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CASE 1. TERATOMA, IMMATURE (BIOLOGIC POTENTIAL UNDETERMINANT) WITH SUBSEQUENT MATURATION.

CASE 2. MATURE, SOLID TERATOMA WITH GLIOMATOSIS PERITONEI.

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CASE 4. PLASMA CELL GRANULOMA (INFLAMMATORY PSEUDOTUMOR)

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Case I: Soft tissue, neck (cervico-thyroid) - Teratoma, immature (biologic potential undeterminant) with subsequent maturation.

There is no more appropriate area of pediatric pathology to begin a seminar than with a discussion of the teratoma, an embryologic neoplasm if there was ever a candidate. The teratoma qualifies fully as an example in the words of Ruppert Willis as the "borderland of embryology and pathology". This case and the next have been selected as representatives of extra-gonadal and gonadal germ cell tumors in childhood. Each case illustrates some of the practical problems which confront the pathologist in terms of prognosticating future behavior and secondly, the ponderable considerations of histogenesis.

Overall, gonadal and extra-gonadal germ cell tumors do not constitute a major problem in the scheme of pediatric neoplasia. Robert Miller at the Epidermiologic Branch of the National Cancer Institute has been the best keeper and analyzer of the statistics and as you can see from a modification of his figures that germ cell tumors rank rather close to the bottom of the list (Table). In 1973, Fraumeni and coworkers examined the epidemiologic features of teratomas in childhood and noted that female death rates exceeded those of males, a reversal of the usual trend for malignancies in childhood. Sacrococcygeal teratomas in girls under 3 years of age accounted for many deaths.

The first case involves a newborn who presented with a mass in the submandibular region of the neck. An excision was performed and a yellowish-tan mass measuring 10 x 9 x 6 cm., weighing 230 gm. was excised. On cut section, it had a multicystic appearance with a mucoid-myxoid quality. Within a few weeks of the original excision, the mass had recurred with extension toward the esophagus and trachea. A second excision was performed. At the age of 1 1/2 years, there was another recurrence and as far as I am aware, no metastases were identified.

I have had the opportunity of reviewing the sections from the primary tumor and the recurrences. The original sections show a tumor with a complex histologic appearance which varies from tubo-glandular foci with an endodermal sinus pattern, elongated glandular structures resembling primitive medullary canals, small nests of pigment-containing cells, cartilage and sheets of large pink cells resembling granular cells. Mucoid or gelatinous areas constitute a part of the background. Some differentiating somatic elements are noted. The structures composed of the hyperchromatic cells appear to be undergoing degeneration in many areas. Sections from the first recurrence are somewhat similar but I could recognize more mature elements, especially smooth muscle and nests of degenerating tumor were even more prominent. Focal infiltration of the submandibular gland was present. The most dramatic aspect of this case is represented in the second recurrence. At this time, the tumor has seemingly matured and represents a fully mature and presumably benign teratoma.
This case illustrates the fact that most germ cell tumors presenting in the newborn period are generally extra-gonadal and secondly, the histologic appearance may be deceptive in the prediction of future biologic behavior. In a review of the 4 major series of germ cell tumors in childhood (Ref. 1, 2, 3, 6), the cervicothyroid region accounted for 3-9% of all cases. Two series (Ref. 3, 6) had no examples. Over 90% of cervicothyroid teratomas present in infancy and 17% of cases have occurred in stillborns. Polyhydramnios has been documented in 20% of cases. These tumors kill as a result of the local manifestations and according to Hawkins and Park (1972), there have been no examples of malignant teratomas of the neck in childhood but a few in adults. Roediger and coworkers (1974) have recently speculated about the histogenesis but I like to subscribe to the midline migration theory of germ cells and their persistence and neoplastic transformation as an explanation for extra-gonadal germ cell tumors. The events leading to maturation of the teratoma in this patient are not well understood but the work of Leroy Stevens (Ref. 9) with the testicular teratoma in mouse strain 129 has shed considerable light on the biology of these tumors.

References


Case 2: Ovary, oophorectomy - Mature, solid teratoma with gliomatosis peritonei

In a 3-year-old child with a large abdominal mass showing calcification by X-ray, the most common diagnosis is neuroblastoma. The catecholamine levels were normal but we have seen a small percentage of biochemically inactive neuroblastomas. An exploratory laparotomy was performed and multilobular adnexal mass measuring 15 x 14 x 12 cm., weighing 1225 gm. was excised. The surface of the tumor was smooth with some fresh hemorrhage. There were some
capsular adhesions and attached omental fat. The cut surface was mainly solid but a few, small cystic areas were noted. In addition to the large solid tumor, the peritoneum was diffusely studded with tiny white nodules measuring 1-3 mm. Several of these nodules were biopsied.

Multiple sections were examined from this ovarian neoplasm and those used in the seminar are representative of the tumor. Almost without exception, the morphologic elements are somatic rather than embryonic or extra-embryonic and there is evidence of maturation. The predominant tissue type is mature neuroepithelium. A rare cluster of small, dark cells resembling neuroblasts and an elongated immature medullary canal are noted. Other elements included skin with appendages, respiratory mucosa, cartilage, mature ganglia, smooth muscle, fat and bone. Although you did not have a section of one of the peritoneal nodules, they were composed elusively of mature neuroglia surrounded by a dense chronic inflammatory reaction. These implants are characteristic of so-called "gliomatosis peritonei."

Approximately 20-35% of all germ cell tumors in childhood originate in the ovary and one-half or more of these ovarian neoplasms are mature cystic teratomas. In a review of 353 tumors of the ovary at the Armed Forces Institute of Pathology, 58% of neoplasms were derived from germ cells followed by surface epithelium (19%) and gonadal stroma (18%) (Ref. 8). It has been estimated that 10-15% of ovarian germ cell tumors in childhood are malignant.

The solid teratoma of the ovary is rare neoplasm among the germ cell tumors. Thurlbeck and Scully (Ref. 11) and even earlier, Peterson (Ref. 9) described the clinical and pathologic features of the solid teratoma. As is true for most germ cell tumors of the ovary, the patients are usually diagnosed during the first three decades of life and an abdominal mass is the most common mode of presentation. Most solid teratomas are unilateral (95%) and the characterization of the tumor as "solid" is somewhat misleading since multicystic areas are invariably present. A system of histologic grading was devised by Thurlbeck and Scully (Ref. 11) in an attempt to predict future clinical behavior. Their system is as follows:

HISTOLOGIC GRADING OF SOLID TERATOMAS OF THE OVARY
(Thurlbeck-Scully, 1960)

Grade 0 All cells well differentiated.
Grade 1 Cells well-differentiated except in rare small foci of embryonal tissue.
Grade 2 Moderate quantities of embryonal tissue present; cells show atypicality and mitotic activity.
Grade 3 Large quantities of embryonal tissue present; cell shows atypicality and mitotic activity

Two recent studies by Beilby and Parkinson (Ref. 2) and Norris and coworkers (Ref. 7) have applied this system of histologic grading to such tumors. In 16 of the 20 cases in one series (Ref. 2), the authors concluded that the determination of the amount of immature embryonic tissue was unreliable. A more important feature was the presence of the endodermal sinus.
pattern in the tumor which was indicative of a poor prognosis. Norris and coworkers (Ref. 7) in an examination of 58 immature ovarian teratomas were more optimistic about the application of the Thurlbeck-Scully system but also felt that the size of the tumor and the clinical stage were other significant prognostic factors. Based upon the Thurlbeck-Scully system, the tumor in the seminar straddles between grade 0-1 since there are small neuroblastic-appearing cells. I have not found that the presence of neuroblasts in a germ cell tumor should be viewed with any great concern, however, the occurrence of the elongated, primitive medullary canals in a teratoma is another story. These structures and the “glomeruloid” or Schiller-Duval bodies are indicative of malignancy.

