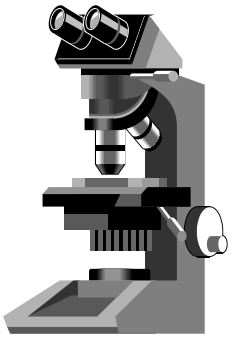
CALIFORNIA
TUMOR TISSUE REGISTRY

PEDIATRIC PATHOLOGY

Minutes – Subscription B

October 2015



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FILE DIAGNOSES

CTTR Subscription B October 2015

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October B 2015

CASE #1: **Accession No. 32041**

DIAGNOSIS: PERSISTENT OMPHALOMESENTERIC DUCT, Abdomen

Diagnoses submitted in decreasing order of frequency:

Omphalomesenteric Remnant / Duct / Cyst with heterotopic gastric tissue
Vitellointestinal Remnant
Meckel Diverticulum
Urachal Cyst with gastric heterotopia

Discussion

Persistent Omphalomesenteric Duct: In the developing fetus the Omphalomesenteric or Vitellointestinal Duct connects the Yolk Sac to the developing Midgut. It first appears towards the end of the fourth week and fully obliterates at the end of the ninth week. Failure of obliteration and regression may be complete or partial, with presentation as a cyst, fistula, or sinus.

Complete persistence of the duct results in a vitellointestinal fistula with discharge of meconium or mucus from the umbilicus. 2% of cases only the proximal portion of the duct persists as a small diverticulum (Meckel Diverticulum) two feet from the ileocecal junction on the anti-mesenteric border of the small intestine. Meckel diverticulum anomaly is twice as common in males. This diverticulum may still be attached to the umbilicus by an obliterated fibrous cord. The cord may cause problems of intestinal volvulus and obstruction. The persistent duct is lined by small intestinal tissue. In some cases ectopic gastric and pancreatic tissue may also be present.

Our case shows sections of a duct lined by a mixture of gastric and small intestinal mucosa.

CASE #2: **Accession No. 32112**

DIAGNOSIS: LARGE LYMPHATIC MALFORMATION, Right Axilla

Diagnoses submitted in decreasing order of frequency:

Lymphangioma
Cystic Hygroma

Discussion

Multiple thin walled dilated vascular channels of varying size with a flat endothelial lining are seen. Some of the vascular channels contain pale proteinaceous material and scattered clusters of lymphocytes.

Lymphangiomas are hamartomatous, congenital malformations of the lymphatic system that involve the skin and subcutaneous tissues. Deep tissue lymphangiomas consist of larger vessels and are termed cavernous lymphangioma or cystic hygroma. Lymphangiomas can occur anywhere in the skin and the mucous membranes. The most common sites are the head and the neck, followed by the proximal extremities. They may also occur in the wall of the intestines, the pancreas, and the mesentery. Deeper cystic lesions usually occur in areas of loose and areolar tissue, typically the neck, the axilla, and the groin. The overlying skin may show secondary acanthosis and hyperkeratosis. There is a strong tendency for local recurrence unless completely excised.

Etiology: Postulated to be due to failure of primitive lymph sacs to connect to the rest of the lymphatic system. Lymphangiomas are rare, and account for 4% of all vascular tumors and approximately 25% of all benign vascular tumors in children. Lymphangioma can become evident at any age, but the greatest incidence occurs at birth or early in life. About 50% of lymphangiomas are seen at birth, and most lymphangiomas are evident by the time the patient is aged 5 years. Cystic hygroma can be associated with Turner, Down and Noonan syndromes. Lymphatic dilatation may be seen in patients after surgery and radiotherapy for breast cancer.

CASE #3: **Accession No. 32131**

DIAGNOSIS: MULTICYSTIC RENAL DYSPLASIA, Left Kidney

Diagnoses submitted in decreasing order of frequency:

Cystic Renal Dysplasia
Renal Dysplasia, Multicystic
Infantile Polycystic Kidney Disease

Discussion
The kidney sections show cysts and disorganized renal parenchyma. Foci show immature tubules and ducts with immature mesenchymal collars and cartilage.

