ADDENDA
CALIFORNIA TUMOR TISSUE REGISTRY
SIXTY-SEVENTH SEMI-ANNUAL SLIDE SEMINAR
ON
TUMORS OF URINARY TRACT AND MALE GENITAL SYSTEM

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TRAVEL LODGE
LOS ANGELES, CALIFORNIA
### TUMORS OF URINARY TRACT AND MALE GENITAL SYSTEM

**George M. Farrow, M. D.**

**June 10, 1979**

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JUNE 10, 1979 - CASE NO. 1
ACC. NO. 23341

MODERATOR'S DIAGNOSIS: GONADS OF TESTICULAR FEMINIZATION SYNDROME, RIGHT AND LEFT GONADS

HISTORY:

This patient, a phenotypic female, was 18 years old when she first saw a physician because she had never menstruated. She had noted onset of breast development at age 12 and although she shaved her legs weekly there had never been growth of axillary and little growth of pubic hair. She recorded good health and no surgery. She was noted to have a normal female habitus and fat distribution. Her external genitalia were infantile and underdeveloped. The vagina ended as a blind pouch 4-5 cm. deep. No cervix, uterus or adnexae could be detected. At surgical exploration, no uterus or adnexae were found, however, on the right and left brim of the pelvis, two oval masses, about 2.5 cm. in length were resected.

This patient, a phenotypic female, was 17 years old when she first saw a physician because she had never menstruated. Onset of breast development was noted at age 11. There had been minimal growth of pubic hair and no growth of axillary hair. She was noted to have a normal female habitus and fat distribution. The external genitalia appeared normal but the vagina ended as a blind pouch 5 cm. in depth. No cervix could be palpated or visualized and no uterus or adnexae were palpable. At surgical exploration, no uterus or adnexae were found, however, on the right and left brim of the pelvis, paired oval structures about 3 cm. in length were resected.

DISCUSSION:

This case, a composite of two teenage patients of female phenotype, illustrates the classical findings in the gonads of the complete form of the testicular feminization syndrome. Both patients have normal external genitalia but with absence of uterus and adnexae and with gonads, undescended and situated at the brim of the pelvis. These testicular structures are slightly smaller than normal testes, surrounded by a thickened tunica albuginea and bear a mass of fibromuscular tissue at one pole. The cut surfaces of the testes are light tan and within the parenchyma are multiple circumscribed nodules.

Microscopically these testes consist of immature seminiferous tubules, which are uniformly small, prepubertal in type and closely packed with poorly developed Sertoli cells. The gross nodules consist mainly of congeries of these tubular structures similar to those of a cryptorchid testis. Prominent collections of mature Leydig cells are present in the interstitial tissues, and these may also form nodular masses. Germ cells are not noted in the complete form of the syndrome.
The term testicular feminization was first used by Morris (1). The chromosome karyotype is almost always 46 XY, but the patients exhibit a female habitus and external genitalia with well developed breasts but no uterus or tubes and absent or scanty axillary and pubic hair. Gonads are located intra-abdominally (21%), in the groin (60%), or the labia majora. The syndrome is familial with a pattern of inheritance suggestive of either an X-linked recessive or a male-limited autosomal dominant gene. The biochemical defect is said to be a failure of end organ response to testosterone, which is formed normally during intrauterine life, resulting in a somatic female (3). It is clear that there are varying degrees of end organ failure at the cellular level. Testosterone must first enter the cell in an energy dependent step involving the enzyme 5 alpha reductase. This enzyme is never completely absent, but a deficiency characterizes the incomplete form of the syndrome resulting in an eunuchoid individual. The complete form, as illustrated by our Cases, is due to an as yet incompletely understood defective mechanism of testosterone metabolism at the cellular level. The testes are removed mainly because of the risk of ensuing malignant neoplasia. Morris and Mahesh report an incidence of 22% in 50 reported cases 50 years and older consisting mainly of dysgerminomas, but with one each of malignant arrhenoblastoma, teratoma, alveolar carcinoma, and sarcoma. (2).

Both of these patients were sex chromatin body negative and had chromosome karyotypes of 46 XY. Both are alive, well, living as adult females, married and taking cyclic estrogen therapy.

REFERENCES:


JUNE 10, 1979 - CASE NO. 2
ACC. NO. 23132

MODERATOR'S DIAGNOSIS: ADRENAL CORTICAL ADENOMAS OF THE TESTES (BILATERAL), RIGHT AND LEFT TESTES

HISTORY:

This patient was 15 years old when first seen in 1970 for Cushing's syndrome with typical chemical and laboratory findings. Bilateral total adrenalectomy yielded diffusely hyperplastic glands of 7.94 and 7.73 grams. One year later he returned because of pronounced tanning of the skin. The sella turcica was radiographically expanded to which was administered 4000 rads of radiation. Because of continued enlargement of the pituitary on two occasions pituitary adenomatous tissue was removed surgically. The patient returned with no alleviation of his Cushing's syndrome, ACTH levels were in excess of 2000 pg/ml. and an iodocholesterol scan demonstrated intense concentration of radioactivity of the testes. In May, 1978, bilateral orchietomy was performed. Both testes contained multiple dark brown tumors ranging from 0.6 cm. up to 3.5 cm. in diameter.

DISCUSSION:

This 23 year old male with severe Cushing's syndrome, which had been treated by bilateral adrenalectomy and whose course was complicated by pituitary tumors (Nelson's syndrome), continued to secrete high levels of corticosteroids. Secretory activity was localized to the testes, and upon bilateral orchietomy multiple dark brown adrenal cortical adenomas (ranging from 0.6 cm. up to 3.5 cm. in diameter) were found, both within the testes and in the spermatic cord immediately adjacent to the epididymis.

Microscopically the adenomas consist of well demarcated, but unencapsulated densely packed collections of rather large cells with abundant eosinophilic or oxyphilic cytoplasm, some with a brownish lipofuscin type pigment in the cytoplasm. The cells often show distinct rounded groupings of a half dozen cells. Occasionally bizarre nuclei are noted, but mitotic figures are very rare to absent. No crystalloids of Reinke are noted. The remaining testicular tissue shows a notable absence of Leydig cells and spermatogenesis appears completely arrested, as described in severe Cushing's syndrome (3).

Histologically it is difficult to be certain if these tumors are of adrenal or Leydig cell origin. The clinical picture and the biochemical abnormality point to the former. Adrenal rests in the testes are not uncommon being noted in 15 of 200 testes from 11 male infants examined at autopsy (2). In patients with prolonged elevations of ACTH tumors have been
observed in both testicular and paratesticular locations. Testicular tumors have also been reported in congenital adrenal hyperplasia, but biochemical evidence of the adrenal origin has been sparse. Rare similar cases have been reported in Nelson's Syndrome where testicular tumors were proven to be the source of excessive cortisol production. (1, 4, 5, 6).

FOLLOW-UP:

This patient is alive one year later without evidence of progression of the hypercortisonism experienced before orchidectomy and he is taking replacement corticosteroid therapy.

REFERENCES:


MODERATOR'S DIAGNOSIS: NON-SPECIFIC GRANULOMATOUS ORCHITIS, LEFT TESTIS

HISTORY:

This 51 year old male gave a history of rather acute onset of mildly painful left testicular enlargement. There was no history of trauma. A diagnosis of epididymo-orchitis was made and he was treated with several courses of antibiotics over a several month period without resolution of the testicular swelling. Examination revealed a normal right testis but in the left scrotum there was a "large, non-illuminating mass." A left orchidectomy was performed. The testis measured 7 x 4.5 x 4 cm. and was diffusely expanded by a pale yellow process. Near the center of the testis there appeared to be a zone of suppuration. Cultures from this area yielded E. coli.

DISCUSSION:

This 51 year old male had a left orchectomy because of mildly painful left testicular enlargement. The testis was diffusely expanded and replaced by a pale yellow process. A central suppurative zone grew E. coli. Microscopically the process is one of massive replacement of the testicular by an inflammatory process. Most of the inflammatory cells are lymphocytes, plasma cells, and histiocytes, but within the remnants of the seminiferous tubules there is a distinct non-necrotizing granulomatous process with numerous multinucleated giant cells with resultant replacement of all elements within the tubular lumen.

Non-specific granulomatosis orchitis is a chronic inflammatory lesion which may simulate malignancy (1). These patients are usually middle-aged or older. There are often associated symptoms of fever, malaise, followed by testicular swelling, induration pain, and tenderness. The process is unilateral in the vast majority of cases, but the Testicular Tumor Panel found 3 of 32 cases which either presented bilaterally or became so within a few months (3). The etiology is not known, but considerations include: 1) trauma, 2) infection, or 3) autoimmune factors. Trauma seems to be a definite factor in some cases and minor trauma may be easily overlooked or forgotten. Sperm, as recognized in sperm granuloma, following vasotomy are capable of inciting an intense granulomatous reaction. A similar process could be induced by release into the tissues of sperm by an infectious process. The rarity of bilaterality makes a systemically mediated autoimmune disease less tenable as an etiologic consideration although sperm agglutinating antibodies are demonstrated in some patients. (2).
FOLLOW-UP:

This man is alive and well 15 years after orchidectomy. He never developed evidence of a systemic infectious disease. His opposite testis has remained normal to palpation. No studies such as sperm count have ever been done.

REFERENCES:


HISTORY:

This 76 year old male had noted a lump in the inferior pole of his testes six months before. Over this interval he had noted progressive enlargement but no pain. There was a history of testicular trauma in his youth. The right testes was found to be uniformly enlarged, hard and nontender.

The right testes and 6 cm. of spermatic cord were removed. The testes was uniformly replaced by a homogeneous soft yellow-gray mass. The spermatic cord appeared normal.

DISCUSSION:

This 76 year old man with a six month history of a progressively enlarging testicular mass had a homogeneous soft yellow tumor uniformly replacing his testes. Microscopically the testes was entirely replaced by a neoplasm forming diffuse sheets without trabeculae. The individual neoplastic cells exhibit nuclei with considerable size variation but with uniformly rounded shape. The nuclear chromatin of the smaller nuclei is extremely dense and course while among the large nuclei the chromatin is finely granular or filamentous. The abundant cytoplasm of each cell is lightly eosinophilic. No lymphoid elements are present.