In any other context when the peritoneum is seeded with tumor implants as this child had at the time of surgery, a poor prognosis would be undisputed. The unique situation of so-called "gliomatosis peritonei" sets it apart. Thurlbeck and Scully (Ref. 11) documented this phenomenon in one of their patients (Case 3) who was still alive 26 years later with omental and peritoneal metastases which were composed solely of mature glial tissue. Since that report, Robboy and Scully (Ref. 10) analyzed 12 cases and nearly all represented examples of grade 0 solid teratoma. In 10 of the 12 cases, a tear and/or omental adhesions were noted on the surface of the tumor. The follow-up ranged from 9 months to 38 years. The 38-year follow-up was the original patient reported by Thurlbeck and Scully. Additional cases of gliomatosis peritonei since the 1970 report have been published by Favara and Franciosi (Ref. 3), Livaditis and coworkers (Ref. 5) and Nogales and Oliva (Ref. 6).

References

Case 3 - Lung - Cystic adenomatoid malformation

The causes of respiratory difficulties in the neonatal period are most conveniently divided into surgical and non-surgical etiologies (Ref. 5, 14). Although the anatomic material from the current case was obtained at autopsy, the uncommon cystic adenomatoid malformation of the lung is well-known cause of respiratory distress in the newborn. The child in this seminar weighed 6 pounds, 2 ounces at birth and was the product of a pregnancy complicated by prolonged rupture of membranes (18-20 hours). At delivery, the infant was flaccid and cyanotic. She required resuscitative efforts and the respirations were characterized as grunting with subcostal retractions. The breath sounds were poor to absent and a chest film revealed non-aeration of the left lung and almost complete consolidation of the right lung with one large emphysematous bleb. As far as could be determined, the tracheobronchial tree was patent. A reasonable clinical diagnosis may have been congenital or perinatal pneumonia secondary to the prolonged rupture of membranes (Ref. 1). Beyond a period of 36 hours with ruptured membranes, the risk of pneumonia climbs precipitously. Meconium aspiration, diffuse pulmonary hemorrhage, neonatal atelectasis and with the emphysematous bleb, congenital lobar emphysema were other possibilities. Hyaline membrane disease is not likely in the light of the time interval and the roentgenographic findings.

The patient died at 8 hours. At autopsy, the right lung weighed 52 gm. and the left, 26 gm. With the exception of the right lower lobe, the remaining lobes were described as aletecatic. The right lower lobe was mottled, dark reddish to grey and on cut section, it had a soft, fleshy appearance with numerous cysts measuring from 0.3 - 1.8 cm. in diameter. Histologically, the sections from the right lower lobe revealed rather uniform appearing epithelial-lined spaces. There were some cystically dilated structures and in occasional foci, the lining cells were columnar and contained cytoplasmic mucin. Most epithelial cells were cuboidal. Fibrous septa containing a prominent vascular component were also present. Throughout the various sections, bronchial cartilage was obviously absent. Differentiated alveolar spaces were extremely uncommon. This case fulfills, for the most part, the 5 criteria which Bain (Ref. 3) considered necessary for the diagnosis: 1) absence of bronchial cartilage; 2) absence of bronchial tubular glands; 3) presence of tall columnar mucinous epithelium; 4) overproduction of terminal bronchiolar structures without alveolar differentiation except in subpleural areas; and 5) massive enlargement of the affected lobe displacing other thoracic structures.

Malformations of the lung have been classified in various ways. Potter and Craig (Ref. 13) have divided pulmonary malformations into 4 basic categories (Table 1) and this child's problem is listed under the heading of "abnormal composition". Congenital cysts and cystic malformations of the lung have been the source of much confusion in terms of basic pathogenesis and nomenclature. Levine and coworkers (Ref. 9) as part of an overall classification of pulmonary anomalies have devised one workable categorization (Table 2).

In addition to respiratory difficulties in the neonatal period, fetal hydrops-anasarca and polyhydramnios are other associated findings (Ref. 8, 12). The respiratory distress that a newborn experiences increases over time as air
becomes entrapped within the cysts. It should be remembered that there is no cartilaginous support to the major air-ways. Eventually, there is shift of the mediastinum. There have been cases that have had a delayed presentation after a period of weeks or months when persistent or repeated pulmonary infections were present.

Most clinicopathologic studies of the cystic adenomatoid malformation have involved no more than 1-3 cases, however, Madewell and coworkers (Ref. 10) have examined the features of 31 cases at the Armed Forces Institute of Pathology. As in our case, the lower lobes were principally affected and most malformations have a macroscopic cystic appearance. Dempster (Ref. 6) and Van Dijk and Wagenvoort (Ref. 15) have reported a solid variant. Radiographically, a persistent soft tissue density was noted in the lung.

An immediate lobectomy is necessary if a child is going to survive this malformation (Ref. 7).

References

TABLE I: PULMONARY MALFORMATIONS
(Potter and Craig, 1975)

I. Abnormal size
   A. Primary hypoplasia
      1. Bilateral (rare, acephauls)
      2. Unilateral (70% left, M:F/2:1, T-e fistula)
   B. Secondary hypoplasia
      1. Diaphragmatic hernia
      2. Craniospinorachischisis (anencephaly)
      3. Renal agenesis, occ. infantile polycystic kidneys

II. Abnormal position

III. Abnormal lobation
   1. Sequestration

IV. Abnormal composition
   1. Cystic adenomatoid malformation
   2. Solitary cysts
   3. Congenital pulmonary lymphangectasia (Laurence)
   4. Heterotopic tissue

Table II: CONGENITAL CYSTS AND CYSTIC MALFORMATIONS OF THE LUNG
(Levine, et al., 1966)

I. Congenital cysts
   A. Solitary
      1. Asymptomatic
      2. Tension and communicating
   B. Multiple cysts
   C. Cystic bronchiectasis

II. Cystic malformations
   A. Solitary cysts
   B. Multiple cysts
   C. Cystic sequestration
   D. Cystic adenomatoid malformation
   E. Diffuse cystic lymphangiectasis
Case 4 - Lung - Plasma cell granuloma (inflammatory pseudotumor)

When this 2-year-old child was admitted to the University Hospitals, there was some confusion and uncertainty about the clinical diagnosis. The mass in the chest was initially interpreted as being located in the anterior mediastinum and there was a question of leukemia. It was finally resolved before surgery that leukemia was not present. At thoracotomy, the mass resided in the right upper lobe and a wedge resection was performed.