Multicystic dysplastic kidney, a variant of renal dysplasia, is one of the most frequent congenital anomalies of the urinary tract. This is associated with ureteral or ureteropelvic atresia and the affected kidneys are nonfunctional. Renal dysplasia is the leading cause of an abdominal mass in newborns and end-stage renal disease in children. The multicystic dysplastic kidney results from an abnormal induction of the metanephric mesenchyme by the ureteral bud during embryogenesis. It is usually sporadic, but may be familial and bilateral and associated with various syndromes, such as Alagille, Beckwith-Wiedermann and Meckel-Gruber. Patients with bilateral disease will also have oligohydramnios and pulmonary hypoplasia

CASE #4: **Accession No. 32113**

DIAGNOSIS: HEMANGIOMA, Right Chest

Diagnoses submitted in decreasing order of frequency:

Hemangioma
Cavernous hemangioma
Capillary hemangioma
Intramuscular hemangioma

Discussion
The excised mass consisted of thin walled vessels filled with red blood cells. Elsewhere large feeding vessels of the lesion focally showed evidence of embolization with organizing thrombus formation.
Hemangiomas are common childhood tumors, some may represent hamartomas. Most pediatric lesions are present at birth, and may show early proliferation with later involution and regression. Endothelial cells of Infantile hemangiomas show Glut-1 positivity. Hemangiomas are usually superficial involving the head and neck areas, but may be deep and involve viscera. Malignant transformation is rare. Subtypes include capillary, cavernous, large vessel and intramuscular. Cavernous hemangiomas may be present in the eye, cerebellum and brain stem in von Hippel Lindau disease. Dysplastic cutaneous hemangiomas, bone and soft tissue hypertrophy are present in Klippel-Trelauney syndrome. Multiple arterio-venous malformations, hereditary telangiecstasia are present in Osler-Weber Rendu syndrome. Congenital hemangiomas are a rare cause of Kasabach-Merritt Syndrome (severe thrombocytopenia and life threatening coagulopathy).

CASE NO #5: **Accession No. 31999**

DIAGNOSIS: CYSTIC TERATOMA, WITH FOCAL IMMATURE ELEMENTS,
Right Ovary

Diagnoses submitted in decreasing order of frequency:

Teratoma
Mature Teratoma
Immature Teratoma
Dermoid Cyst

Discussion
The multi cystic ovarian mass consisted of predominantly mature elements showing numerous ectodermal, mesenchymal and endodermal structures, including hair, skin, bone and respiratory epithelium. Focal immature neuroglial elements were present comprising less than 1 high power field. Please note that not all tissue sections showed the immature elements, which is reflected in the responses received from our participants.
Germ cell tumors are composed of different tumor types derived from primitive germ cells of the gonad. Teratomas are a subgroup of these tumors. Teratomas may be solid or more commonly cystic. They may contain tissue from one or a mixture of tissue types. Immature elements are present in 3% of teratomas of the ovary, 1% of all ovarian cancers and 20% of malignant ovarian germ cell tumors, and are more common in the first two decades of life. Immature teratomas may occur in a pure form or as a component of a mixed germ cell tumor (yolk sac, dysgerminoma, embryonal carcinoma, choriocarcinoma). Histologic grading is based on the proportion of immature elements (usually neuroectodermal and blastemal tissue). Grading is based on the modified three tier Norris system graded on the quantity of the immature neuroglial tissue present. Grade 1 neoplasms contain immature tissue (neuroepithelial, blastemal, or stromal) that involve no more than a single low-power (4×) field per slide; grade 2 neoplasms contain immature tissue that involve two to three low-power fields on any slide; and grade 3 neoplasms contain immature tissues that involve four or more low-power fields on any slide.