Spermatocytic seminoma was first separated out by Masson (1) and his summary of the tumor constitutes a classic in pathology:

"The author has observed six testicular tumors which differ from the seminomas of Chevassu (dysgerminomas of R. Meyer, embryonal carcinomas of Ewing) by their greyish-white color, their edematous aspect and by the absence of necrotic and hemorrhagic foci.

These tumors are made of irregular cells, smaller than those of the classical seminomas, their cytoplasm is devoid of glycogen, the stroma is scanty and not infiltrated by lymphocytes. Many of the nuclei have a filamentous structure and present a persistent spireme which resembles that of the spermatocyte of the first order.

The cells have a marked tendency to invade the seminiparous tubes, and in one case the genesis of the neoplastic focus has been observed in one of the tubes.

No case of teratoma could be found in all the cases ..."
Scully (2) in reporting 3 examples among 81 tumors diagnosed as seminoma called attention to this largely overlooked report. In the Testicular Tumor Panels large series of 729 seminomas there were 27 spermatocytic seminomas or 3% (3). Because of the uniquely benign nature of the subsequent course of these patients (no documented case of metastasis), it is important to recognize and separate this type of testicular tumor.

FOLLOW-UP:

This man is alive and free of any evidence of neoplasm 1 1/2 years following orchidectomy. Radiation was given to the retroperitoneal lymph nodes empirically after surgery.

REFERENCES:

MODERATOR'S DIAGNOSIS: MALIGNANT LYMPHOMA OF THE TESTES, LARGE CELL, DIFFUSE TYPE, LEFT TESTIS

HISTORY:

This 80 year old male with a past history of benign prostatic hyperplasia and renal stones was seen with a slowly enlarging painless left testicular mass of two months' duration. This caused slight diffuse enlargement of the testis and was described as hard and non-tender. The other testes show atrophy consistent with age. No lymphadenopathy was noted. The testes and spermatic cord were removed. The testes was slightly enlarged and diffusely infiltrated by a homogeneous brown-gray mass.

DISCUSSION:

This 80 year old man with no past history or other findings of malignant lymphoma presented with a slowly enlarging painless testicular mass. The testes were found to be infiltrated diffusely by a homogeneous brown-gray process.

Microscopically residual atrophied seminiferous tubules are widely separated by an interstitial infiltrate of neoplastic cells which feature large nuclei of variable size and irregular shape. Most nuclei have a vesicular chromatin pattern and one a more prominent nuclei. Cytoplasm among the cells is not prominent, there is no specific grouping of the cells and no presence of mature lymphoid elements is noted. Immunoperoxidase histochemical techniques reveal many of the neoplastic cells to possess cytoplasmic immunoglobulins monoclonal for the lambda light chain.

Malignant lymphoma of the testis usually affects older men and these cases comprise one to seven percent of all testicular tumors (1, 3). Malignant lymphoma is the most common form of secondary neoplastic involvement of the testis, the most common testicular tumor in men over 50 years, and the most frequent tumor to involve the testes bilaterally. Patients with long term follow-up have illustrated the existence of primary malignant lymphoma confined to the testes.

The prognosis for lymphoma clinically localized to the testis at the time of original diagnosis is relatively favorable after orchidectomy and radiation to the regional lymph nodes. In a series from our own institution of 31 patients only 2 tumors were bilateral and one arose in a cryptorchid testes. Seventeen patients appeared clinically to have lymphoma confined to the testes while 14 had evidence of disseminated disease. Five patients lived five years or longer, and another five were alive from one to three years, all from the
"primary" group. Histopathologically all tumors were immature types and all the five year survivors had histiocytic large cell lymphoma.

FOLLOW-UP:

This patient is alive and apparently free of lymphoma five months following orchidectomy.

REFERENCES:


MODERATOR’S DIAGNOSIS: SEMINOMA, ANAPLASTIC TYPE, LEFT TESTIS

HISTORY:

This 34 year old man complained of soreness of the left testis for six months and very recently he noted testicular enlargement. The testis was found to be enlarged, swollen and tender to palpation. The left scrotum was explored and a tumor found in the left testes and an orchidectomy was performed. Sections of testis revealed within the parenchyma a well circumscribed yellow firm mass 4 x 3 x 3 cm. There was a 2 cm. central zone of necrosis bordered by a hemorrhagic rim.

DISCUSSION:

This 34 year old man has a testicular tumor characterized as a well circumscribed yellow mass with a central zone of necrosis. Microscopically the neoplasm is composed of cells arranged in well-defined groupings often with an alveolar or occasionally a trabecular pattern. The cells are large and exhibit extremely variable and bizarre nuclei with marked nuclear irregularity and coarseness and hyperchromasia. Nucleoli are not prominent. Many cells exhibit prominent eosinophilic cytoplasm. No stromal lymphoid elements are present. Frequent mitoses are noted, the most important histopathological feature of anaplastic seminoma as defined by Mostofi (4).

Although it is not universally agreed, seminomas are generally classified into three subtypes: classical, spermatocytic and anaplastic. The Testicular Tumor Panel (5) does not accept the term "anaplastic" but rather prefers "atypical" which accounts for about 3% of their seminoma group. The M. D. Anderson Group (1) finds 7% of seminomas to be this type and the University of Wisconsin 12% (2). All observers agree that the prognosis following standard therapy is worse for the anaplastic seminoma but several point out that the prognosis is approximately the same when stage is taken into account (1, 3).

FOLLOW-UP:

Radiation therapy was administered empirically to the retroperitoneal nodal areas after surgery since no metastases were demonstrated. The patient is alive and apparently free of neoplasm six months later.

REFERENCES:


JUNE 10, 1979 - CASE NO. 7
ACCESSION NO. 23133

MODERATOR'S DIAGNOSIS: SERTOLI CELL TUMOR, RIGHT TESTIS

HISTORY:

This 36 year old man noted right scrotal enlargement for six months. The grapefruit-sized mass was painless. He had noted gradual onset of sexual impotence. Two years before a right hydrocele had been excised and the surgeon noted at that time that the "Right testicle is three times its normal size but there is no evidence of any tumor involving the right testis." The left testis has been normal to examination.

The specimen consisted of scrotum and testis. The testis measured 5 x 4 x 2.5 cm. and weighed 35 grams, and on cut section presented a reddish-gray variegated appearance.

DISCUSSION:

This testicular tumor occurred in a 36 year old man with a history of progressive sexual impotence, but with no other documentation of hormonal function. The tumor was within the testicular parenchyma where it presented as a poorly circumscribed mass. Microscopically the basic neoplastic component is a small epithelial type cell of 12 to 15 microns with a rounded nucleus with fine chromatin and a rather indistinct, often clear cytoplasm. The theme of the histology appears to be an exercise wherein nature experiments with variations in tissue structure to which this simple cell may be adapted. The most prominent pattern is one of epithelial appearance with double layers of cells arranged in ribbony trabeculae. In many places a prominent intercellular stromal substance is present, ranging from a myxoid to a hyaline, almost amyloid appearance. In some places the cells are arranged into prominent tubular structures and in others they cover the surfaces of papillary projections. Finally, by a process of gradual transformation the cells assume an elongated and spindled appearance. The neoplasm appears to be infiltrated into structures of the adjacent epididymis.

Although this testicular tumor is entirely unique in my experience, I believe that it is benign and represents a variant of Sertoli cell tumor. Talerman (2) has reported an ovarian tumor in a normal 46 XX 10 year old girl which he believes is a distinctive gonadal tumor related to gonadoblastoma. This neoplasm showed an intimate mixture of sex cord stroma derivatives (primitive Sertoli and granulosa cells) intimately mixed and forming a cord-like or trabecular pattern. He found, however, both Leydig cells as well as primitive germ cells both of which are absent from our tumor.
Sertoli cell tumors are uncommon comprising one to two percent of the series of testicular tumors. They are more common under the age of 40 and generally present as well circumscribed yellowish tan solitary tumors in the testes, although cystic variants are recognized. They often function to produce feminization often manifested by gynecomastia. The majority of the tumors are benign, although Symington and Cameron report a 22% incidence of malignancy in their series of 32 cases (1).

FOLLOW-UP:

This man is alive and apparently free of neoplasm at six months post-orchidectomy.

REFERENCES:


MODERATOR'S DIAGNOSIS: INCOMPLETELY DIFFERENTIATED GONADAL STROMAL TUMOR
IN AN INFANTILE TESTIS, TESTIS

HISTORY:

This testicular tumor, approximately 1.5 cm. in diameter, was discovered incidental to a herniorrhaphy in a 3 month old infant.

This right testicular tumor was removed along with 6 cm. of spermatic cord from a 5 month old male, one of identical twins, who had been noted to have a scrotal mass. The testicular neoplasm measured 1.7 x 0.7 cm. and was firm and yellow tan in color and situated within the testis proper.

DISCUSSION:

This case composite of two tumors of essentially identical histopathology in male infants of three and five months of age, illustrate an extremely rare neoplasm, only one other report of which I am aware (1). The major portions of the tumor have an encapsulated solid growth pattern composed mainly of elongated or spindled cells with poorly defined cytoplasm, often finely fibrillar in appearance. Other foci illustrate more rounded cells with somewhat clear cytoplasm and occasionally these cells are arranged in a trabecular or fascicular pattern reminiscent of Sertoli cell tumors. No differentiation along Leydig cell line is demonstrated. Infantile type seminiferous tubules are present in the adjacent testis with mainly Sertoli cells but with occasional primordial germ cells apparent. These tubules are engulfed and surrounded in portions of the neoplasm. Focal calcification is noted. Two disturbing features which impart the aura of malignancy to the morphology are the presence of an infiltrative quality peripherally, into the adjacent epididymis in one of the cases, and the quite plentiful numbers of mitoses, four to five per high power field, in many areas.