Grossly, the mass was contained within the pulmonary parenchyma and had a well-circumscribed lobular contour. It was firm and measured approximately 3.5 x 3.5 x 3.0 cm. A gritty consistency was noted on cut surface. The tumor had a yellowish-grey color, a slightly-whorled appearance and focal stippled calcification. A frozen section had been performed and a diagnosis of an inflammatory process was made. Histologically, the predominant microscopic elements were mature fibrous tissue and sheets and aggregates of mature plasma cells. Entrapped, residual respiratory structures were present within the mass. A rare binucleated plasma cell and occasional Russell bodies were identified. The focus of dystrophic calcification was also confirmed. Although the mass appeared well-demarcated in the gross examination, the inflammation and fibrosis blended into the adjacent parenchyma. It has been 6 months since surgery and the child is doing well.

Tumor and tumor-like disorders of the lung are relatively uncommon in childhood as attested by one's personal experience and the paucity of literature (Ref. 9). Individual case reports of pulmonary tumors in children serve as testimonials to the rarity of lung neoplasms in this age group. Of the primary malignant tumors, the carcinoid type of "bronchial adenoma" is the most common neoplasm of the lung in childhood. Wellons and coworkers (Ref. 11) reported 2 cases and collected 56 from the literature. The usual varieties of pulmonary carcinoma encountered in adults are among the rarest of pediatric neoplasms. Niitu and coworkers (Ref. 6) have reviewed the experience in Japan and the other countries of the world. In our own institution, solitary or multiple, small peripheral metastatic lesions to the lungs are the commonest malignant tumors which we have a chance to examine as surgical specimens. Osteosarcoma and Wilms' tumor together account for 90% of all such cases. Pulmonary biopsies from children with malignant disease are not at all infrequent when the diagnosis of an opportunistic infection is being considered. In most cases, the diagnosis of Pneumocystis carinii pneumonia is being attempted. Histiocytosis X (differentiated histiocytosis), malignant histiocytosis and Ewing's tumor have been the other pathologic disorders for which pulmonary biopsy or resection has been attempted in the past 2 years at the University Hospital.

The plasma cell granuloma certainly qualifies as a tumor-like process and, in fact, "inflammatory pseudotumor" has been a term used in the past. Bahadori and Liebow (Ref. 2) prefer the appellation of plasma cell granulomas. Histiocytoma, xanthogranuloma and xanthoma are just some of the other less frequently used synonyms. This circumscribed mass-lesion is generally located in the peripheral lung fields, less frequently as an endobronchial mass. In Bahadori and Liebow's experience, over one-half of 40 patients that they
studied were initially asymptomatic. Those with symptoms had a cough, shortness of breath or hemoptysis. Approximately 27% of the patients in the latter study were 10 years of age or younger at diagnosis and one-third were less than 20 years. Pearl (Ref. 7, 8) has described the clinical and roentgenographic features of this lesion under the heading of "postinflammatory pseudotumor" in a group of children. One of her cases had a respiratory infection and developed a circumscribed mass which was followed by a second lesion that extended into the mediastinum and encroached upon the right inferior pulmonary vein.

The plasma cell granuloma has a predilection for the lower lobe, measures from 1 - 12 cm. in greatest diameter and has the firm, greyish to yellowish-brown appearance that the mass in the seminar had. Histopathologically, some variations in cell types may be apparent. For instance, histiocytes, lymphocytes, mast cells and eosinophils are also present, especially the foamy histiocytes. Necrosis was evident in only 3 of the 40 cases in the Bahadori and Liebow series. Limited resection is generally curative (Ref. 5, 10).

Most cases have not been historically associated with a preceding pulmonary infection. Ackerman and coworkers (Ref. 1) drew attention to the similarities of localized organizing pneumonia to carcinoma of the lung. Microbiologic examination of the plasma cell granuloma has been unproductive in terms of identifying a pathogen. There have been 2 recent ultrastructural studies (Ref. 3, 4) which have further defined the morphology but have shed very little light on the pathogenesis.

References

Case 5 - Mediastinum - Enteric duplication (foregut duplication, mediastinal dorsal enteric cyst)

This case is illustrative of 2 problems in pediatric surgery and surgical pathology and those being a mediastinal mass in a child and gastrointestinal duplication. The patient was 5 years old when first seen with symptoms and signs of pneumonia which was treated with antibiotics. We are not told whether a chest x-ray was taken at that initial presentation but 2 months later when he re-presented, a 5.5 cm. mass was noted in the left retro-cardiac area. It was not indicated whether an air-fluid level was associated with the lesion nor if the vertebral bodies were normal.

The cyst was grossly unilocular and was somewhat larger than the dimensions from the x-ray. Microscopically, the lining epithelium has been ulcerated in many foci and replaced by inflammatory cells, granulation tissue and fibrosis. Where the surface is intact, it ranges from stratified cuboidal to clearly gastric in type. In these latter areas, a muscularis is identified. Aggregates of lymphocytes are present in the submucosa. There was no evidence of ciliated stratified epithelium nor islands of cartilage. If these tissues are noted in a duplication cyst, then the diagnosis is that of a "bronchopulmonary foregut malformation".

A survey of 283 tumor and tumorlike disorders of the mediastinum from 4 pediatric series revealed that approximately 8% of such lesions were diagnosed as gastroenteric duplications (Ref. 3). Bronchogenic cysts represented 3% of the combined series. The largest single group of neoplasms of the mediastinum in childhood was the neurogenic category (35%), followed by the germ cell tumors (14%) and malignant lymphomas (14%).

The enteric cyst of the mediastinum is one of the two types of foregut cysts, the other being the bronchogenic cyst (Ref. 9). Most duplications of the intestinal tract are located in the small intestine, particularly in the region of the ileum (Ref. 5-7). About 20% of duplications occur above the diaphragm and most are associated with the esophagus or paraesophageal (Ref. 11). Thoracic duplications are usually diagnosed in the first year of life but obviously our patient managed to escape detection. Respiratory distress due to tracheal and/or pulmonary compression and dysphagia are some of the more frequent presenting features. A unique presentation has been reported with the duplication cyst of the mediastinum lined with gastric mucosa (Ref. 2). Gross ulceration and peptic digestion of adjacent anatomic structures with pulmonary suppuration and/or hemorrhage are the major findings. Anomalies of the vertebrae (split notochord system) are other related abnormalities especially when the duplication originates in the mediastinum (Ref. 12). The embryologic aspects of the duplication have been reviewed by Bremer (Ref. 1), Kissane (Ref. 9) and Favara and coworkers (Ref. 4). A vascular theory is proposed by the latter authors.