CASE #6: **Accession No. 31985**

DIAGNOSIS: WILMS TUMOR, Left Kidney

Diagnoses submitted in decreasing order of frequency:

Wilms Tumor
Wilms Tumor with favorable histology
Nephroblastoma

Discussion
The renal mass section demonstrates a Wilms tumor (WT, Nephroblastoma), with a variety of growth patterns. The dominant pattern is of serpentine cords of blastema in a markedly edematous and myxoid stroma. Some areas also show a classic triphasic appearance with neoplastic stroma, abortive tubules and glomeruli and undifferentiated blastema, while a minority is more stroma rich. Frank anaplasia is not identified, qualifying this tumor as NWTS “favorable histology”. The native kidney showed no nephrogenic rests.
Wilms tumor is the most common renal tumor in children, 90% of cases are diagnosed in children less than six years of age. Rare congenital cases have been reported. Males and females are equally affected. Syndromes associated with Wilms tumor include Denys-Drash (gonadal dysgenesis, WT, intralobar nephrogenic rests), WAGR (WT, Aniridia, GU

anomalies, mental Retardation, intralobar nephrogenic rests), Beckwith-Wiedermann syndrome (hemihypertrophy, adrenal cytomegaly, aniridia, perilobar nephrogenic rests).
Anaplasia may be focal or diffuse and is defined as pleomorphic, hyperchromatic nuclei 3x larger than adjacent tumor cells, and the presence of atypical mitoses. Anaplasia is associated with poor treatment response. Tumors are WT1 and EMA positive.

CASE #7: Accession No. 31754

DIAGNOSIS: PNET / EWING SARCOMA, Right Chest

Diagnoses submitted in decreasing order of frequency:

PNET / Ewing Sarcoma
Melanoma
Small Round Blue cell Tumor
Rhabdomyosarcoma (Alveolar, Embryonal)
Pleuropulmonary Blastoma
Neuroendocrine carcinoma
Extrarenal Rhabdoid Tumor
Small Cell Lymphoma

Discussion
Sections demonstrate a primitive "small round blue cell" tumor, with sheets of monotonous cells with scant cytoplasm. Focal old and fresh hemorrhage with minimal active necrosis is present, showing minimal chemotherapy effect. The differential includes rhabdomyosarcoma, rhabdoid tumor, neuroblastoma, desmoplastic small round cell tumor and lymphoma. Special stains and studies are necessary for precise classification. This is a case of PNET of the chest wall (Askin Tumor).
Primitive Neuroectodermal Tumor (PNET) is the most frequent malignant tumor of the chest wall in children. It is an aggressive tumor, which is treated surgically, and adjuvant chemotherapy is administered to control distant metastases. Common sites for metastasis are lungs and bone. Tumor cells show high nuclear to cytoplasmic ratios and scant cytoplasm. Nuclei are round or angulated with small nucleoli. A peritheliomatous perivascular growth pattern may be seen in areas of necrosis. Electron microscopy demonstrates abundant intracellular glycogen in the tumor cells. Tumor is positive for glycogen, vimentin, CD 99/MIC2/O13 (strong membrane staining), and FLI1. NSE, S100 and synaptophysin may be positive depending on the degree of neuroectodermal differentiation. . RT-PCR demonstrates t(11;22)(q24;q12) fusion transcript of FLI1-EWS.

CASE #8: Accession No. 32121

DIAGNOSIS: ATYPICAL TERATOID / RHABDOID TUMOR (ATRT)

Diagnoses submitted in decreasing order of frequency:

Atyypical Teratoid / Rhabdoid Tumor
Medulloblastoma
Oligodendroglioma
Anaplastic Ependymoma
Choroid Plexus Carcinoma