Evans and Glick (1), in a testicular tumor from a four year old male with gynecomastia and identical histopathological features to our cases, report the ultrastructural features of the neoplasm to resemble the immature fusiform interstitial cells and the peritubular contractile cells present in the normal testis as described by Sniffen (4), Fawcett and Burgos (2) and by Ross and Long (3).

FOLLOW-UP:

Follow-up on the case of Evans and Glick was only for three months at
which time the patient was well. That was three years ago and the patient's records have been lost. Our two patients are followed for only eight months and my latest information is that there has been no recurrence of neoplasm in either patient. The subsequent status of the identical twin in Dr. von Schmidt's case will be extremely interesting to observe.

REFERENCES:


MODERATOR'S DIAGNOSIS: METASTATIC CHORIOCARCINOMA TO THE LUNG FROM A MEDIASTINAL PRIMARY, LUNG BIOPSY

HISTORY:

This 54 year old male, previously well, had hemoptysis and sudden weakness of the right arm and leg. Abnormal physical findings were limited to the chest and the neurological examination. A brain scan revealed a left mass lesion and chest x-ray, multiple pulmonary nodules suggestive of advanced metastatic neoplasm. One of these pulmonary nodules was biopsied.

DISCUSSION:

This case illustrates the classical morphology of choriocarcinoma. Hemorrhagic nodules in the lung consist of chorionic-villous like structures composed of inner well-defined cytotrophoblastic cells, with well-defined cell borders and clear or finely granular cytoplasm, capped on the surface by huge, eosinophilic, multinucleated syncitio-trophoblastic cells. By an immunoperoxidase anti-human chorionic gonadotrophin technique, these large cells are demonstrated to be the site of production H.C.G. At the time of thoracotomy, an orange-sized mass was palpated by the surgeon in the anterior mediastinum. The postoperative serum H.C.G. titer was the highest ever recorded in our laboratory, 180,000 units. The testes were entirely normal to palpation, there was no evidence of retroperitoneal involvement. The patient died three weeks after surgery; no autopsy was performed.

Malignant germ cell tumors found in the testes can originate in the anterior mediastinum as well as the retroperitoneum. Virtually every histopathologic type has been reported. In the most recent survey of our own material, 1970, (5) of 18 cases of these extragonadal tumors, all males, 12 occurred in the mediastinum, 5 in the retroperitoneum, and there was one seminoma-like tumor of the pineal body. The patients ranged in age from 11 to 54 and averaged 27 years. Seminomas were the most common, comprising six cases in the mediastinum and among this group are the only long term survivors where one patient succumbed to tumor after six and two-thirds years and the remainder were alive one-and-a-half to nineteen years after surgery plus radiation, although one patient still has tumor ten years after treatment was begun and had a chest wall metastasis excised. There was one case of choriocarcinoma in a patient who died after two months and the one case of embryonal carcinoma and the four cases of mixed embryonal carcinoma and teratoma have all died of tumor except for one patient alive with tumor at one year. Reports of similar series have also emanated from Walter Reed Hospital (2) and from Memorial Sloan-Kettering (3), with a distribution of 22 males and 8
females. It should be emphasized that the metastasis of choriocarcinoma from occult testicular primary tumors is common, and the phenomenon of regression of the primary must be considered. Azzopardi, Mostofi and Theiss (1) have described that the fossilized remains of regressed choriocarcinoma in the testis contain a distinctive hematoxylin-staining pigment and a calcium phosphatase deposit. Eleven, mainly single, case reports of yolk sac tumors of the mediastinum have also appeared, most of which have proved fatal. (4).

REFERENCES:


IMMUNOPEROXIDASE (PAP) TECHNIQUE FOR
HUMAN CHORIONIC GONADOTROPIN
(HCG)

FIXATION: 10% Buffered neutral formalin. (To help prevent non-specific staining, immediate fixation of tissue is essential.)

TECHNIQUE: Cut paraffin section, 3 - 4 microns in thickness.

PROCEDURE:
1. Deparaffinize sections (Xx101, absolute alcohol, graded alcohols) to distilled water.
2. Place slides in 3.0% solution of hydrogen peroxide for 5 minutes at room temperature.
3. Rinse slides in distilled water.
4. Place slides in 1.0% solution Egg Albumin (FISHER, powder) in PBS, for 30 minutes at room temperature.
5. Rinse slides in distilled water, then rinse in PBS (Phosphate buffered saline, pH 7.2).
6. Add RABBIT anti HUMAN CHORIONIC GONADOTROPIN, 1/1000 (Cappel Laboratories, Cochranville, PA. 19330) to one set of slides; add NORMAL RABBIT SERUM, 1/1000, to duplicate set of slides as the control set. Incubate at room temperature for 60 minutes.
7. Rinse in 3 changes of PBS, 5 minutes each.
8. Add SWINE anti RABBIT SERUM IgG (DAKO - Accurate Chemical and Scientific Corp. 28 Tec Street, Hicksville, New York 11801) 1/20. Incubate for 30 minutes at room temperature.
9. Rinse in 3 changes of PBS, 5 minutes each.
10. Add PAP 1/20 (DAKO - Accurate Chemical & Scientific Corp.) Incubate at room temperature, in the dark, for 30 minutes.
11. Rinse in 3 changes of PBS 5 minutes each.
12. Place in AEC reaction for 30 minutes.

AEC REACTION:
1. Dissolve 3-Amino-9-ethylcarbazole (AEC) 30 mg.
   (ALDRICH CHEMICAL COMP., INC. Milwaukee, Wis.) IN
2. N - N Dimethyl formamide 7.5 ml.

3. Add to 0.1M Acetate buffer, pH 5.2 142.5 ml.

4. Just before use, add 3.0% Hydrogen peroxide 1.5 ml.

5. Filter, and incubate at room temperature for 30 minutes 150 ml. total

6. Rinse with distilled water.

7. Counterstain with hematoxylin.

8. Mount with Kaisers glycerine jelly. (DO NOT DEHYDRATE. DO NOT USE PERMOUNT)

PHOSPHATE BUFFERED SALINE (PBS):

Sodium Phosphate Dibasic (Anhydrous (Na₂HPO₄)) 165.12 grams

Potassium Phosphate Monobasic (KH₂PO₄) 59.52 grams

Sodium Chloride (NaCl) 204 grams

DISSOLVE the above, with the aid of a little heat, in 2000 ml. distilled water.

ADD distilled water to make a total amount of 24,000 ml. (24 liters)

CHECK pH: 7.2

STORE at room temperature.

KAISERS GLYCERINE JELLY:

DISSOLVE: 20 grams Gelatin

IN 105 ml. distilled water

ADD: 125 ml. Glycerin

2.5 grams Carbolic acid crystals (Phenol)

HEAT: Gently for 10 to 15 minutes, stirring all the while until mixture is smooth.

STORE: In dropper bottle in 37°C oven.
0.1M ACETATE BUFFER:

DISSOLVE 21.50 grams Sodium Acetate 3H₂O

IN 42 ml. 1N Acetic Acid (Glacial Acetic Acid = 17N)

ADD 2000 ml. distilled water

CHECK pH 5.2

STORE In refrigerator (4°C)
MODERATOR'S DIAGNOSIS: METASTATIC TESTICULAR TERATOMA TO THE RETROPERITONEUM FEATURING MAINLY RENAL CELL CARCINOMA AND WILMS' TUMOR, RETROPERITONEAL MASS

HISTORY:

This 41 year old man presented in February, 1972, complaining of a mass in the left upper quadrant of the abdomen. In December, 1967, he had had a left orchidectomy for a testicular teratoma. Review of the one block of the testicular tumor available revealed that most of the neoplasm was composed of fully differentiated elements including squamous epithelium, ciliated columnar epithelium and smooth muscle. A zone of partial differentiation exhibited a spindled cell element with occasional mitoses. At surgery a huge retroperitoneal mass extended from above the left renal pedicle to the left common iliac artery. The kidney although displaced, was not involved by neoplasm. This mass was removed. Most of it was solid with occasional cystic areas and one nodular area 4 cm. in diameter of golden yellow color.

DISCUSSION:

This 41 year old man who four-and-a-half years previously had a left orchidectomy for a testicular teratoma, (from which the only block available for review reveals a mainly differentiated teratoma but with a zone of partially differentiated spindled cells), developed a large retroperitoneal metastasis which almost entirely contained a neoplasm showing a range of renal differentiation from Wilms' tumor to renal cell carcinoma (hypernephroma type). By x-ray studies and by surgical exploration the kidneys were not involved by the neoplasm. The patient died four months after the latest surgery and no autopsy was performed.

Grossly the metastatic tumor was well circumscribed, most of it was solid, but with occasional cystic areas and areas of hemorrhage and necrosis. One nodular area, 4 cm. in diameter was distinctly yellow. Microscopically the tumor contained derivatives of all germinal layers, often well differentiated, adult tissues, however, the bulk of the lesion contained malignant elements. The 4 cm. yellow nodule was renal cell adenocarcinoma composed of clear and granular cells and most of the remainder of the tumor was composed of Wilms' tumor. Adjacent to and intermingled with many of these areas were foci of partly differentiated but readily recognizable renal tissue.

Since renal origin for the tumor was not established, other sources
must be considered. One alternative origin in a retroperitoneal teratoma seems less likely because of the finding in the lesion of mature elements similar to those in the testicular primary tumor. The unique association of expressions of renal neoplasia gives the case interest. De Muylder (2) has described a similar combination of tumors in the kidney of a three year old boy, and other reports of wilms' tumor arising in a teratoma are listed below (1*, 3, 4)

*This case.

REFERENCES:


MODERATOR'S DIAGNOSIS: VILLOUS ADENOCARCINOMA OF THE BULBOUS URETHRA

HISTORY:

This 76 year old man complained of intermittent, terminal gross hematuria for about one year. Cystoscopy revealed a stricture of the urethra at the penoscrotal angle and just proximal to this there was an extensive villous growth extending well into the bulbous urethra. The proximal bulbous urethra as well as the membranous and prostatic urethra contained no neoplasm. At surgery a 4 cm. segment of bulbous urethra was resected and a villous neoplasm, occupied a 3 cm. length of this structure around the full circumference of the lumen.

