



PEDIATRIC SURGERY Update © **Vol. 44 No. 06 JUNE 2015**

Anti-NMDA receptor Encephalitis

Anti-N-methyl-D-aspartate (NMDA) receptor encephalitis is a rare autoimmune paraneoplastic syndrome characterized by escalating confusion, amnesia, agitation and paranoid or delusional thoughts. Most patients with anti-NMDA receptor encephalitis have the following characteristics: young females with a median age of 24 years, prominent neuropsychiatry symptoms such as behavioral or personality changes that could progress to seizures, stereotyped movements, autonomic instability or central hypoventilation, harboring of a matured ovarian or mediastinal teratomas, with detectable quantities of serum or cerebrospinal fluid antibodies that interacted with the cell membrane of rat hippocampal neurons in vivo. The teratoma produces autoantibodies to the NMDA Receptor 1 subunit of the NMDA receptor site detectable in serum and cerebrospinal fluid (anti-NMDA receptor immunoglobulin G antibody). Not all patients presenting with NMDA receptor encephalitis are females with ovarian teratomas, but the frequency is so significant that work-up should include ultrasound, CT Scans, and MRI to rule out a causative tumor. Infants and toddlers with such paraneoplastic syndrome lack an associated tumor. Common presenting symptoms of patients with NMDA receptor encephalitis include neuropsychiatric symptoms, seizures, dyskinesias, loss of consciousness, amnesia, and autonomic dysfunction. Management of anti-NMDA receptor encephalitis caused by a teratoma is removal of the tumor and immunotherapy. Removal of the teratoma is associated with decrease in serum and cerebrospinal fluid levels of the pathologic autoantibody with improvement or full recovery. Immunotherapy includes steroids, intravenous immunoglobulin and plasmapheresis. Since most cases present with neuropsychiatry symptoms, recognition by mental health professional is key to early diagnosis.

References:

- 1- Leshner AP, Myers TJ, Tecklenburg F, Streck CJ: Anti-N-methyl-D-aspartate receptor encephalitis associated with an ovarian teratoma in an adolescent female. *J Pediatr Surg.* 45(7):1550-3, 2010
- 2- Tanyi JL, Marsh EB, Dalmau J, Chu CS: Reversible paraneoplastic encephalitis in three patients with ovarian neoplasms. *Acta Obstet Gynecol Scand.* 91(5):630-4, 2012
- 3- Goldberg EM, Titulaer M, de Blank PM, Sievert A, Ryan N: Anti-N-methyl-D-aspartate receptor-mediated encephalitis in infants and toddlers: case report and review of the literature. *Pediatr Neurol.* 50(2):181-4, 2014
- 4- Seifi A, Xia BT, Felte RF: Thinking outside the box about young female patients with sudden-onset bizarre behavior: a case of anti-N-methyl-D-aspartate receptor encephalitis. *Prim Care Companion CNS Disord.* 15(4): 1-2, 2013
- 5- Acien P, Acien M, Ruiz-Macia E, Martin-Estefania C: Ovarian teratoma-associated anti-NMDAR encephalitis: a systematic review of reported cases. *Orphanet J Rare Dis.* 9:157-65, 2014
- 6- Li S, Zhao A: A case of anti-NMDAR encephalitis induced by ovarian teratoma. *Cell Biochem Biophys.* 71(2):1011-4, 2015

Hereditary Pancreatitis

Hereditary pancreatitis (HP) is a rare etiology of chronic pancreatitis in children and adults. HP is an autosomal dominant inherited disorder with an incomplete penetrance affecting mostly the white population. HP is characterized by a younger age of onset and a longer course of recurrent episodes of acute pancreatitis before reaching pancreatic insufficiency. It also is associated with a high cumulative risk of developing pancreatic ductal carcinoma more commonly seen with a paternal inheritance pattern. HP is correlated to a mutation in the PRSS1 gene located on 7q35 locus identified as R122H. PRSS1 mutation induces an inability of endogenous trypsin inhibitor binding to inactivate intrapancreatic trypsin, leading to pancreatic autolysis. Other gene mutations implicated are SPINK1 and CFTR. Accurate and reproducible genetic testing for PRSS1, SPINK1, and CFTR has improved the efficiency of diagnosis. The diagnosis of HP is usually based on the recognition of recurrent pancreatitis, usually starting in childhood, in two or more members of a family in the absence of other causes for pancreatitis. HP is characterized by acute onset of recurrent epigastric pain associated with nausea, vomiting and abdominal pressure presenting before the age of ten years. Complications such as pancreatic duct stones, duct strictures and pseudocysts are more frequent in children with HP. They are diagnosed using MRCP and ERCP. Late complications include pancreatic insufficiency with steatorrhea and insulin-dependent diabetes. Management of hereditary pancreatitis includes several objectives: pain-control, prevention of recurrence, treatment of exocrine and endocrine dysfunction, management of complications and early detection of pancreatic ductal adenocarcinoma. Endoscopic management consists of biliary/pancreatic sphincterotomy, pancreatic duct stricture dilatation, stent placement and removal of stones from the pancreatic duct. Endotherapy delays development of chronic pancreatitis and pancreatic cancer. Surgical procedures consist in lateral pancreaticojejunostomy, resection of the tail of the pancreas and duodenal sparing pancreatectomy.