Anatomically, the duplication has a cystic appearance in this case or alternatively, it is tubular. In the abdomen, most duplications are contained within the leaves of the mesentery and more often than not there is no communication with the normal lumen of the bowel. The mucosal lining of the duplication does not always correspond to that of the adjacent bowel. A complete muscular tunic is identified in those cases in which the separation is complete between the bowel and the duplication.
The "bronchopulmonary foregut malformation" (BPFM) is worthy of a few comments since it represents a bridging anomaly between the respiratory-related and gut-related defects (Ref. 8). By definition, the BPFM is a patent communication between accessory lung tissue and esophagus or stomach. In addition to intra- and extralobar sequestration with or without communication with the GI tract, the congenital esophageal diverticulum and foregut malformations are part of the embryopathogenetic spectrum.

References


Case 6 - Kidney - Multilocular cystic kidney (multicystic nephroma)

The multicystic mass in the kidney of this 1-year-old child presents the differentiated diagnostic problem of "polycystic lesions" of the kidney in children (Ref. 5, 6). There are certain features of the gross specimen in this case which should give us some direction in the correct diagnosis. Although the kidney is quite large and obviously contains a mass, the overall contour and outline of the organ is retained. This distinction is made because the so-called multicystic dysplastic kidney has an extremely irregular outline and lacks the reniform appearance. The cysts are irregular in size whereas in the multilocular cystic kidney, the individual cysts are more or less the same size. These cysts do not interconnect with each other nor with the renal pelvis. Another finding in the gross specimen in the latter lesion is circumscription and apparent encapsulation of the mass from the compressed but otherwise normal rim of kidney. The "total" or complete multicystic dysplasia fails to have any identifiable normal renal parenchyma (Ref. 3, 7, 8). Finally, the pedicle should be carefully examined since the renal vessels and ureter are quite attenuated and in the case of the ureter, it is atretic or absent in the multicystic dysplastic kidney. These structures are generally normal in the multilocular cystic kidney.
Microscopically, the multilocular cystic kidney is composed of cysts and fibrous septa with a few bundles of smooth muscle (Ref. 4). Some cysts are lined by a low cuboidal epithelium whereas others do not have a lining epithelium. The septa may contain atrophic glomeruli or tubules. Neither normal or dysplastic nephron elements are present in the septa. On occasion, immature mesenchyme is identified within these septa and in fact, nodules with the features of Wilms' tumor have been noted. The question is then of a Wilms' tumor arising in a multilocular cystic kidney. A contrasting microscopic appearance is present in the multicystic dysplastic kidney in which immature glomeruli, tubules, mesenchymal and even cartilage are the typical findings. These various structures occur as solid nests or they are located within the septa.

The histogenesis of the multilocular cystic kidney remains a disputed point in that some consider it a developmental anomaly and others, a neoplasm (multicystic nephroma). Baldauf and Schulz (Ref. 1) have recently reviewed the approximately 70 cases in the literature of multilocular cystic kidney. About half the cases have been described in childhood and the mean age has been 17 months. As expected, Wilms' tumor was the most frequent pre-operative diagnosis. None of the cases to date with Wilms' tumor occurring in a multilocular cystic kidney have metastatized (Ref. 2).

References


Case 7 - Kidney - Mesoblastic nephroma (fetal hamartoma of kidney)

There were probably few among the many examiners of this tumor that did not recognize this mesenchymal neoplasm of the kidney as a mesoblastic nephroma. In the past, this tumor was diagnosed as a congenital or neonatal Wilms' tumor. Not only a nephrectomy but irradiation therapy would have been the treatment.

Bolande has been much of the credit for his clinical and pathologic description of this tumor in 1967 with a report of 8 cases (Ref. 4). With few
exceptions, the mesoblastic nephroma presents as an abdominal mass in the neonatal period. The gross features of the tumor are rather typical in that most of the renal parenchyma has been replaced by a circumscribed but non-encapsulated greyish-white to yellowish-grey mass. A whorled to trabeculated appearance is characteristic of the cut surface and the features are very similar to the uterine leiomyoma. The lobulated, myxoid character of the Wilms' tumor is absent as well as hemorrhage and necrosis in most cases. Although the renal capsule is intact in the majority of mesoblastic nephromas, we have seen extension through the capsule and involvement of the perirenal soft tissues. A local recurrence is certainly possible and has been reported but we have recommended watchful waiting rather than immediate re-exploration or irradiation therapy. To the best of our knowledge and others, all cases to date have been unilateral (Ref. 2, 3, 5, 10).

Histologically, the mesoblastic nephroma has a rather monotonous morphology in that the tumor shows a predominantly spindle cell, interlacing pattern. The tumor cells resemble smooth muscle cells. Mitotic activity may be abundant and some areas of the tumor may show not only increased mitoses but the cells are distinctly atypical and hyperchromatic. Bizarre cellular forms are extremely unusual. Isolated glomeruli and tubules are present among the spindle cells but these are thought by most to represent entrapped normal structures. Small tongues of spindle cells extend among the glomeruli and tubules at the periphery of the tumor. Dysplastic tubules and islands of fetal cartilage have also been described in these tumors (Ref. 2, 5).

The mesoblastic nephroma like the Wilms' tumor is thought to originate from the metanephric blastema. Whether the spindle cell is a fibroblast or smooth muscle cell has been the subject of tissue culture and ultrastructural studies without total resolution of the question (Ref. 7). Our moderator on the basis of ultrastructural examination has proposed that the tumor is derived from "secondary" mesenchyme which unlike the mesoblast (primary mesenchyme) is incapable of epithelial differentiation (Ref. 11).

From the prognostic standpoint, nearly all cases to date have pursued a benign clinical course. The exception to this indolent behavior has been documented in case reports (Ref. 8, 9) and Beckwith (Ref. 1) has sounded a note of caution about the "shades of grey" mesoblastic nephromas.

References


Case 8 - Kidney - Wilms' tumor

Although this 18-year-old female definitionally does not fall into the pediatric age group (0-15 years), she has a renal tumor with the features of a Wilms' tumor that is moderately well-differentiated. There have been scattered case reports of Wilms' tumors in adults but the histopathology has often been difficult to evaluate in some of these (Ref. 10). An interesting clinical-laboratory aspect of this patient was the presence of polycythemia. As you noted from the protocol, the pre-operative erythropoietin level was within normal limits. A hemoglobin determination performed 1 month after surgery was 14 gm/dl. Erythropoietin-producing Wilms' tumor have been reported in the past (Ref. 6,11). A nephrectomy was performed and a well-encapsulated tumor measuring 4.5 cm. in greatest diameter was present in the lower pole. There was no evidence that the tumor had extended beyond the capsule and the blood vessels were grossly uninvolved.

Histologically, the better differentiated areas of the tumor are composed of closely packed immature or dysplastic appearing tubules and dilated structures with papillary tufts resembling embryonic glomeruli. Other fields are characterized by dense sheets of small basophilic tumor cells without differentiating features. At the periphery and within the tumor, there are bands of hyalinized collagen. Multiple calcispheres or psammoma bodies are present within the cellular portion of the tumor and within the hyalin bands. There is no evidence of vascular invasion.

The initial question which was posed was the histopathologic diagnosis of the tumor. Some consideration was given to the possibility of a renal cortical adenoma of the "embryonic type." On the basis of size alone, it was difficult to reconcile the diagnosis of an adenoma since cortical tumors in excess of 2-2.5 cm. are thought by many to represent carcinomas. The overall histology of a tumor composed of immature tubules, glomeruli and mesenchyme must logically be interpreted as a nephroblastoma or Wilms' tumor regardless of the age of the patient.