DISCUSSION:

"Adenocarcinoma of the male urethra is so rare that no clear-cut documentation of its clinical or pathologic features exists in the literature. The few adenocarcinomas that have been found in reviews of the male urethra have generally been considered of periurethral gland origin." - Mostofi and Price, 1973 (1).

This 76 year old man had a grossly villous growth in the bulbous urethra which was not connected to the prostate or associated with the periurethral glands. A 4 cm. segment of urethra was resected. The patient is alive and well five years later.

Microscopically the neoplasm bears a close similarity to villous carcinomas occurring in the rectum or large intestine. The surface configuration is distinctly villous and many of the cells, although they cannot be regarded as benign, show features of goblet cell differentiation and mucus production. Beneath the villous surface elements there is less differentiated highly invasive adenocarcinoma composed mainly of small gland structures.

Carcinomas of the male urethra is not a rare disease, more than 400 cases are reported. The most important tumors are 1) primary transitional cell carcinoma, 2) squamous cell carcinoma of the membranous urethra, and 3) tumors of the meatal area, seen mostly in young adults (3). Carcinoma affects the posterior more frequently than the anterior portion. Meatal tumors are usually papillomas or condyloma acuminata.

Primary malignancies of the female urethra are also rare. In 49 cases reported from the Mayo Clinic (2), the following cell types and sites were encountered.
### JUNE 10, 1979 - CASE NO. 11
ACCESSION NO. 23332

<table>
<thead>
<tr>
<th></th>
<th>Anterior Urethra</th>
<th>Entire Urethra</th>
<th>Totals</th>
</tr>
</thead>
<tbody>
<tr>
<td>Squamous cell</td>
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<td>Transitional cell</td>
<td>3</td>
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<td>Melanoma</td>
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<tr>
<td><strong>Totals</strong></td>
<td><strong>25</strong></td>
<td><strong>24</strong></td>
<td><strong>47</strong></td>
</tr>
</tbody>
</table>

**REFERENCES:**


HODERATOR'S DIAGNOSIS: LOCALIZED (TUMEFACTIVE) AMYLOIDOSIS OF THE BLADDER

HISTORY:

This 36 year old male complained of bladder irritation for three to four years and more recently had noted several episodes of gross hematuria. Although previously well, there occurred 20 pounds recent weight loss. The cystoscopist noted a necrotic, solid, broad-based lesion involving most of the left wall of the bladder which appeared to be a malignant neoplasm. The surface was necrotic and satisfactory viable tissue for biopsy was not obtained. Subsequently a segmental resection of the left lateral wall and dome of the bladder was performed.

The specimen consisted of a 7.5 x 7 cm. segment of bladder. Occupying the center of the specimen was a thickened irregular raised, multifocally ulcerated and hemorrhagic lesion.

DISCUSSION:

This 36 year old man exemplifies many of the features of localized or tumeformative bladder amyloidosis. After a three to four year history of bladder symptoms associated with episodes of gross hematuria, the cystoscopist initially misinterpreted his findings for a malignant bladder neoplasm. The correct diagnosis was established only after a segmental resection of the bladder was performed. Subsequently the patient continued to be symptomatic and to bleed and he eventually required a total cystectomy and a urinary diversion. The patient lived another twenty-four years to suffer the effects of coronary artery disease, but laboratory workup on several occasions never showed proteinuria, Bence-Jones or otherwise, an elevation or electrophoretic abnormality of serum proteins nor evidence of systemic amyloid or plasma cell neoplasia.

Grossly the segmentally resected specimen showed multiple ulcerations of the surface mucosa. The wall of the bladder was firm, thickened and somewhat wax-like. Microscopically heavy amyloid deposits of the usual morphologic appearance were present in the submucosa, muscularis and vessel walls of the bladder. All the usual special staining procedures yielded findings typical for amyloid including methyl violet metachromasia, thioflavin T fluorescence (3) and congo red birefringence with dichroism.

In a recent review of the Mayo Clinic experience with 236 cases of
Amyloidosis of all types, Kyle and Bayrd (1) show the following distribution:

<table>
<thead>
<tr>
<th>Category</th>
<th>Cases</th>
<th>Percentage</th>
</tr>
</thead>
<tbody>
<tr>
<td>Primary systemic</td>
<td>132</td>
<td>56%</td>
</tr>
<tr>
<td>Myeloma</td>
<td>61</td>
<td>26%</td>
</tr>
<tr>
<td>Localized</td>
<td>22</td>
<td>9%</td>
</tr>
<tr>
<td>Secondary</td>
<td>19</td>
<td>8%</td>
</tr>
<tr>
<td>Familial</td>
<td>2</td>
<td>1%</td>
</tr>
</tbody>
</table>

Among the localized cases, involvement of the bladder, lung, skin and larynx accounted for more than half the cases. In a 1971 review of the subject (2), we found 42 reported cases of amyloidosis of bladder, including nine from our own institution. One of our cases and several of the other reported cases eventually proved to have systemic amyloidosis. These 42 cases included 22 women and 20 men ranging in age from 31 to 80 years (mean, 51 years). The vast majority complained of gross hematuria. The most common cystoscopically described abnormality was that of an infiltrating neoplasm. In all 42 cases multiple areas of the bladder were involved. The cases, for purposes of treatment and prognosis, fall into three groups:

1. Patients with only localized "tumefactive" lesions, had a favorable course with few recurrences widely spread in time. Best treatment: transurethral resection.

2. Patients with diffuse lesions of the tumefactive type. These usually require cystectomy and urinary diversion.

3. Patients with the diffuse lesion and systemic amyloidosis. Have a prognosis mainly dependent on the status of their systemic disease.

REFERENCES:


THIOFLAVIN T - For Amyloid

**FIXATION:** 10% buffered neutral formalin

**TECHNIQUE:** Cut paraffin sections at 6 microns

**SOLUTION:**

1.0% Thioflavine T Solution:

- Thioflavin T: 0.5 grams
- Distilled water: 50 ml.

**NOTE:** Make fresh solution every two weeks

Differentiating Solution:

- Glacial acetic acid: 1.0 ml.
- Distilled water: 100.0 ml.

**d-Levulose Syrup:**

- d-Levulose (D-Fructose): 30 grams
- Distilled water: 20 ml.

Dissolve levulose in water by placing solution in 37°C oven for 24 hours. Filter before removing from oven.

**STAINING PROCEDURE:** Use control slide.

1. Deparaffinize and hydrate to distilled water.

2. Stain for 10 minutes in 1.0% Thioflavin T (STIR SOLUTION FIRST)

3. Differentiate for 10 minutes in 1.0% Acetic acid.

4. Wash briefly in distilled water for 2 - 3 minutes.


6. Seal with clear nail polish.
History:

This asymptomatic 24 year old male was referred for evaluation of a scrotal mass noted on an insurance physical examination. There was no history of scrotal trauma or previous surgery. The right hemiscrotum was found to be enlarged and multiple firm masses ranging from one to three cm. were palpated adjacent to the testes.

Examination of the gross specimen revealed multiple (approximately 25) nodules situated in the parietal layer of the tunica vaginalis ranging from 2 mm. up to 3.3 cm. in diameter. The testes and epididymis were normal.

Discussion:

This asymptomatic 24 year old male with a unilateral multinodular scrotal mass on the right illustrates a lesion which in the experience of Mostofi and Price, constitutes an entity second only to the adenomatoid tumor in frequency of involvement of the testicular adnexae (2). The lesion is much more common than the number of case reports would indicate masquerading under a number of synonyms including nodular periorchitis (1), calcified hydrocele, vaginalis, chronic perivaginalis, chronic proliferative peri-orchitis, periorchitis prolifera, fibrous pseudotumor, etc. The process represents a chronic hypertrophic serositis of unknown etiology characterized by collagenous thickening and rounded nodularity of the tunica vaginalis. Microscopically these nodules consist of a proliferation of fibroblasts with dense occasionally acellular zones of collagenization and an infiltrate of inflammatory cells, mainly lymphocytes which may form nodular aggregates, plasma cells and occasional eosinophils. Occasional cases have been reported in association with sclerosing retroperitonitis or even sclerosing mediastinitis.

References:


MODERATOR'S DIAGNOSIS: LEIOMYOSARCOMA OF THE SPERMATIC CORD

HISTORY:

This 86 year old male entered the emergency room for a Foley catheter change and was found to have a "huge incarcerated left inguinal hernia and some variety of tumor." This tumor had been fist sized before the hernia became symptomatic and had been present for several years. A left orchiectomy was performed with removal of a portion of the spermatic cord and a suprapubic prostatectomy and removal of bladder stones was done for benign prostatic hyperplasia. The specimen consisted of a massive tumor weighing 790 gms. and measuring 23 cm. in length and 13 cm. in diameter. There were multiple bulging nodules up to 4 cm. in diameter composed on cut section of firm light yellow tissue with zones of central necrosis. Remnants of a testis surrounded and invaded by tumor were noted at one extremity of the specimen.

DISCUSSION:

This 86 year old man exhibited a huge tumor in the inferior portion of his left spermatic cord which invaded the adjacent epididymis. The malignant nature of the neoplasm is further evidenced by the death of the patient from metastases about seven months from initial surgery. The neoplasm weighed 790 grams and measured 23 cm. in length and up to 13 cm. in diameter. Microscopically the features are those of an infiltrative malignancy composed of spindled cells with morphologic features of smooth muscle cells. There were foci of necrosis and abundant mitotic figures are evident.
JUNE 10, 1979 - CASE NO. 15
ACCESSION NO. 23346

MODERATOR’S DIAGNOSIS: MIXED MALIGNANT MESENCHYMAL SARCOMA OF THE SPERMATIC CORD.

HISTORY:

This 73 year old man was admitted for repair of a hernia, but at examination was found to have scrotal mass lesion. At surgery the testis and spermatic cord were removed. In the spermatic cord just above the testis a firm, potato shaped, gray-white mass measured 10 x 6 x 6 cm.