References:

- 1- DuBay D, Sandler A, Kimura K, Bishop W, Eimen M, Soper R: The modified Puestow procedure for complicated hereditary pancreatitis in children. *J Pediatr Surg.* 35(2):343-8, 2000
- 2- Choudari CP, Nickl NJ, Fogel E, Lehman GA, Sherman S: Hereditary pancreatitis: clinical presentation, ERCP findings, and outcome of endoscopic therapy. *Gastrointest Endosc.* 56(1):66-71, 2002
- 3- Rebours V, Boutron-Ruault MC, Schnee M, et al: The natural history of hereditary pancreatitis: a national series. *Gut.* 58(1):97-103, 2009
- 4- Schmitt F, Le Henaff G, Piloquet H, Leclair MD, David A, Heloury Y, Podevin G: Hereditary pancreatitis in children: surgical implications with special regard to genetic background. *J Pediatr Surg.* 44(11):2078-82, 2009
- 5- Lal A, Lal DR: Hereditary pancreatitis. *Pediatr Surg Int.* 26(12):1193-9, 2010
- 6- Ceppa EP, Pitt HA, Hunter JL, Leys CM, Zyromski NJ, Rescorla FJ, Sandrasegaran K, Fogel EL, McHenry LW, Watkins JL, Sherman S, Lehman GA: Hereditary pancreatitis: endoscopic and surgical management. *J Gastrointest Surg.* 17(5):847-56, 2013
- 7- Kargl S, Kienbauer M, Duba HC, Schafkl R, Pumberger W: Therapeutic step-up strategy for management of hereditary pancreatitis in children. *J Pediatr Surg.* 50(4):511-4, 2015

Parathyroid Carcinoma

Parathyroid carcinoma is an extremely rare cause of primary hyperparathyroidism in the pediatric population with less than ten cases reported in the world literature. Clinical manifestations of parathyroid cancer in children include palpable neck mass, bone pain, weakness, pancreatitis, malaise, polyuria, polydipsia, nausea and vomiting. Most cases report high levels of PTH associated to severe hypercalcemia with total serum calcium greater than 13 mg/dL and a palpable neck mass. Sestamibi scan corroborated the diagnosis, while CT-Scan provides clues toward tumor resectability. Parathyroid carcinoma is confirmed by histologic examination with findings of trabecular pattern, mitotic figures, capsular and bloods vessel invasion. Management of parathyroid cancer is en bloc removal of the tumor along with the ipsilateral thyroid lobe avoiding rupture of the tumor capsule and spillage of tumor cells. Removal of adjacent enlarged or abnormal lymph nodes is recommended. The tumor metastasize to the lung primarily, followed by bone, liver and brain. Serum calcium and iPTH levels should normalize after surgery, unless unresected tumor or metastatic disease is present. Recurrence and systemic metastases occur in 50% of patients with parathyroid carcinoma. When metastatic disease is present metastasectomy is recommended to reduce hypercalcemia. Chemotherapy, adjuvant radiotherapy and medical management including calcitonin, mithramycin bisphosphonates and NPS R-568 calcimimetic agent may be used for patients with uncontrollable hypercalcemia with unresectable or metastatic disease. Prognosis is poor with mortality caused by severe hypercalcemia when widespread metastatic or unresectable disease is present.

References:

- 1- Rock K, Fattah N, O'Malley D, McDermott E: The management of acute parathyroid crisis secondary to parathyroid carcinoma: a case report. J Med Case Rep. 4:28, 2010
- 2- Wang CA, Gaz RD: Natural history of parathyroid carcinoma. Diagnosis, treatment, and results. Am J Surg. 149(4):522-7, 1985
- 3- Kim YS: Parathyroid carcinoma with lung metastasis in a thirteen-year-old girl. J Korean Surg Soc. 82(6):385-8, 2012
- 4- Ito Y, Iwase H, Tanaka H, Yuasa H, Kureyama Y, Yamashita H, Toyama T, Kimura M, Kobayashi S: Metachronous primary hyperparathyroidism due to a parathyroid adenoma and a subsequent carcinoma: report of a case. Surg Today. 31(10):895-8, 2001
- 5- Kebebew E: Parathyroid carcinoma. Curr Treat Options Oncol. 2(4):347-54, 2001
- 6- Kung B, Winokur R, Cognetti D, O'Hara B, Rosen D: Parathyroid carcinoma: a rare cause of primary hyperparathyroidism. Ear Nose Throat J. 88(9):E10-3, 2009

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