PEDIATRIC SURGERY *Update* ©
Vol 14 No 01 JANUARY 2000
'Official Publication of the Puerto Rico Association of Pediatric Surgeons'

Rhabdomyosarcoma - Genetics

Most rhabdomyosarcomas (RMS) occurs sporadically. A few are associated to syndromes such as Beckwith-Wiedemann, Li-Fraumeni, and Neurofibromatosis I. Risk factors in the development of RMS include maternal use of marijuana & cocaine, exposure to radiation, and maternal history of stillbirth. Alveolar (aRMS) and embryonal RMS (eRMS) are the most genetically studied sarcomas in children. The most consistent genetic mutation identified in more than 70% of aRMS is translocation of chromosomes 2 and 13, t(2;13)q35-37;q14). The PAX3 loci in chromosome 2 fuses to the FKHR (fork head in RMS) domain of chromosome 13 creating a powerful chimeric PAX3-FKHR gene. Another of the reported translocation is t(1;13)(p36;q14) involving chromosome 1 and 13 in 10% of aRMS. In this variant Chromosome 1 locus encoding PAX7 fused to FKHR in chromosome 13 resulting in another chimeric transcript PAX7-FKHR.PAX7-FKHR tumors tend to occur in younger patients, more often in the extremity, more often localized lesions and are associated with significantly longer event-free survival. Identification of fusion gene status may be a useful diagnostic tool in differentiating RMS from other round cell tumors. eRMS contains frequent allelic loss on chromosome 11 (11p15), a genetic feature specific for this type of tumor.The presence of a consistent region of allelic loss is indicative of the presence of a tumor suppressor gene that is inactivated. This leads to overexpression of insulin-like growth factor II gene that is known to play a role in the development of embryonal tumors. Other alterations associated with eRMS are distint patterns of chromosomal gains in contrast with aRMS which shows genomic amplification. Both tumors share alterations in the p53 gene at the germline level contributing to increase susceptibility to other tumors characteristics of the Li-Fraumeni syndrome.

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Intestinal Non-Hodgkin's Lymphoma

In 1.6% of all ileo-colic intussusception in children a malignant Non-Hodgkin Lymphoma (NHL) is the culprit. Primary gastrointestinal NHL usually present with a median age of eight years, colicky abdominal pain, bloody stools and palpable mass. Is the most frequent extranodal lymphoma. Other times symptoms take the form of nonspecific abdominal pain, intestinal obstruction or mimic appendicitis. Intestinal NHL has rapid doubling times (12-36 hrs) making it sensitive to cytotoxic drugs. During presentation localized or disseminated disease is seen evenly. Children with actual or simulated acute abdominal conditions are the ones that receive early therapy and have best survival (Stage I/II disease). Bulk disease in the abdomen as predicted by levels of LDH, interleukin II receptor and B2 microglobulin level determines outcome. Complete resection, absence of bone marrow and CNS involvement offers the best five-year survival rates (80-97%). Suspicious lymph nodes should be removed, but functional impairment is not justified. Most of these children will receive minimal adjuvant chemotherapy. In case of large retroperitoneal tumors, disseminated or metastatic disease aggressive debulking should be avoided and the role of surgery should be aimed at establishing a tissue diagnosis as fast as possible. Debulking is associated with greater complications and delay in instituting primary chemotherapy. Bowel perforation carries the worst prognosis.

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Ectopic Pancreas

Ectopic pancreatic tissue is found incidentally or may cause problems when associated with a duplication cyst, a Meckel diverticulum, in the stomach, in a congenital duodenal diaphragm and in the ileum (as lead point of an intussusception). The presence of ectopic tissue in patients with Meckel's diverticulum is a main risk for occurrence of an acute nonmechanical complication. Most heterotopic pancreas identified incidentally in

asymptomatic children occurs as a patch of tissue in the serosal surface of the proximal jejunum with fully formed acinar tissue, islets and draining ducts. Incidental removal is not indicated unless the location harbingers problems. Ectopic pancreatic tissue is susceptible to drugs also.

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