DISCUSSION:

This 73 year old man was found to have a 10 x 6 x 6 cm. mass in the spermatic cord just above the testes. Although this was excised along with the testes and remainder of the spermatic cord, a tumor metastasis was removed from the inguinal region three months later and now, 15 months from the initial surgery, the patient has pulmonary metastases. Microscopically this tumor presents a variegated appearance. The most common element is composed of malignant spindled cells with features consistent with smooth muscle origin and with staining characteristics with Masson's trichome also consistent with smooth muscle. In many areas there is a transition to a much more bizarre elongated cell, many rounded or strap-like in quality, which resemble neoplastic skeletal muscle cells. (No cross striations demonstrated, but abundant eosinophilic cytoplasm is present.) In other zones there is the striking presence of extracellular deposits of an eosinophilic material which may represent neoplastic osteoid and interspersed among these ramifying masses are numerous multinucleated, osteoclast-like giant cells.

FURTHER DISCUSSION:

Cases 14 and 15: Sarcomas of spermatic cord and its tunics are rare but highly malignant lesions. Banowsky and Shultz, in a most complete review (1), found 101 reported cases by 1970. The most frequent reported type was fibrosarcoma, followed by leiomyosarcoma, rhabdomyosarcoma, liposarcoma, myxosarcoma and a variety of other types. The total mortality in the report was 37 percent.

In a smaller personal series dealing only with adults, the group at Memorial Sloan-Kettering reports six patients comprising three fibrosarcomas, two liposarcomas and one malignant fibrous histiocytoma. (4). They were able to find 212 recorded cases in the literature. (1978). The experience to that time of our institution was reported in 1972 when we had ten patients (3).
Eight of these, all under 17 years of age, had embryonal rhabdomyosarcoma with only one long term survivor. Both adult patients, one with leiomyosarcoma and one with liposarcoma survived tumor free for many years. Case 15 is of interest because of the unique nature of the histology. The interested reader may wish to read the article by Darby, et al. entitled "An Unusual Leiomyosarcoma of the Uterus Containing Osteoclast-like Giant Cells" (2), and form his own opinion as to the correct diagnosis in this case.

REFERENCES:


MODERATOR'S DIAGNOSIS: METASTATIC TUBULOPAPILLARY ADENOCARCINOMA FROM A RENAL CORTICAL PRIMARY.

HISTORY:

This 22 year old female first noted an enlarged lymph node in the right neck immediately post-partum. An excisional biopsy was performed. The thyroid gland revealed no abnormalities to palpation.

DISCUSSION:

This 22 year old female who first noted an enlarged right neck lymph node was found after biopsy to have metastatic papillary adenocarcinoma. The differential diagnosis based upon the histology brought out the possibility of primary sites in the thyroid, lung, and ovary as the major contenders. However, the thyroid gland was small and no nodules were detected. A radioisotope scan was negative. The chest x-ray was entirely normal and no ovarian abnormalities could be detected. Because of an episode of hematuria excretory urography was performed which revealed a large destructive mass lesion of the right kidney. A nephrectomy was performed with the findings of a large invasive renal parenchymal tumor and with several metastatically involved renal hilar lymph nodes. Subsequently a right neck dissection was performed and 22 lymph nodes were found to contain metastatic tumor deposits. The patient is alive eight months post-nephrectomy with recurrent tumor in the right neck but no other known metastases.

The histology of this tumor represents one of the variations of renal cortical carcinoma. In the lymph node the major feature is that of a neoplasm which is predominantly papillary composed of a single layer of columnar cells. In some areas tubular structures are found which often contain an eosinophilic proteinaceous material which might be confused with colloid of thyroid origin. No psammoma bodies are found, but rarely foci of foamy histiocytes situated within the interstitial or stroma of a papillae are noted. This latter feature coupled with scattering of mitoses among the tumor cells help to distinguish the lesion from metastatic papillary carcinoma of the thyroid. In the kidney a neoplasm of essentially identical histologic make-up was found. Interstitial foam cells were a much more prominent feature here. No clear cell areas of usual renal cell carcinoma were found.

Although this tumor presents an unusual histopathologic appearance, a
tubulo-papillary configuration, there is no solid data to my knowledge to indicate that this bears any histogenetic or prognostic significance. However, it has been my experience that among young patients, this histologic variant is more common than among the more usual older patient.
MODERATOR'S DIAGNOSIS: MULTIFOCAL, BILATERAL WELL DIFFERENTIATED RENAL CORTICAL CARCINOMA, TUBULO-PAPILLARY TYPE

HISTORY:
This patient is a 46 year old male farmer, in otherwise excellent health, who presented with asymptomatic gross hematuria. In the course of the diagnostic evaluation, renal arteriography revealed multiple, bilateral renal tumors. In January, 1979, the kidneys were explored surgically and each kidney was described as having forty to fifty nodules, many greater than 2 cm. which were firm and pale white to yellow in color. In the upper pole of the right kidney and the medial portion of the left kidney there were confluentes of these nodules forming masses 4-5 cm. in diameter. Biopsies were taken from smaller nodules in both the right and left kidneys.

DISCUSSION:
This 46 year old male farmer, who was in otherwise good health, complained of painless gross hematuria. Renal arteriography revealed multiple bilateral renal tumors. At a subsequent surgical exploration each kidney was described as having 40-50 cortical nodules, tan to yellow, many greater than 2 cm. In the upper pole of the right kidney a confluent mass of tumor measured 4-5 cm. A small nodule from each kidney was biopsied.

This case presents both a diagnostic as well as a therapeutic dilemma. The surgeons on the one hand, recognizing because of the bilateral and multicentric nature of the problem, as well as the large size of the confluent mass, that a diagnosis of renal cell carcinoma was most likely, still shrank from the aspect of bilateral nephrectomy, with the resultant need for chronic dialysis or for renal transplantation. The latter consideration was complicated by the lack of any known relatives in this patient who had been adopted from unknown parentage. They therefore would not move without a tissue diagnosis of cancer which landed the responsibility clearly upon the pathologist.

If we take on basis of faith that all the lesions within both kidneys are of similar histopathologic makeup, then we must make our diagnosis based upon the features of the smaller nodules available to us in the biopsy. We see that
situated within the cortex of the kidney there are nonencapsulated, but generally well circumscribed neoplastic proliferations of cuboidal to low columnar cells which are, for the most part, arranged in delicate papillary structures and with other zones of tubular configuration. The cytoplasm is often nondescript but some of the tumors showed abundant clear (hypernephroid) cytoplasm. At the periphery of these neoplastic zones there is often infiltration into and between existing renal cortical tubules and glomerulae, although there is no stromal reaction in the form of fibroplasia or inflammation as often greets the invasion of a neoplasm into the host tissues. The nuclei of the cells are very regular, containing finely dispersed chromatin, indeed, differing minimally from the adjacent normal renal tubular epithelial cells. Mitoses cannot be demonstrated. Even in the relatively small biopsy sections the feature of multicentricity can be appreciated with several small, apparently independent tumors in each section. Many of the lumina of the renal tubules in the adjacent renal parenchyma contain apparently exfoliated masses of 4-10 cells which appear to have more the morphologic appearance of neoplastic cells rather than normal renal tubular epithelial cells. Can these be related to intrarenal spread via tubular dissemination and account for the multicentricity?

Because of the multicentricity and because of the large size (4-5 cm.) of some of the lesions, a cautious diagnosis of well differentiated tubulopapillary renal cortical carcinoma, multicentric and bilateral, was offered. Bilateral nephrectomy was performed. Both kidneys contained 40 to 50 grossly visible renal cortical nodules usually bright yellow in color, ranging in size from 1 to 2 mm., up to masses 3 cm. in diameter on the left. No invasion outside the renal capsule was noted nor into the renal vessels or calyceal system or hilar lymph nodes: One mass, about 2 cm. in diameter, in the lower portion of the right kidney showed a cut surface slightly more golden in color with slight central hemorrhage and small foci of necrosis. Sections from the area had a more solid pattern of clear or hypernephroid cells with more variable and pleomorphic nuclei which we interpreted as renal cell carcinoma, clear cell type. All of the remainder of the nodules sampled showed a pattern identical to that of the biopsy material. The patient is now three months postnephrectomy, doing well on dialysis and without evidence of tumor.

Although the problem of the differential diagnosis of cortical adenoma
was compounded by the bilateralism of the lesions in this patient, it is
much more common to be faced with this decision in the patient with a solitary,
often small tumor in one kidney. In days past, most operations done on the
kidney were those to remove it and problems of this sort more or less academ-
ic. In these days of renal angiography for hypertension, CAT scanners and
renal transplantation, the problem is more acutely focused. An old rule of
3 cm. advocated by the late Dr. E. T. Bell held well for autopsy cases although
in our practice we have rarely seen metastases from renal cortical tumors of
well differentaited, clear cell appearance less than that size.

Bennington and Beckwith (1) have summarized available knowledge and a
logical approach. I would refer the reader to their excellent publication
and paraphrase some of their points which I find helpful and add one of
my own.

1. There are no light microscopic, histochemical or electron microscopic
features that distinguish cortical adenoma from carcinoma.

2. There is a direct relationship between tumor size and the frequency of
metastasis in the autopsy case or in the nephrectomy situation.

3. Renal cortical neoplasms, irrespective of size, when found at explora-
tion of the kidney in the living patient should be regarded as carcino-
mas even when small.

4. Tumors, even when small, composed of sheets of clear cells, (hyper-
nephroma type) should be regarded as malignant with appropriate therapy,
but neoplasms manifesting the very well differentiated tubulo-papillary
pattern might be treated by more conservative methods such as en bloc
resection when solitary.

REFERENCES:

1. Bennington, J. L. and Beckwith, J. B.: Development of Renal Adenocarcin-
oma and its Relation to Renal Adenoma. Tumors of the Kidney, Renal Pelvis
and Ureter. Atlas of Tumor Pathology, Armed Forces Institute of Pathology,
MODERATOR'S DIAGNOSIS: HEMANGIOPERICYTOMA OF THE KIDNEY

HISTORY:

This 47 year old man was referred because of recurrent episodes of confusion and diplopia. Fasting blood sugar was 50 mg.% and his symptoms were relieved by sugar ingestion. Symptoms became more severe in spite of dietary measures and he was hospitalized in a comatose condition. A diagnosis of islet cell tumor was considered but at abdominal laparotomy the pancreas was carefully examined and no tumors found. In the left kidney a firm mass was palpated and a left nephrectomy was performed. A partial pancreatectomy was also performed.

