EDITORIAL

Pancreatitis in children: A diagnosis missed in Pakistan?

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This editorial, hopes to make the general paediatrician aware of important causes of abdominal pain and or malabsorption, bloating, significant weight loss, diarrhoea, failure to thrive (FTT) and irritability (more in infants) which they may see on a daily basis, in our part of the world. This may not be co-related to the organ pancreas, hence missing out on important differential diagnosis. Detailed information regarding each disease has not been mentioned, as it is not the scope of the editorial. However, further reading of each disease is suggested.

Pancreas is located in the upper left abdomen. There may be 3 cell types involved endocrine, exocrine and stellate cells of the pancreas. The islet cells of Langerhans produce hormones that regulate glucose metabolism and pancreatic function. The secretory cell types, four in number produce glucagon, insulin, somatostatin and pancreatic polypeptide (PP). Exocrine cells comprise of acinar cells which secrete enzymes. The acinar basolateral membrane has receptors for secretion of cholecystokinin, acetylcholine and vasoactive intestinal peptide. The basolateral portion with the nucleus and endoplasmic reticulum synthesize the digestive enzyme. Apices of acinar cells contain zymogen granules in which are vesicles containing inactive digestive enzymes. The ducts secrete fluid containing bicarbonate and other electrolytes. The Stellate cells are responsible for the formation of epithelial structures. In pathological states such as chronic pancreatitis, these cells transform and promote inflammation and fibrosis.[1] Hence, Exocrine function of pancreas include, secretion of water, bicarbonate and enzymes required for digestion of Carbohydrate (CHO), protein and fat.

Exocrine pancreatic insufficiency (EPI) manifests itself in the patient as, FTT, anaemia, electrolyte abnormalities, deficiencies in fat-soluble vitamins and prolonged PTT. Tests include faecal elastase-1 measured by immunosorbent stool assay and serum immunoreactive trypsinogen. Though the "gold standard" is a 72-hour faecal fat collection, it is a difficult process. Other tests include serum amylase and breath H2 excretion, direct collection of duodenal fluid by naso-duodenal tube has a sensitivity and specificity of 90%, it is an expensive and invasive procedure. Inherited disorders of EPI include cystic fibrosis, Shwachman-diamond syndrome, Pearson bone marrow-pancreas syndrome (mitochondrial syndrome), Johanson-Blizzard syndrome, and congenital rubella syndrome.[2]

Congenital anomalies of the pancreas must also be considered in terms of a differential diagnosis and this includes pancreatic divisum present in about 10% of population with the child having clinically intermittent abdominal pain and mild to severe recurrent episodes of pancreatitis. Diagnosis is confirmed by Computed tomography (CT)/magnetic resonance imaging (MRI), endoscopic retrograde cholangiopancreatography (ERCP) and magnetic resonance cholangiopancreatography (MRCP) with secretin. Other causes may include ectopic pancreas, mostly incidental and annular pancreas which is a rare anomaly.[3]

Pancreatitis can also be triggered by viral infection which has an increased risk in children less than 7 years with weight less than 23 kg. The viral infection of the pancreas may be associated with other systemic illness, biliary obstruction, malformations, trauma, drugs, genetic mutations and metabolic abnormalities. The diagnosis of pancreatitis requires $\geq$2 of 3 following criteria; abdominal pain, acute localized upper abdominal pain with or without radiation to the back, the pain can be vague or nonspecific, increased serum amylase and or lipase to >3× the upper limit of normal and radiographic evidence of pancreatitis by ultrasound or CT.[4] Serum lipase increases in 2-12 hours and is elevated for up to 5 days. Serum lipase can be increased in other conditions such as diabetic ketoacidosis, renal failure, burns, mumps, anorexia, and bulimia, which should be kept in mind, when considering the differential diagnosis. Lipase is a more sensitive indicator of pancreatic injury than amylase and is increased within 4-8 hours and remains increased for 8-14 days. Increased transaminases and both transaminases and γ-glutamyl transferase will suggest a

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possible biliary obstruction. Ultrasound is a good initial test; CT scan is helpful in a prolonged course of the disease and MRCP can identify both anatomic and obstructive anomalies.[5]

Other than viral pancreatitis, aetiology includes, Haemolytic uraemic syndrome, Systemic lupus, Henoch-Schonlein purpura, Juvenile rheumatoid arthritis, inflammatory bowel disease, Cystic fibrosis (CF), Sickle cell disease, Kawasaki disease, Shock/hypo perfusion injury, cholelithiasis, choledochal cyst, biliary sludge and trauma due to motor vehicle accidents or bike handlebar injuries.[6] Latter are on the increase in cosmopolitan cities such as Karachi, Lahore and Islamabad.