The subject of Wilms' tumor is one that has been extensively reviewed from the clinical, pathologic and therapeutic standpoint over the past 25-30 years (Ref. 1,3,4,12). More recently, the literature has emphasized the tremendous therapeutic success which has occurred as a result of irradiation and chemotherapy (Ref. 4). The National Wilms' Tumor Study in this regard has been the model of cooperative studies (Ref. 2). A standardized system of staging has evolved from this study which intimately involves the pathologist and his evaluation of the extent of tumor. In the gross examination, the observation of whether the capsule is intact is extremely important and the presence or absence of gross vessel invasion (rare compared to renal cell carcinoma). Histologically, the differentiation of the tumor does appear to influence the prognosis but the point remains somewhat controversial (Ref. 5,8). Kumar and coworkers (Ref. 7) have recently indicated the prognostic significance of microscopic vascular invasion within the tumor. Wilms' tumor in adol-
escents and adults has been described in previous studies and one point relevant to our case is the frequency of calcification in the tumor in older individuals (Ref. 9,10). The demonstration of calcification both roentgenographically and pathologically is no greater than 5% in children but is 30 - 40% in adults.

As of late August, 1976, the patient was doing well and has no evidence of recurrent disease.

References


Case 9 - Liver - Biliary cirrhosis secondary to extrahepatic biliary atresia

The diagnosis of biliary cirrhosis secondary to extrahepatic biliary atresia is not a subtle one in the microscopic section from this case. As most of you know, the differential diagnosis between "neonatal hepatitis" and biliary atresia is not always straightforward especially in a needle biopsy. Any number of laboratory determinations have been utilized over the last few years in an attempt to establish the diagnosis without an exploration and biopsy. Serum 5'-nucleotidase, alpha-fetoprotein and most recently the determination of serum lipoprotein-X levels (LP-X) before and after cholestyramine have been used. Campbell and Williams have reported that a fall in LP-X after cholestyramine is evidence of patent extrahepatic bile ducts; an elevation is indicative of an atresic system. One of the principal reasons to avoid exploratory surgery is based, in part, upon the studies of Thaler and Gellis (Ref.12) and others that only 5% of extrahepatic atresia are potentially correctable and that the morbidity and mortality of neonatal hepatitis are increased with surgery. A recent study by Lawson and Boggs (Ref. 10) contradicted the Thaler and Gellis experience regarding the surgical risk of operating upon a child with neonatal
hepatitis.

There have been a number of clinicopathologic studies relating to the differentiation of neonatal hepatitis from extrahepatic atresia. Many of these strike a rather pessimistic note about the morphologic distinction but the following features have been the most useful to me: 1) excessive bile duct proliferation in the portal areas, extension of these ducts along bands of fibrous tissue into the lobule and bile thrombi - all in extrahepatic atresia, 2) panlobular giant cell transformation in neonatal hepatitis versus perportal giant cell change in extrahepatic atresia, 3) acidophilic bodies in neonatal hepatitis and 4) extensive extramedullary hematopoiesis in neonatal hepatitis (Ref. 3). Although the presence or absence of these findings are not full proof, the correct diagnosis can be established and confirmed at surgery or follow-up in 90% or more of cases.

The major developments or topics in the area of neonatal hepatitis-extrahepatic atresia are the following: 1) the concept of infantile obstructive cholangiopathy (IOC), 2) multiple etiologies of neonatal hepatitis and 3) the hepatic portoenterostomy or the Kasai operation. Landing (Ref. 9) has formulated the concept of IOC as a common pathogenesis of injuries to the cholangiolar-ductal system of the liver leading to neonatal hepatitis, biliary atresia and the choledochal cyst. Hepatitis B has been implicated by Landing and others (Ref. 6) but cytomegalovirus, rubella and inborn errors of metabolism such as alpha-1-antitrypsin deficiency are other worthy candidates. The dynamics of the destructive process and the timing may well explain the success of the Kasai operation which is almost exclusively confined to the first 12 weeks of life. Both Landing's papers and Witzelben's editorial comments are worth reading (Ref. 8, 9, 13). It is generally appreciated that the giant cell transformation of the neonatal hepatocyte is a unique response at this age but is nonspecific in regard to an etiologic agent. This point has been made in the preceding comments about IOC. The therapeutic frustration which has been associated with extrahepatic biliary atresia is as well known to the pathologist and surgeon alike. Recently, Kasai (Ref. 4,5) has devised the hepatic portoenterostomy based upon his earlier experimental work and later clinical observations that there were salvagable remnants of extrahepatic bile ducts during the neonatal period. Since these ducts are evanescent, it is critical that this operation is performed very early in life. The demonstration of microscopic bile ductules is mandatory to the success of the operation. Kasai has reported favorable results with the establishment of bile drainage in 70-80% of cases but in the United States, the success of the procedure has approached Kasai's or failed miserably as Campbell and his coworkers have reported. One of the major complications of the operation is the development of ascending cholangitis (Ref. 7). In spite of this, the hepatic portoenterostomy potentially represents a significant therapeutic advance in an area stagnated by surgical failure.

References

Case 10 - Liver - Reye's syndrome variant (?) with submassive necrosis

The protocol indicated the complicated nature of this child's clinical presentation and subsequent course which terminated in death approximately 13 days from the earliest symptom. A needle biopsy of the liver was performed on the third hospital day and it showed extensive fatty change (metamorphosis) of the micro- and also macrovesicular type in the hepatocytes. In addition, there was hepatocellular degeneration and necrosis in the midzonal areas with some involvement centrally. The histologic appearance was puzzling in this regard but all of the other clinical and laboratory findings supported the impression of Reye's syndrome. Various supportive measures were employed but the patient died. At autopsy, there was marked edema of the brain (800 gm); the heart was large (42 gm) and pale yellow; the kidneys were swollen (75 gm) and pale and the liver (210 gm) had a mustard-yellow colon and a fine, reddish mottling on cut surface. The sections of the heart and kidneys within (tubules) contained prominent amounts of cytoplasmic lipid. There was extensive fatty change throughout those areas of the liver where the parenchyma was preserved. Rather than the fine lipid vacuoles which are characteristically seen in Reye's syndrome, the droplets were larger and tended to displace the nucleus. An additionally striking feature was the presence of hepatocellular necrosis, primarily centri- and midzonal as initially appreciated in the biopsy but more extensive and confluent at autopsy.

What was the nature of this child's disease? From the clinical standpoint, an infant who becomes progressively irritable and has hepatomegaly shortly after a non-specific viral illness should be considered a likely victim of Reye's syndrome (Ref. 6, 8, 10). The laboratory values, including an elevated blood ammonia not described in the protocol, were thought to be compatible with the diagnosis. After the liver biopsy was examined, there was some bewilderment because of the hepatocellular necrosis. The question of some environmental hepatotoxin, anoxia, and a virus, possibly herpes simplex was posed. Toxicologic screening and viral cultures were performed and all were negative.