Gross examination of the kidney revealed a well encapsulated, firm tumor 10.5 x 10 x 8 cm. which markedly compressed the renal parenchyma and appeared to arise from the renal capsule. The specimen weighed 770 grams. No tumors were found in the pancreas.

DISCUSSION:

This 47 year old man had episodes of spontaneous hypoglycemia. A large left renal tumor was removed which appeared to arise from the renal capsule, but which appeared to be encapsulated and to compress the renal parenchyma. The cut surface of the tumor was firm and fibrous. Postoperatively, the patient did well. He had no more episodes of hypoglycemia until eight years later when he returned because of a recurrence of attacks. Pulmonary and hepatic metastases were demonstrated and two years later, ten years after his nephrectomy, he died in hypoglycemia coma.

Microscopically this tumor is composed of plump spindled cells generally arranged about small slit-like spaces which appear to be lined by endothelial cells and constitute capillaries. In many areas these capillaries are quite flattened and might be described as occult. Irregular fibrillar extracellular masses of collagen are a prominent feature in many fields. The cells are regular, plump and spindled and mitoses are difficult to demonstrate.

The syndrome of hypoglycemia associated with neoplasia is a well recognized entity. A few years ago when this subject was reviewed at our institution (3) there were more than 150 case reports, mostly in middle-aged or elderly adults, but at least three children are also described. Fifty percent of the reported cases were hepatomas or "fibrosarcomas", the latter group undoubtedly including a constellation of nonrecognized distinct entities. Eighty percent of the tumors were located intra-abdominally and the remainder within the thorax.
An outstanding feature has been the large size of the tumors varying from 400 to 900 grams with most over 1000 grams. Two major mechanistic possibilities exist: (1) excessive tumor utilization of glucose or (2) the tumor elaborates a substance(s) capable of depressing normal glucose formation or increasing glucose utilization. Observations favoring the former mechanism include studies which have demonstrated increased tumor glycolytic rates, increased glycogen content and amino acid content in tumors, increased concentrations of lactic acid in the blood during the active phase of the syndrome and marked tumor arterio-venous glucose differences.

Tumor secretion of an insulin-like substance has been observed in at least ten studied patients and among three of our own patients (4) there have been increased concentrations of tryptophan metabolites in the blood and urine during periods of hypoglycemia. These tryptophan metabolites result in profound hypoglycemia in certain lymphoma-bearing mouse strains.
# HYPOGLYCEMIA WITH NEOPLASIA

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<td>Unrecorded</td>
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<td>Range</td>
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<td>Majority</td>
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## SITE OF ORIGIN

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</tbody>
</table>

Other sites: cecum, jejunum, ovary, bladder, lung, buttock, mediastinum

## HISTOLOGY

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Of 2386 surgical specimens of renal malignancy in patients 16 years and older seen consecutively at the Mayo Clinic in a 60 year period there were only 26 cases which with careful pathologic review were classified as sarcomas of the kidney (2). Capsular location was a feature of more than half the tumors, although some of the tumors were situated in relation to the renal pelvis or within the parenchyma. There were 15 leiomyosarcomas, 5 hemangiopericytomas, 5 liposarcomas, and 1 rhabdomyosarcoma. Three of the 5 hemangiopericytomas were well-circumscribed firm fibrous tumors intimately attached to the renal capsule. Compression atrophy of the adjacent kidney without definite invasion was a feature of these cases. The other two cases were unencapsulated and multinodular invading the renal parenchyma, capsule and perirenal tissues. Twenty-one of the 26 sarcoma patients died from tumor including four of the five cases of hemangiopericytoma. The differential diagnosis of hemangiopericytoma should include a consideration of renin-secretory tumors. Although I have never personally observed a case, Bennington (1) describes them as resembling hemangiopericytoma microscopically but the cells contain cytoplasmic granules which produce a positive immunofluorescence with anti-human renin. These tumors, which are small, appear to arise in the juxtaglomerular cells and are thus a specialized form of hemangiopericytoma, occurring usually in young adults with hypertension and behaving in a benign fashion.

REFERENCES:


MODERATOR'S DIAGNOSIS: MALIGNANT FIBROUS HISTIOCYTOMA, INFLAMMATORY TYPE

HISTORY:

This 44 year old male complained of vague abdominal and flank pain. His physician palpated a huge left flank and upper abdominal mass which was said to have doubled in size in two weeks. At exploratory surgery the mass involved the left kidney and extended throughout much of the retroperitoneum and into the base of the small intestinal mesentery. The lesion was bright yellow in color. A debulking operation was performed with removal of 2800 grams of tissue.

DISCUSSION:

This 44 year old man who complained of abdominal pain was found to have a huge left flank and upper abdominal mass which had rapidly increased to size. At exploratory surgery this mass involved the left kidney and extended throughout much of the retroperitoneum and into the small bowel mesentery. The tissue was bright yellow in color and 2800 grams was removed in a debulking operation. Laboratory data showed no significant alteration except for mild thrombocytopenia, a peripheral leukocyte count of 14,500 with 63% neutrophils which showed striking hypersegmentation of their nuclei. The bone marrow aspirate was slightly hypercellular with an E:G ratio of 1:4. Normal maturation of granulocytes was noted. Plasma cells comprised 7% and there were some slightly atypical forms. Numerous megakaryocytes with budding platelets were present. No foreign or metastatic tumor cells were noted.

In the month after surgery the palpable mass doubled in size. External radiation therapy to a total dose of 2975 rads was administered, without appreciable reduction in the mass. Now at 7 months after surgery, the patient is alive, without evidence of distant metastases, but with an even enlarging abdominal and retroperitoneal mass.

The histopathology of this lesion is characterized on low power examination by an abundance of leukocytes, mainly segmented neutrophils imparting a distinctly inflammatory aura. Most of these are segmented neutrophils but occasional eosinophils, lymphocytes and plasma cells are noted. Curiously, in the face of such a granulocytic response, no zones of necrosis or suppuration are noted, implying some stabilization of the granulocytic lysosomal elements. No atypical or immature leukocyte forms are noted. Scattered among these elements and nearly overshadowed are larger cells possessing a
prominent, often vesicular, nucleus often with somewhat vacuolated, at times foamy, cytoplasm. These larger cells vary considerably in size and shape of nuclei, often featuring markedly atypical forms. Mitoses among these cells may be found.

Malignant fibrous histiocytoma is the appellation for a neoplasm that has appeared out of the maze of soft tissue malignancies only in the recent one to two decades. Kauffman and Stout (2) are credited with first bringing the entity to general attention and later Stout with O'Brien (4) culled 53 cases out of a large number of fibrohistiocytic tumors. The experience with 65 patients at our institution was later reviewed (5) with 11 of the cases originating in the retroperitoneum but kidney origin was not noted. Variations on the typical histopathology have appeared, the most recent of these being the myxoid malignant fibrous histiocytoma reported by Weiss and Enzinger (6). Of most significance to this case is the report in 1972 by Kempson and Kyriakos (3) of a remarkable histologic variant of this tumor associated with a massive infiltrate into the neoplasm of neutrophils in combination with the large, both bland and atypical, histiocytes. Follow-up on these patients was consistent with a neoplasm of malignant behavior with death from tumor in all 7 of these cases after an often protracted course punctuated by local recurrences and eventual metastases.

Although this case may represent secondary involvement of the kidney from the retroperitoneum, we have seen one other (unreported) case clearly localized to the kidney initially, which ultimately metastasized widely. This tumor was the inflammatory type and initially misdiagnosed as xanthogranulomatous pyelonephritis. Bennington and Beckwith (1) mention another renal case which was the more usual histologic variant.

REFERENCES:


5. Soule, E. H. and Enriquez, P.: Atypical Fibrous Histiocytoma, Malignant Fibrous Histocytoma, Malignant Histiocytoma and Epithelioid Sarcoma. A

MODERATOR'S DIAGNOSIS: RENAL CELL CARCINOMA, SARCOMATOID TYPE

HISTORY:

This 64 year old man presented with gross hematuria of 2 weeks and hypotension. Physical examination was non-contributory but x-ray studies revealed a left lower pole renal mass. Chest x-ray and bone scans were negative. A left radical nephrectomy was performed. The kidney weighed 200 gms. and the inferior half was nearly replaced by a mass of firm fleshy gray-white and pink-tan tumor measuring 7 x 6 x 4.5 cm., which infiltrated into the perinephric fatty tissues. The renal vessels and regional lymph nodes revealed no tumor.

DISCUSSION:

This 64 year old man with 7 x 6 x 4.5 cm. renal tumor illustrates beautifully a renal neoplasm of distinctive type, often mistakenly diagnosed as some variant of sarcoma. This is particular apt to occur, when as is often the case, the patient presents himself because of a metastatic deposit in some peripheral location especially an extremity. This patient, although he now suffers pulmonary metastases eight months after his nephrectomy, had findings pointing to a renal tumor.

We studied 43 cases of malignant renal tumor in adults with mixed histopathologic features (1) and found typical Wilms' tumor is five patients, and mixed transitional cell-carcinosarcoma in one patient. Thirty-seven patients had a distinctive renal parenchymal tumor characterized by recognizable renal cell carcinoma usually of the clear cell type, intimately associated with a more pleomorphic spindle-cell or giant cell cell malignancy resembling sarcoma. Zones of apparent transition of carcinoma cells to sarcomatoid cells could often be demonstrated.

In ten cases the pleomorphic component showed a predominance of giant cell and strap-like forms which closely resembled pleomorphic rhabdomyosarcoma although cross striations were never demonstrated. In 24 cases the sarcomatoid component consisted of malignant spindle cells, closely resembling fibrosarcoma, and in three cases in addition to fibrosarcoma-
like zones, there were many areas where neoplastic cartilage and osteoid could be demonstrated. The cases with metastatic deposits which were studied reproduced the histologic features of the primary tumor although proportions of carcinoma to sarcomatoid tumor varied.