Medications include; Valproic acid and L-asparaginase which are most commonly associated with pancreatitis at therapeutic doses. Azathioprine, mercaptopurine, mesalamine, metronidazole, tetracyclines, cytarabine, furosemide, and steroids also associated[7] with pancreatitis.

Other causes of pancreatitis include annular pancreas, duodenal ulcer, tumour of the papilla, duodenal Crohn disease, tumour, or mass. Infections, such as Mycoplasma, Coxsackie virus, Mumps virus, Adenovirus, Varicella, herpes simplex virus, cytomegalovirus, Rubeola, Hepatitis A and B, Influenza A and B, Human immunodeficiency virus.

Genetic Syndromes include; PRSS1 mutations, CFTR mutations, SPINK-1 mutations. If there is recurrent pancreatitis or with a significant family history, children should be evaluated for at least PRSS1 and CF.[7] While metabolic related causes of pancreatitis include; hypercalcaemia, hypertriglyceridemia, malnutrition and toxins such as acetaminophen overdose, organophosphates, alcohol, spider or scorpion venom, heroin, and amphetamines.[8]

Management includes early aggressive fluid resuscitation with Ringers' lactate and preferably parenteral narcotics. Early feeding is recommended. About 20% of children have complications, such as peri pancreatic fluid collection and pseudocyst formation.[9]

In Chronic pancreatitis (CP)[6] there is progressive inflammation of the pancreas, with irreversible structural changes with permanent loss of both the exocrine and endocrine function. CP can be preceded by acute recurrent Pancreatitis (ARP). Risk factors include genetic, obstructive, toxic/metabolic, autoimmune, and idiopathic. Abdominal pain, usually in the upper abdomen is episodic or persistent, and can be mild-moderate to severe. Nausea and/or vomiting; anorexia may be present. Symptoms and signs of EPI include steatorrhea, weight loss, and fat-soluble vitamin deficiencies.[1,6] Characteristic imaging findings can be identified by ultrasound (US), magnetic resonance cholangio-pancreatography (MRCP), endoscopic retrograde cholangiopancreatography (ERCP), endoscopic US (EUS), and computed tomography (CT).[10-12]

Genetic testing and pancreatic imaging by secretin-enhanced MRCP is the first choice as it is non-invasive in nature, there is lack of ionizing radiation, and the procedure gives accurate imaging of the pancreatic parenchyma and ductal system. Fasting lipids and total serum Ca2+, Sweat Cl-are other tests, which can be used.

Treatment of CP includes conservative management, pain control and hydration. Endoscopy may help if there is a stricture with pancreatic duct obstruction. Total pancreatectomy (TP) with islet cell autotransplantation involves removal of the pancreas and harvesting and perfusion of isolated islets to the portal vein. Approximately, 60% of children are off narcotics and insulin independent at the 20-year follow-up, with improvement in quality of life.[10,11] Pancreatic exocrine insufficiency results in maldigestion and absorption of fat due to inadequate activity of pancreatic enzyme in the small bowel.[10]

A child with pancreatitis may have abdominal pain in 81%, while 43% have constant pain. Diagnosis of paediatric acute pain (AP) is done by INSSPIRE.[11] The child should meet 2 out of the three criteria; abdominal pain compatible with AP, serum amylase or lipase levels greater or equal to three times the upper limit of normal and imaging findings consistent with pancreatitis.[11]

In conclusion, paediatricians must be aware of, to include a few; causes and details of acute and chronic pancreatitis, Shwachman Diamond syndrome, Johansson-Blizzard syndrome, congenital anomalies and cystic fibrosis in which the pancreas can be involved and hence warrants a specific clinical examination, investigation and management respectively.

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