Does this patient have Reye's syndrome or fulminant viral hepatitis with submassive necrosis? It can be argued that the hyperbilirubinemia is a feature against the diagnosis of Reye's syndrome as well as the submassive hepatic necrosis. If this case represents viral hepatitis, the initial liver biopsy was certainly most unusual for that disease. Toxic hepatitis is a distinct possibility especially with the zonal distribution of changes and the fatty change. A reasonable effort was made to exclude some toxin through fluid and tissue toxicologic examination at autopsy.

This patient reminds me of the three cases which Gall and coworkers (Ref. 7) reported in 1975 as "acute liver disease and encephalopathy mimicking Reye syndrome" and the review of 7 cases by Brown and Ishak (Ref. 5). The children in the former study were 23-months, 4-years, and 6-years old. Histologically, centriflobular necrosis and minimal fatty changes were present in the liver. Circulatory failure, carbon tetrachloride, toxins, drugs and infectious disease were discussed by Gall and coworkers as possible related etiologies but unproven. Ultrastructurally, similar mitochondrial alterations were present in the hepatocytes as those described in Reye's syndrome (Ref. 9). Brown and Ishak (Ref. 5) suggest that fatty acids represent the hepatotoxin.
The gross and microscopic features of Reye's syndrome in the liver have been documented on a number of occasions (Ref. 1, 2, 4). Bove and coworkers (Ref. 2) have recently reviewed their experience with liver biopsies from 49 children. They make the point which has previously been made that hepatocellular necrosis is either absent or inconspicuous. Isolated necrosis of hepatocytes may occur in the periportal area. It was interesting to note that 1 of 49 children had centrilobular necrosis in a biopsy and in 2 children at autopsy who did not have a previous liver biopsy. These authors made the following statement, "We have considered central necrosis to be a superimposed lesion, and if unaccompanied by severe fatty change in the intact portions of the lobules, we would be reluctant to make a diagnosis of Reye's syndrome."

References


Case 11 - Colon - Necrotizing enterocolitis (NEC) of infancy

A low-weight for dates or premature infant who has sustained some stress such as anoxia is the usual victim of necrotizing enterocolitis. Although NEC was seemingly recognized as early as 1825 by Siebold, the past 10 years have witnessed the publication of numerous reports in the pediatric and surgical literature. Most pathologists' initial introduction to this disorder took the form of frozen sections looking for ganglion cells in a child suspected of having Hirschsprung's disease or at the autopsy table. George Fetterman, the former pathologist at the Children's Hospital of Pittsburgh, editorialized in 1971 about NEC and whether it was an old problem with a new name or bone fide new entity (Ref. 4).

Perforation of the bowel especially the colon either spontaneously or associated with exchange transfusion has been appreciated in the neonate for some time (Ref. 6). Two types of lesions have been reported in bowel: 1) an
isolated perforation in a normal segment of colon; or 2) multiple perforations with diffuse necrotizing enterocolitis.

Clinically, the age of onset of NEC is approximately 6-8 days old (range 1-25 days). Abdominal distention, apnea, vomiting, diarrhea (sometimes bloody), hypothermia and mild jaundice are some of the more common presenting features (Ref. 2, 3). In the experience at the University of Minnesota, 91% of the children with NEC were premature and 4.7% of the neonatal admissions were for NEC (Ref. 5). Roentgenographically, adynamic ileus and pneumatosis cystoides intestinalis were the commonest findings. In the various series, pneumatosis intestinalis was present in 75-90% of the children. Pneumoperitoneum and gas in the portal vein were other less frequent but more ominous radiographic changes (Ref. 1). Both medical and surgical regimens have been utilized in the management of these children. At Babies Hospital, New York, intestinal obstruction, pneumoperitoneum and peritonitis were the indications for surgery (Ref. 8). Disseminated intravascular coagulation and metabolic acidosis were additional indications for surgery at the University of Minnesota (Ref. 5). In the former series, the overall survival was 22% (medical, 16%; surgical, 30%) and the latter series was 35% (medical, 44%; surgical, 31%). The earlier clinical recognition of NEC has reflected itself in a significant improvement in survival and more cases are now being managed conservatively (Ref. 9).

The gross and microscopic findings in the seminar case are typical for NEC. It is apparent from the protocol that the baby was desperately ill and a resection could not be performed. Grossly, the ileum and the colon are the most frequent sites of involvement followed by the jejunum. In the more severe cases, the ileum appears to represent the central site from which there is proximal (jejuno-ileal) and distal (colon) involvement. The affected segment has a dusky, hemorrhagic appearance to the serosal surface and perforations are occasionally recognized in the gross examination. When the pneumatosis is severe, blebs are discernible on the external surface. The mucosa is hemorrhagic and microscopically, as in this case, there is coagulative necrosis of the epithelium. In spite of the extensive mucosal and submucosal necrosis, there is a minimal inflammatory reaction. The cysts are confined to the submucosa. There is no reaction in the cysts which contrasts with pneumatosis cystoides in adults. A giant cell reaction is present in the wall of the cysts in the benign adult form. Transmural necrosis or perforation were not identified in the sections which I examined.

Among those children who survive, a long-term complication is the development of focal stenosis of the bowel (Ref. 7).

References

Case 12 - Spleen - Histiocytosis, malignant

The section of spleen which I examined disclosed an infiltrative process mainly confined to the red pulp areas. Most of the tumor cells were relatively uniform in size, outline and other cytologic characteristics. The nuclei were moderately hyperchromatic, and there was some indentation of the nuclear membrane. Mitoses were present but I did not see any abnormal forms. An acidophilic to amphophilic rim of cytoplasm was identified in most of the ovoid cells with their distinct cellular membranes. Erythrophagocytosis was inconspicuous in my section.

These cells had nearly all the features which I associate with a histiocyte and there was sufficient atypia to strongly suggest that the disorder was malignant. Certainly, the attenuated clinical history lasting no more than 4 days lends credence to that interpretation. I would like to say that we have encountered atypical histiocytic infiltrates in lymph nodes, spleen, liver and skin in children with acute, fulminant Epstein-Barr virus and cytomegalovirus infections. It is sometimes difficult at the light microscopic level to be certain whether the cells represent immunoblasts or histiocytes. I have not been informed whether viral cultures were obtained.

Assuming that this case represents an example of histiocytosis, how does it relate to the general histiocytic disorder known as histiocytosis (Ref. 3, 4). The monocytes-macrophages are the basic cellular elements of the neoplastic "histiocytoses." Based upon clinical and pathologic considerations, Rappaport (Ref. 5) distinguished three groups: a reactive proliferation of histiocytes with a known metabolic, immunologic or infectious origin; a malignant proliferation of histiocytes (malignant histiocytosis) and the elusive histiocytosis X or "differentiated histiocytosis." Since the reactive histiocyte may be quite atypical, I would like to reserve the option that a pathogen may be involved in our patient since the symptoms of fever, a productive cough, irritability and the exanthemous rash are so suggestive of an infection. It is also known from the two larger series of malignant histiocytosis that the clinical presentation can rapidly involve and terminate in death within a few days, weeks or months (Ref. 2, 7).