The highly malignant nature of the tumors was attested to by the ultimate tumor death of 33 of 36 patients who were followed.

REFERENCES:

MODERATOR'S DIAGNOSIS: NEPHROGENIC ADENOMA OF THE BLADDER

HISTORY:

This 18 year old female in an auto accident in May, 1974, sustained multiple injuries including rupture of both the anterior and posterior walls of the bladder with a large vesicovaginal opening. After several corrective operations she continued to complain of painful and frequent urination. A cystoscopic examination September, 1975, revealed an extensive papillary tumor involving the floor of the bladder. Intravesical thio TEPA was administered on multiple occasions and a transurethral resection and electrocoagulation of the tumor was attempted November, 1975. By December, 1975, the tumor had flourished and now occupied the entire lower half of the bladder. A total cystectomy and urinary diversion was performed.

The inferior two-thirds of the bladder was lined by an erythematous shaggy papillary lesion. The urethra and ureters were free of neoplasm. No regional lymph nodes were submitted.

DISCUSSION:

This 18 year old woman, with irritative bladder symptoms, presented with an extensive, shaggy-appearing papillary neoplasm which involved the entire lower half of the bladder. Attempts at local resection and electrocoagulation failed to control growth, as did intravesical chemotherapy, eventuating in a total cystectomy. The patient gave the pertinent past history of a ruptured bladder one-and-a-half years before (attended with prolonged indwelling catheter drainage). Three-and-one-half years after cystectomy the patient is well without evidence of neoplasm.

The histologic pattern of this lesion is one of a tubulopapillary neoplasm which is composed of regular cuboidal cells arranged in both extensive delicate frond-like papillae but also with many zones where there is a resemblance to renal tubular structures. The neoplasm is situated upon the mucosal surface of the bladder, but many tubular structures are within the submucosal connective tissue stroma. Extension into muscle is not demonstrated. The cells are regular and mitoses cannot be readily demonstrated. In some of the sections there is a zone of metaplasia of the bladder mucosa composed of large goblet cells.
Synonyms for this lesion have been "adenomatoid tumor", and "mesonephric adenoma and adenocarcinoma" of the bladder. Apparently the first report of a bladder lesion of this type was that of Davies, 1949, (2) which he called a hamartoma, but the pathologic description is that of our case. In 1950, Friedmann and Kuhlenbeck (4) found seven cases in the records of the AFIP in patients between the ages of 18 and 29 years. Mostofi (6) and Hasen (5) each reported patients who developed the tumor after bladder trauma and the two cases of Christopherson and Moller (1) had preceding multiple surgical procedures to the bladder. Both these latter tumors recurred after local electrocoagulation therapy and one was considered "histologically" malignant.

The report by Dow and Young (3) was the first to document malignancy in one of these cases in a patient who died with generalized metastases. Although local recurrence is common after conservative therapy, this is the only tumor to pursue a truly malignant course. My experience includes five cases not recorded in the literature ranging in age from 18 to 67 years. The lower portion of the bladder is the site of predilection. In my five cases and in at least half the reported cases there has been a history of bladder trauma, either accidental or surgical, followed by prolonged catheter drainage of the bladder. This may be an important etiologic factor.

REFERENCES:


HISTORY:

This 59 year old male complained of intermittent gross hematuria for one year. He gave the history that in 1964 after an abdominal exploratory operation, he was told that he had cancer of the pancreas. No biopsy was obtained. He was then treated with cytoxan which was continued on an intermittent basis until 1969. At this time another doctor told him it must have been a pancreatic cyst. Hematuria and symptoms of bladder irritation began five years later in 1974.

X-ray examination revealed a cystic partially calcified structure in the region of the pancreas and highly anaplastic malignant cells were detected on the urine cytologic examination.

Cystoscopy revealed diffuse, edematous and erythematous raised granular areas throughout the lower half of the bladder and multiple biopsies revealed in situ transitional cell carcinoma, highly anaplastic. A total cystectomy and urinary diversion was then performed. The bladder showed extensive mucosal changes as cystoscopically described. No gross tumor was noted. The regional lymph nodes were free of neoplasm.

DISCUSSION:

This 59 year old man with a history of gross hematuria was found to have extensive in situ transitional cell carcinoma of the bladder for which a total cystectomy was performed. Step sections on the resected specimen and mapping studies revealed a poorly differentiated transitional cell carcinoma, mainly in-situ, throughout most of the bladder mucosa but with multiple zones of submucosal invasion. One year postoperatively the patient complained of a bloody discharge from his urethral stump and a subsequent urethrectomy specimen revealed more in situ carcinoma. He is now alive and apparently free of tumor four years later. A most significant facet of his medical history related to his intake for a period of more than four years of cyclophosphamide (cytoxan) for a diagnosis of pancreatic malignancy which apparently did not exist.

Cyclophosphamide (cytoxan) is a chemical widely used in cancer chemotherapy. Although generally classified with the alkylating agents, the drug as administered is a cyclic phosphamide ester of nitrogen mustard,
and it is unique to this class of compounds in that enzymatic removal of
the phosphamide group must be accomplished to release the active compound.
This occurs primarily in the liver, but there is rapid systemic distribute-
on of the active principle which appears promptly in the urine. Up to
40 percent of patients receiving the drug experience some degree of bladder
toxicity in the form of sterile cystitis often accompanied by hematuria.
For this reason the supicion of bladder neoplasm may arise and if urine
cytologic examination is performed, bizarre cytologic alterations induced
in the urothelial cells by the drug may be readily confused with those of
a malignant neoplasm. Because most patients received the drug for a malig-
nant neoplasm and usually survived only short periods of time, it did not
become immediately apparent that these cellular changes did possibly indi-
cate incipient evolution through a premalignant state into bladder cancer.
Finally reports began to appear of carcinoma of the bladder developing in
some of these patients. (1, 4). There are now more than 25 known cases
of bladder cancer among patients who received the drug for malignant
disease, the youngest of these to my knowledge being an 18 year old fe-
male (2). Most of these cancers have been anaplastic and many have shown
squamous features. The drug is now widely used for such non-neoplastic
conditions as systemic lupus erythematosus and rheumatoid arthritis. Our
case and two others soon to be reported from the National Institute of
Health (3) constitute the first cases appearing in patients without as-
sociated malignant disease.

REFERENCES:

1. Dale, G. A. and Smith, R. B.: Transitional cell carcinoma of the


in Patients Receiving Cyclophosphamide for Systemic Lupus Erythe-

4. Wall, R. L. and Clausen, K. P.: Carcinoma of the Urinary Bladder in
Patients Receiving Cyclophosphamide. N. Engl. J. Med. 293:271-273,
1975.
**MODERATOR'S DIAGNOSIS:** TRANSITIONAL CELL CARCINOMA OF THE BLADDER WITH EXTENSION INTO THE PERIURETHRAL PROSTATIC DUCTS

**HISTORY:**

This 72 year old man gave a four year history of burning dysuria, frequency and urgency of urination. His prostate was noted to be enlarged, firm but non-nodular. Cystoscopy revealed a diffusely reddened and inflamed bladder mucosa. Urine cytology was positive for malignant cells. Biopsies of the prostatic urethra revealed a malignant neoplasm for which a total cystectomy-prostatectomy was performed. The bladder mucosa appeared diffusely reddened and slightly granular. No gross neoplasms were noted in the bladder or prostate.

**DISCUSSION:**

This 72 year old man with irritative bladder symptoms and a diffusely inflamed-appearing bladder mucosa and a urine cytology which contained malignant cells was found on multiple biopsies both of the bladder and the prostatic urethra to have an extensive transitional cell carcinoma, in situ, mainly, but with one focus of microinvasion in the bladder and with extension of the neoplasm into the periurethral prostatic ducts. These findings were documented by step-sectioning and mapping the entire specimen of prostate, bladder and urethers after a total cystectomy and urinary diversion. The lymph nodes contained no metastases. The patient is alive and well four years later with no evidence of neoplasm.

The vast majority of carcinomas in the prostate are adenocarcinoma and primary there. A quite uncommon primary tumor of the prostate is transitional cell carcinoma beginning in the major prostatic ducts. Greene, et al. (2) reported clinical and pathologic findings in 26 patients gleaned from 5500 patients with prostatic carcinoma seen at the Mayo Clinic between 1957 and 1971. Histologically these neoplasms present as plugs, composed of large transitional epithelial cells with no evidence of glandular differentiation. Many zones may show distention of prostatic ducts by centrally necrotic plugs of the tumor and in most cases invasion into the adjacent prostatic stromal tissue can be demonstrated. Treatment of these cases must be different than for ordinary prostatic adenocarcinoma since the neoplasms are not sensitive to hormonal manipulation. Indeed, the outlook for these patients is grim. Twenty-one of 26 having died from their tumors and the longest of the survivors had been followed only 31 months. Radiation and/or radical surgery seem to offer the only hope for cure.
Although none of these 26 patients had a demonstrated bladder tumor, secondary involvement of the prostate by transitional cell carcinoma is much more common than that by a primary tumor. Seemayer, et al. (3), have emphasized this feature of bladder cancer. The implications for therapy and for staging are important since the prostate may be shielded from certain forms of therapy such as topical intravesical chemotherapy or external irradiation aimed at the bladder. Invasion may occur within the prostate while the tumor remains in situ or occult within the bladder. Prostatic ductal extension even with in situ transitional cell carcinoma occurs frequently. In a step-sectioning and mapping study of the lesions in 21 cystectomy specimen for in situ carcinoma we found extension into the prostatic ducts in seven of 19 males (1), which usually occured as a direct extension from an in situ change in adjacent urethral mucosa, but often a unique type of pagetoid extension of individual malignant cells into intact benign mucosa could be observed.