Discussion
Sections demonstrate a primitive malignant neoplasm with high-grade cytology, prominent rhabdoid features, stroma production, and coagulative tumor necrosis. The histologic features, in concert with the lack of INI1/BAF47 immunoexpression are consistent with an Atypical Teratoid / Rhabdoid tumor (ATRT).
ATRT is a rare, highly aggressive central nervous system tumor with a poor prognosis, and predominantly affects infants and young children (2% – 3% of primary CNS tumors in children). This cranial neoplasm is usually supratentorial or in the posterior cranial fossa. Tumor cells are intermediate in size, pleomorphic and rhabdoid (abundant granular bright eosinophilic cytoplasm), with eccentric nuclei with prominent nucleoli. Other neuroectodermal and mesenchymal elements are present (hence the designation teratoid). Mitoses and apoptotic cells are readily identified. Ultrastructurally the rhabdoid cells show intracytoplasmic paranuclear whorls of intermediate filaments. Definitive diagnosis of ATRT is based on the detection of deletions and/or inactivating mutations of the chromosome 22-localized hSNF5/INI1 tumor-suppressor gene in tumor tissue, and/or the absence of nuclear immunoreactivity for the hSNF5/INI1 gene product in the tumor cells. The surrounding non-tumor reactive tissue cells show positive staining. The loss of one copy of INI1 in the germline results in the Rhabdoid Tumor Predisposition Syndrome, in which patients develop renal and extrarenal rhabdoid tumors, including ATRTs, and choroid plexus tumors. Differential diagnosis includes: PNET / Medulloblastoma, germ cell tumors, choroid plexus carcinoma, ependymoma, oligodendroglioma, gemistocytic astrocytoma.

CASE # 9: Accession No. 32139

DIAGNOSIS: EPENDYMOMA, WHO GRADE II, Brain

Diagnoses submitted in decreasing order of frequency:

Ependymoma
Oligodendroglioma
Astrocytoma

Discussion
Sections show a monomorphic population of tumor cells with a fibrillary background. Pseudorosettes and true rosetting is present. The morphology and the immunoprofile are consistent with a classic ependymoma (WHO Grade II). Ependymomas are the most common CNS tumors in children. They may present in both supratentorial and infratentorial locations. Conventional, grade II ependymomas, are moderately cellular tumors, with a solid growth pattern and distinct demarcation from surrounding brain tissue. Cells are monomorphic, with round nuclei and coarse chromatin. Mitotic activity is rare. Fibrillary stroma with calcifications may be present. Tumor cells form perivascular pseudorosettes and true ependymal rosettes and canals. Necrosis may be present, however endothelial proliferation and pseudopalisading necrosis are not features seen in Grade II ependymomas. Tumor cells are GFAP, S100, Vimentin, COX2, P53, and EMA (punctate) positive. Differential diagnosis includes glioma (rosettes are not present in this tumor).

CASE #10: Accession No. 31989

DIAGNOSIS: MEDULLOBLASTOMA, Posterior Fossa, Brain

Diagnoses submitted in decreasing order of frequency:

Medulloblastoma (Nodular, Desmoplastic)
Neuroblastoma
PNET

Dysembryoplastic Neuroepithelial Tumor

Discussion
The posterior fossa tumor in this young child shows primitive undifferentiated "small round blue cells", with hyperchromatic nuclei and many areas of nodularity. No large cell or anaplastic changes are identified. Synaptophysin positivity is seen in areas of neuronal differentiation. Reticulin rich and poor areas are identified consistent with Nodular/Desmoplastic variant of medulloblastoma. Ki-67 staining was lacking in the nodular areas.

Medulloblastoma occurs predominantly in the first decade of life, arising in the cerebellum or roof of the fourth ventricle. It is a highly aggressive subtype of Primitive Neuroectodermal tumor (Grade IV), shows leptomeningeal spread and may metastasize systemically. Medulloblastomas may be associated with Turcot (familial adenomatous polyposis) and Gorlin (nevoid basal cell carcinoma) syndromes. Isochromosome (17q) or 17p- is seen. C-myc expression is associated with a poor prognosis. There are four histologic variants: classic, nodular/desmoplastic, large cell anaplastic, and medulloblastoma with extensive nodularity. Desmoplastic/nodular medulloblastoma has a nodular pattern with surrounding collagen bands. This variant is more common in infants and may have a better prognosis than the classic form. Medulloblastoma with extensive nodularity shows similar features also occurs in infants and it too is associated with a better prognosis.

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