According to most authorities, the monocyte is derived from a pluripotential stem cell through the sequence of monoblast, promonocyte and the mature circulating form (Ref. 1, 6). Further differentiation occurs in the monocyte as it becomes a tissue macrophage or histiocyte through the acquisition of increased phagocytic and lysosomal activities. The Golgi apparatus and lysosomal granules
are more prominent in the macrophage-histiocyte than the monocyte. As anticipated, DNA replication is markedly diminished. It has been accepted by most investigators that the Langerhans cell with its characteristic cytoplasmic marker, the Birbeck granule or X body is the neoplastic cell of the differentiated histiocytoses. Initially, there were those who considered the Langerhans cell in its native state in the epidermis as a type of melanocyte but only the dendritic nature of these cells was the common denominator. Cytochemically, the melanocytes contain tyrosinase but, in contrast, the Langerhans cells contain hydrolytic enzymes such as acid phosphatase and nonspecific esterases. These cells in tissue culture are also capable of phagocytic activity although it is uncommon to identify phagocytosis in the lesions of histiocytosis X. The weight of evidence, although not indisputable, is that the Langerhans cell is mesenchymal in derivation, migrates into the skin during fetal life and is most closely related to the monocyte-macrophage.

The histologic differential diagnosis of lesions with sinusoidal proliferation includes sinus histiocytosis with or without massive lymphadenopathy (Rosai-Dorfman disease), metastatic carcinoma especially malignant melanoma and lymphoepithelioma, leukemic reticuloendotheliosis (primarily adults), granulocytic sarcoma (chloroma) and histiocytic lymphoma. Immunoblastic lymphadenopathy and infectious mononucleosis with partial or complete effacement of the follicular architecture and interfollicular hyperplasia are other considerations.

References


Case 13 - Lymph node, axillary, right - Malignant lymphoma, poorly differentiated lymphocytic (lymphoblastic) type

The only diagnostic point that the majority of pathologists will agree upon in this case is that this 19-year-old male has malignant lymphoma, that it is diffuse and that there are no Reed-Sternberg cells. There are some who probably have fit this case into their own classification or one that they are currently espousing. To say that the situation in terms of nomenclature of non-Hodgkin's malignant lymphomas is chaotic may well be one of the current understatements (Ref. 5, 6). In our institution, there is still an attempt to adhere to the
Rappaport-Gall classification of non-Hodgkin's malignant lymphomas, that is malignant lymphoma, histiocytic type; poorly differentiated lymphocytic; well-differentiated lymphocytic and undifferentiated (Burkitt's lymphoma) (Ref. 9).

In this case, it is apparent that the entire node has been replaced by a diffuse proliferation or poorly differentiated lymphoid cells. There is some convolution of the nuclear membranes. Chromatin clamping rather than dispersion is present. Mitoses are abundant and a focal "starry-sky" appearance is apparent.

The differential diagnosis of this malignant lymphoma resides between malignant lymphoma, poorly differentiated (lymphoblastic) type and undifferentiated (Burkitt's) type. From the clinical standpoint, generalized peripheral lymphadenopathy is an extremely unusual presentation for Burkitt's lymphoma. A gastrointestinal neoplasm or abdominal-retroperitoneal lymphadenopathy are the presenting features of American Burkitt's lymphoma (Ref. 1, 2, 8). We are not told, but if a mediastinal mass, bone marrow or peripheral blood involvement were present then lymphoblastic lymphoma would be the diagnosis on clinical grounds (Ref. 7). Histologically, the tumor cells were certainly immature but without the "stem-cell" appearance of the Burkitt's cells. Functional studies would have been helpful in that the Burkitt's cells have monoclonal immunoglobulins on the surface indicative of a B-cell (Ref. 4). In this case, the marker studies may well have characterized the tumor as T-cell or even nil-cell. A very convoluted nucleus would have been more suggestive of a T-cell neoplasm.

Prognostically, both American Burkitt's lymphoma and poorly-differentiated (lymphoblastic) lymphoma have a very poor outlook (Ref. 10, 11). Death usually occurs in less than a year after diagnosis.

References


Case 14 - Soft tissue, lower extremity - Synovial sarcoma

When this 13-year-old boy presented and after an X-ray was taken, there was little question that he did not have a malignancy of some type. A large soft tissue density was present and there was destruction of the proximal tibial metaphysis. The three diagnostic considerations were an osteosarcoma, Ewing's tumor or a primary soft tissue malignancy. Of these choices, osteosarcoma was thought to be the least likely because of the lack of bone production by the tumor and the relative lack of a periosteal reaction. It was elected therefore, to perform an incisional biopsy with frozen section consultation to insure that diagnostic tissue had been removed. The orthopedic surgeon was not terribly concerned about a specific histopathologic diagnosis. For many of you, this approach is certainly a reversal of a standard procedure of a few years ago when an immediate amputation hung in the balance of a frozen section interpretation. It has been shown that a delay of 24-48 hours does not compromise the prognosis and the extra assurance of permanent section is well worth the delay. In fact, I have not participated in a frozen section consultation in the past 5 years at Barnes Hospital or University Hospitals in which the amputation for an osseous or soft tissue malignancy was performed at that operation. In our case, we told the surgeon that the frozen section showed a spindle cell neoplasm. Our differential diagnosis included synovial sarcoma and fibrosarcoma with less consideration to a malignant fibrous histiocytoma and the spindled component of an osteosarcoma. The permanent sections revealed a spindle cell tumor with small epithelioid nests which we thought sufficiently biphasic to warrant a diagnosis of synovial sarcoma.

In the past, the diagnosis of synovial sarcoma was a dreaded one. An early review of synovial sarcomas in childhood by Crocker and Stout (Ref. 7) showed that 62.5% of patients were either dead or living with tumor. Most tumors in that series (84%) were located in the lower (20 cases) or upper extremities (16 cases). The region of the knee, the thigh and hand were the specific sites of predilection.

Amputation has been the treatment of choice but recently, there has been a trend to perform a wide excision, if possible, followed by local irradiation and chemotherapy. This was the plan for our patient and an en bloc excision including the proximal tibia was performed. Unfortunately, the patient has required 5-6 admissions for a staphylococcal wound infection. He was back in the hospital about 2 weeks ago for a repeat debridement. Irradiation and chemotherapy had not been instituted as of 6 months post-operatively. There has been no evidence of local recurrence or metastasis.

Synovial sarcoma was third in frequency among the 135 soft tissue sarcomas in children reviewed at the Mayo Clinic (Ref. 7). Rhabdomyosarcoma and "sarcomas of undetermined histogenesis" were more common. The Memorial Hospital group
have examined their series of 24 cases of synovial sarcoma in children with an age range of 20 months to 15 years but over 50% of patients were between 13 and 15 years (Ref. 5). A feature of synovial sarcoma is the prolonged duration of symptoms which can last for 3-5 years before a definitive diagnosis. We have seen a case of a 15-year-old boy with symptoms for at least 3 years. His pediatrician-father thought that he was a hypochondriac. Another feature of synovial sarcoma is the frequent calcification in the tumor as demonstrated roentgenographically. Approximately 15% of cases have, at some time, nodal metastases (Ref. 4).