REFERENCES


MODERATOR'S DIAGNOSIS: EMBRYONAL RhabdomyOSARCOMA OF THE PROSTATE

HISTORY:

This 3 1/2 year old male experienced severe intermittent pain before urinating for two months. For one week there was bilateral leg pain and the day before his first hospital admission both legs became swollen. Examination revealed a firm, rubbery, irregular fixed mass over the pubis and a baseball-size rubbery firm mass was palpated rectally in the region of the prostate filling the hollow of the sacrum. A needle biopsy of this mass was performed followed by radiation therapy. The patient expired 3 1/2 months later. At autopsy the prostate gland was completely replaced by a large tumor which completely filled the pelvis and weighed 880 gms. The cut surface was homogeneous, white and fleshy in consistency. There were metastatic deposits in lymph nodes, liver, pleura, and around the vena cava and portal veins.

DISCUSSION:

This three-and-a-half year old male, who died with disseminated metastatic neoplasm after radiation to a large prostatic mass, illustrates the classical pathological features of embryonal rhabdomyosarcoma. The large prostate was rubbery, homogenous, white and fleshy. Microscopically the neoplasm is composed of embryonal rhabdomyoblasts showing varying degrees of differentiation, the occasional cell exhibiting well developed striations.

Sarcomas of the prostate account for less than 0.1 percent of all prostatic malignancies but are important among the pediatric group, especially rhabdomyosarcoma. Among the 636 cases of the Intergroup Rhabdomyosarcoma Study (1) up to November, 1978, the head and neck region, the most frequent site (38%) was followed by the genitourinary region (21%), extremities (18%), trunks (7%), retroperitoneum (7%), and miscellaneous sites. Twelve percent were less than two years of age at entry, 33 percent were two to five years, 22 percent between six and 10 years, 24 percent between 11 and 15 years, and 9 percent between 15 and 20 years. Thus 67 percent were ten years of age and under. Head and neck and retroperitoneal lesions in the majority of cases were not amenable to resection. In contrast, tumors confined to the genitourinary were resectable more often than not. Of the four classical histologic types, embryonal was the most frequent, accounting for 58 percent of the cases, 19 percent for alveolar, 7 percent botryoid and 1 percent pleomorphic. The remainder were classified as special undifferentiated cell types or as type indeterminate.
The major prognostic indicator for children with rhabdomyosarcoma is the clinical group (stage). However, considering prognostic features within clinical groups, the most consistent characteristic related to prognosis was the primary site. Generally patients with disease in the extremities had an unfavorable prognosis while those with genitourinary or orbital tumors had the opposite. Histologic type related to disease-free survival only in localized, resectable disease cases (Clinical group 1) where the alveolar cell type had the least favorable prognosis.

In a study from our institution, 1975, on embryonal rhabdomyosarcoma of the bladder and prostate in children (2), of 30 children treated the primary site was the bladder in 14 cases (9 boys and 5 girls) and the prostate in 16 cases. The mean age at diagnosis was three years for bladder cases and 6.5 years for the prostate. Overall survival after various treatment modalities including various combinations of surgery, radiation and chemotherapy was 23 percent.

REFERENCES:


MODERATOR'S DIAGNOSIS: PROSTATIC ADENOCARCINOMA OF PRIMARY (PERIURETHRAL) DUCT TYPE

HISTORY:

This 73 year old man had symptoms of prostatism for several years. In 1976, elsewhere, a prostatic transurethral resection was performed and again in 1977 for persistent symptoms. (Tissue not available for review.) Referred because of recurrent urethral bleeding. The prostate on rectal palpation was moderately enlarged, irregular, firm and tender. Cystoscopy revealed a "curious polypoid structure" near the verumontanum. This lesion was biopsied. Shortly thereafter a radical prostatectomy was performed. Some sections are from the biopsy specimen, others from the prostatectomy. In the latter specimen within the prostatic urethra there was a papillary tumor which extended grossly into the major periurethral prostatic ducts. The lymph nodes were negative for metastases.

DISCUSSION:

This 73 year old man with symptoms of prostatism for several years was found to have an enlarged, irregular firm and tender prostate gland on digital examination. Cystoscopy revealed a "curious polypoid structure" near the verumontanum. Subsequently a radical prostatectomy was performed and in the specimen there was a villous or papillary tumor which extended grossly into the major periurethral prostatic ducts. The lymph nodes contained no metastases. The patient did well and returned one year later in May, 1979, for a check up. An extrarectal nodule was palpated in the region of the prostatic bed and a needle biopsy yielded recurrent adenocarcinoma of similar histologic pattern.

A portion of the participants received slides from an initial biopsy of the polypoid urethral tumor which illustrate a polypoid and villous neoplasm composed of tall columnar cells resembling more colonic than usual prostatic cancer. For those who received slides from the radical prostatectomy specimen, this neoplasm is seen to emanate from the major prostatic ducts.

I became interested in this type of prostatic adenocarcinoma when asked to consult on an interesting case brought to me by a pathologist in a neighboring town. This case was subsequently reported (2), and he and I then undertook to review all the slide material of 4286 consecutive cases of prostatic adenocarcinoma seen at our institution between 1950 and 1970 (1). We found 55 cases which we felt were pure and pathologically distinct from the usual peripheral acinar adenocarcinomas or 1.3% of the total. Additionally there were 207 cases when there was a mixture of this tumor type with more ordinary prostatic adenocarcinoma. Therefore, elements of the neoplasm were observed in 6.3% of all cases of prostatic adenocarcinoma. Eight of the 55 pure cases origin-
ated from the periurethral, primary prostatic ducts as in our Case 25, and had exuberant papillary fronds. Five of these cases had recorded on cystoscopic examination a polypoid or villous urethral component and two an infiltrative urethral component. The five year survival rate for these cases (42.8%) was similar to that for ordinary adenocarcinoma. A large proportion of the tumors occurred in more peripheral portions of the prostate and were usually multicentric and extensive. This group of 47 cases we classified as adenocarcinoma of the secondary prostatic ducts. The five year survival was only 24.2% for this group. Without the benefit of a well-conducted, controlled study of therapy, it appeared from these patients records that estrogen therapy or orchidectomy was much less effective in controlling local or metastatic disease in these patients than in ordinary prostatic adenocarcinoma.

Although serum acid phosphatase levels are unpredictable in these tumors when metastases exist examination of tissue sections with a highly specific human antiprostacic acid phosphatase immunoperoxidase technique has consistently been negative when the usual acinar carcinomas are strongly positive.

Kopelson, et al., with Myron Tannebaum from Columbia P and S, have recently reported their experience with a similar group of 58 patients with essentially similar conclusions (3).

REFERENCES:


IMMUNOPEROXIDASE (PAP) TECHNIQUE FOR PROSTATIC ACID PHOSPHATASE (pACP)

FIXATION: 10% Buffered neutral formalin. (To help prevent non-specific staining, immediate fixation of tissue is essential.)

TECHNIQUE: Cut paraffin section, 3 - 4 microns in thickness.

PROCEDURE:
1. Deparaffinze sections (Xylol, absolute alcohol, graded alcohols) to distilled water. RUN CONTROL SLIDES OF PROSTATE.
2. Place slides in 1.0% solution of Periodic Acid for 10 minutes.
3. Rinse slides in distilled water.
4. Add Normal Swine Serum (1/20) to slides - incubate for 10 minutes.
5. Blot off excess swine serum - DO NOT WASH.
6. Add Rabbit anti pACP (1/1600) to one set of slides; add NORMAL RABBIT SERUM (1/1600) to duplicate set of slides as the control set. Incubate at room temperature for 60 minutes.
7. Rinse in 3 changes of PBS (Phosphate buffered saline, pH7.2), 5 minutes each.
8. Add SWINE anti RABBIT SERUM IgG (DAKO - Accurate Chemical and Scientific Corp. 28 Tec Street, Hicksville, New York 11801) 1/20. Incubate for 30 minutes at room temperature.
9. Rinse in 3 changes of PBS, 5 minutes each.
10. Add PAP 1/20 (DAKO - Accurate Chemical & Scientific Corp.) Incubate at room temperature, in the dark, for 30 minutes.
11. Rinse in 3 changes of PBS, 5 minutes each.
12. Place in AEC reaction for 30 minutes.

AEC REACTION:
1. Dissolve 3-Amino-9-ethylcarbazole (AEC) .......... 30 mg.
   (ALDRICH CHEMICAL COMP., INC. MILWAUKEE, WIS.)
   IN
2. N - N Dimethyl formamide (FISHER SCIENTIFIC) ........7.5 ml
3. Add to 0.1M Acetate buffer, pH 5.2 .................. 142.5 ml.
4. Just before use, add 3.0% Hydrogen peroxide .......... 1.5 ml.
5. Filter, and incubate at room temperature for 30 150 ml. total
6. Rinse with distilled water.
7. Counterstain with hematoxylin.
8. Mount with Kaisers glycerine jelly. (DO NOT DEHYDRATE. DO NOT USE PERMOUNT)

1.0% PERIODIC ACID:

DISSOLVE Periodic Acid ........................................3.5 grams
IN Distilled water ........................................... 70 ml
ADD Absolute Methyl Alcohol .................................. 280 ml
350 ml total

PHOSPHATE BUFFERED SALINE (PBS):

Sodium Phosphate Dibasic (Anhydrous (Na₂HPO₄)) ....... 165.12 grams
Potassium Phosphate Monobasic (KH₂PO₄) .................... 59.52 grams
Sodium Chloride (NaCl) ........................................ 204.00 grams
DISSOLVE the above, with the aid of a little heat, in ... 2000 ml distilled water
ADD distilled water to make a total amount of ...... 24,000 ml (24 liters)
CHECK pH: 7.0 - 7.2
STORE at room temperature.

KAISERS GLYCERINE JELLY:

DISSOLVE: 21.50 grams Sodium Acetate ·3H₂O
IN: 42 ml 1N Acetic Acid (Glacial Acetic Acid = 17N)
ADD: 2000 ml distilled water
CHECK: pH 5.2
STORE: In refrigerator (4°C)

NOTE:

The RABBIT anti PROSTATIC ACID PHOSPHATASE antisera was obtained from Dr. K. W. Lam, Albany Medical College, Albany, New York.