PEDIATRIC SURGERY *Update**
Vol. 55 No. 01 JULY 2020

Ovarian Immature Teratoma

Ovarian teratomas in children are the most common germ cell tumors. Can be mature, immature and malignant. The vast majority of ovarian teratoma are mature. Ovarian immature teratomas (OIT) represent 1% of ovarian tumors graded according to the proportion of tissue containing immature neural elements. More than 80% of immature teratoma has elevated levels of alpha-fetoprotein. Tumors with higher AFP levels exhibit additional foci of malignant germ cell components. Peak incidence occurs between 15 and 19 years of age presenting as pelvic mass, abnormal uterine bleeding, abdominal pain or abdominal distension. US shows a complex ovarian lesion (solid and cystic components) or a heterogenous lesion in CT-Scan. Fat and scattered calcifications can also be present. Staging represents findings at surgery whether the tumor is confined to the ovary, peritoneum, pelvis, lymph node, adjacent organs, bilateral or has malignant ascites. Grade refers to pathologic presence of immature tissue in lower power field. Immature teratomas behave in a malignant fashion only if foci of malignant germ cell elements (yolk sac tumor) are present or if they are resected incompletely giving rise to the growing teratoma syndrome. Grade at diagnosis is the most important risk factor for relapse across all age groups. In children with grade 1 and 2 tumors there are no relapse regardless of stage. The majority of relapses (20%) occur in children with grade 3 tumors. Grade 3 with stage I/II disease have excellent free survival in comparison with stage III/IV. Completeness of resection influences free survival. Most children with OIT will not need chemotherapy. Grade, stage and completeness of resection are important risk factors for relapse. Recurrent disease occurs within the pelvis at the site of the original tumor. Tumor size does not correlate with tumor grade. The management of ovarian immature teratoma is unilateral salpingo-oophorectomy plus comprehensive staging. Complete resection is a key factor in avoiding tumor relapse. Routine biopsy of the unaffected ovary is unnecessary because immature teratoma is almost always unilateral. Lymphadenectomy does not provide any significant benefit to the survival of patients affected by immature teratoma. The reason to remove the tube with the tumor is to reduce an ectopic pregnancy risk. Initial adjuvant chemotherapy does not reduce future relapse or progression in OIT. Ovarian-sparing surgery during tumorectomy is an option being studied and depends on the anatomic feasibility of each case. Adjuvant chemotherapy is use for residual or recurrent disease though it may cause growing teratoma syndrome. Children with OIT should be follow-up with serial US and AFP levels.

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Sinusoidal Obstruction Syndrome

Sinusoidal obstruction syndrome (SOS) is a hepatic veno-occlusive disease occurring as a frequent complication after high-dose chemotherapy in the setting of hematopoietic stem cell transplantation. It can also be seen after conventional chemotherapy in pediatric patients after receiving dactinomycin-based chemotherapy for Wilms tumor, rhabdomyosarcoma, medulloblastoma and malignant germ cell tumor. Intensive antileukemic regimens that use 6-thioguanine also predispose to hepatic SOS. The initiating event is injury to the endothelial cells at the sinusoidal surface of the hepatocyte by the chemotherapeutic agent. This causes obliteration of the hepatic venules as a result of subendothelial edema and microthrombosis leading to hepatic congestion, sinusoidal dilatation and portal hypertension with hepatocyte injury and death. A cascade of hypercoagulable and proinflammatory pathways causes further damage resulting in obstruction of hepatic venous outflow, portal hypertension and multi-organ failure. Diagnosis is clinical. This usually occurs in the third week after chemotherapy with symptoms such as fever, jaundice, tender hepatomegaly, vomiting, fluid retention, ascites, hypoalbuminemia, elevated serum transaminases, thrombocytopenia and prolonged PT and PTT. In children there is no limitation for time of onset of SOS and two or more of the symptoms described are diagnostic. Imaging could demonstrate signs of hepatic portal hypertension in late stages. The incidence of developing SOS in Wilms tumors receiving chemotherapy is 1.5 to 8%. Liver SOS appears after the 2nd to 6th dose of Dactinomycin, seven to 14 days after the last dose. Special vulnerability occurs in children less than one year of age, right sided Wilms tumor and those receiving abdominal radiotherapy. Management of hepatic SOS is supportive with antibiotics, fluid restriction, diuretics, plasma, albumin and platelets transfusions. Pharmacologic intervention includes anticoagulants such as defibrotide, antithrombin III, heparin, protein C concentrate, N-acetylcysteine and gabexate mesylate. High dose methylprednisolone and aspirin has been utilized in other patients. Most children recover after approximately ten days of medical management.

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Hepatic Hemangioendothelioma Revisited

Infantile hepatic hemangioendothelioma (IHH) is a very rare, benign vascular tumor that appears during the first six-months of life with the potential to regress spontaneously. Considered the most common vascular tumor of the liver in children is associated with a high mortality rate. IHH can be focal, multifocal or diffuse in the liver. Focal IHH are fully grown tumors at birth that rapidly involutes with time. Multifocal IHH are individual lesions separated by normal liver parenchyma. Diffuse IHH is characterized by extensive replacement of hepatic parenchyma with multiple lesions. IHH can be associated with high output congestive heart failure, anemia, hypothyroidism, consumption coagulopathy, thrombocytopenia (Kasabach-Merritt syndrome), hepatomegaly (causing abdominal compartment syndrome), and cutaneous hemangiomas. Prenatal diagnosis has been associated with hydrops fetalis. Postnatal diagnosis is established with US, CT-Scan and MRI. More than five cutaneous hemangiomas lesions are indication for liver US in search of IHH. Alpha-fetoprotein levels should be obtained to differentiate from hepatoblastoma. IHH can be associated with consumptive hypothyroidism due to overproduction of type 3 iodothyronine deiodinase which deactivates thyroid hormones. Mortality results from high-output cardiac failure secondary to arteriovenous shunting within the tumor (up to 50% of the cardiac output can be diverted), respiratory compromise, hepatic failure, intraperitoneal hemorrhage and consumptive coagulopathy. The arteriovenous shunting can result in a decreased of systemic blood volume and increase of pulmonary blood volume thus the cardiac output increase. The younger the age at diagnosis, the more severe the cardiac symptoms. Natural history of asymptomatic IHH is spontaneous involution. Symptomatic lesions need aggressive management. Radiotherapy and chemotherapy have not shown consistently good results. Steroid and alpha-interferon are used as initial treatment to inhibit proliferation of endothelial cells with mixed results. Propranolol, a beta blocker, is now the preferred systemic therapy for problematic IHH due to promotion of pericyte-mediated vasoconstriction and decrease and cease of growth with more rapid involution of the lesion. Severe bilobar disease might need percutaneous hepatic artery embolization or transplantation. Early embolization is recommended for children with focal or multifocal

lesions presenting as shunts or those unresponsive to medication. Hepatic artery ligation or embolization should not be done in patients with shunting from the portal vein to the hepatic vein and minimal systemic arterial collateral circulation since it might result in hepatic necrosis.

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**** PSU 1993-2020***
ISSN 1089-7739