Pathologically, the tumor in the seminar was juxtacortical and invaded bone. The biphasic pattern was well-represented in nearly all sections. One histologic feature which I have found helpful is the multilobular pattern of growth. The lobules expand and compress the adjacent soft tissues. Encapsulation is rarely present and the lack of circumscription can be a problem. Enzinger has pointed out the frequency of mast cells in synovial sarcoma. The differential diagnosis especially when the biphasic pattern is not obvious includes fibrosarcoma, fibrous histiocytoma, malignant Schwannoma and leiomyosarcoma. A clear cell sarcoma of tendon sheath origin should also be mentioned. Cadman and coworkers (Ref. 1) and MacKenzie (Ref. 6) have the largest general reviews of synovial sarcoma. Fernandez and Hernandez (Ref. 3) have discussed the role of electron microscopy in the diagnosis.

References

Case 15 - Soft tissue, lower extremity - Alveolar rhabdomyosarcoma

The patient's history dated back to 6 years of age when her left leg was amputated for a soft tissue malignancy which was diagnosed at that time as a "liposarcoma." She did well without adjunctive therapy or further symptoms until she was 13-years-old. At that time, the symptoms and signs pointed to a cardiac problem characterized by sudden loss of cardiac output. A polyloid neoplasm was partially excised from the left ventricular septum. Grossly, that tumor measured 3.5 x 1.5 cm. and had a smooth, endothelialized external surface. There was extensive fibrosis at the tip of the mass however, at the base, there were nests of hyperchromatic tumor cells. Some of the cells were multinucleated and had acidophilic cytoplasm. It was apparent that the excision was
incomplete since tumor was present at the margin of resection. A comparison was made between the cardiac neoplasm and the one excised 7 years previously. They were both unquestionably alveolar rhabdomyosarcomas. She did well for almost 11 months and then developed a soft tissue mass of the right leg. Your section shows a tumor arranged in large, expansile and infiltrating nests of cells. Within these larger aggregates, the alveolar pattern is very distinct. In spite of the size of the mass, there was little evidence of necrosis. This lesion was excised because at the time, there was no other evidence of tumor. Approximately 4 months later, she died with widespread tumor.

This case was chosen to discuss the rhabdomyosarcoma, the most common soft tissue malignancy in childhood but also to share the unusual natural history of this particular alveolar rhabdomyosarcoma (Ref. 1, 2, 5).

Riopelle and Theriault in 1956 were the first to describe the alveolar rhabdomyosarcoma as a distinctive neoplasm and 2 years later, Enterline and Horn (Ref. 3) reported their 9 cases and compared them with 6 cases of Riopelle and Theriault. One of the most important points stressed by these earlier authors and applicable today is the confusion with other neoplasms. The alveolar rhabdomyosarcoma shares with malignant lymphoma, Ewing's tumor, neuroblastoma, retinoblastoma, embryonal rhabdomyosarcoma as being one of the "small, blue cell neoplasms" of childhood. Ewing's tumor may, on occasion, produce an alveolar-like arrangement when the neoplasm extends into soft tissues. Another histopathologic problem is the differentiation from malignant lymphomas both in soft tissues and within lymph nodes. Of all the sarcomas, alveolar rhabdomyosarcoma has one of the highest frequencies of nodal metastasis (60-75%). I have found that the identification of the multinucleated tumor cell is most helpful in the diagnosis of alveolar rhabdomyosarcoma.

The largest series of alveolar rhabdomyosarcomas in the literature is the one from the Armed Forces Institute of Pathology (Ref. 4). Unlike the more common embryonal rhabdomyosarcoma which occurs in the head and neck region and pelvis in children, the alveolar rhabdomyosarcoma occurs in the extremities (forearm, hand) and trunk. When this tumor is found in the pelvic region, it is generally not associated with an anatomic structure such as the bladder, prostate or vagina but rather in the perianal, perirectal, and perineal soft tissues. The median age in the AFIP series was 15 years. We have seen a peri-orbital alveolar rhabdomyosarcoma in a 2-year-old female, our youngest case. That is another difference - embryonal rhabdomyosarcoma originates in the orbit but the alveolar rhabdomyosarcoma in the soft tissues around the eye. The natural history of the tumor was not typified by the seminar case since the median survival was 8 3/4 months in the AFIP experience. Our patient survived over 8 years.

An obvious question which can be posed is whether this patient developed a second primary tumor (Ref. 6). Morphologically, the only thing that we could say is that they were similar, if not identical neoplasms. From the therapeutic standpoint, she was treated as a second primary tumor. What about a cardiac metastasis from the original alveolar rhabdomyosarcoma? Among the 57 cases with autopsies in the AFIP series, the heart was the site of metastasis in 44%. Pratt and coworkers (Ref. 7) have indicated the apparent predilection for cardiac metastases in childhood rhabdomyosarcoma. In a sense, we are left on the horns of a dilemma.
References


Case 16 - Soft tissue, chest wall - Skeletal hemangioma

The development of this soft tissue mass was at least historically related to trauma occurring 4 years previously. Angiographically, it was strongly felt that the mass was malignant. A wide local excision of an ill-defined tumor was carried out. Histologically, the tumor was initially interpreted as an angiosarcoma. If this neoplasm had occurred in the breast rather than the soft tissues then that diagnosis becomes more tenable. The patient is 6-months post-operative and is doing well without further therapy.

In this case, we have a neoplasm which is composed of a mixture of large, thick-walled vascular channels with cavernous dilatation and aggregates of smaller vascular spaces. It is this latter microscopic pattern which was felt to represent the clearly malignant component. A careful examination reveals that these foci are certainly cellular but there are few, if any, budding and branching structures and the individual endothelial cells lack significant cytologic atypia. Mitotic figures are generally absent. The intimate relationship between the vascular proliferation and the skeletal muscle is appreciated in many of the sections. Dense fibrous connective tissue forming bands are also present. Scattered areas of adipose tissue are noted.

Vascular and fibrous tissue tumors represent the largest groups of benign neoplasms of the soft tissues in childhood (Ref. 2). Because of their cellularity, the vascular tumors, especially in children, are overdiagnosed, at times, as malignant. The trap is set particularly for the cellular (juvenile) hemangioma of the parotid gland in a small child.

Skeletal hemangiomas are generally diagnosed during the first 3 decades of life. Allen and Enzinger (Ref. 1) have reviewed the clinical and pathologic features of 89 cases and have divided them into 3 basic morphologic types 1) small-vessel; 2) large-vessel, and 3) mixed. Our case would correspond histologically with the "mixed" type. The adipose component of the skeletal hemangioma may be quite striking and thus the tumor has also been designated as an "infiltrating angiolipoma." Local recurrences of these tumors have been documented in 18% of the AFIP cases but none have metastasized.
It should be remembered that angiosarcoma of the skin and soft tissues is one of the rarest tumors in the pediatric age group (Ref. 3).

References