JOP. J Pancreas (Online) 2007; 8(4):433-437.

CASE REPORT

Dorsal Pancreas Agenesis and Polysplenia/Heterotaxy Syndrome: A Novel Association with Aortic Coarctation and a Review of the Literature

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ABSTRACT

Context Agenesis of the dorsal pancreas is very rare and may be associated with other congenital disease states. It has a rare association with polysplenia/heterotaxy syndrome. Most commonly, these states occur due to errors in development of the asymmetric organs and may be associated with benign to severe congenital cardiac malformations.

Case report We report a case of a 25-year-old male with known coarctation of the aorta who was otherwise asymptomatic. Following a routine cardiac examination, he was incidentally discovered to have an absent body and tail of the pancreas on imaging. Further testing demonstrated findings consistent with a diagnosis of polysplenia/ heterotaxy syndrome with agenesis of the dorsal pancreas.

Conclusions In patients with congenital heart disease, there is increased likelihood for the presence of other congenital malformations. In particular, polysplenia/heterotaxy syndrome, while very rare, has been shown to be associated with cardiac abnormalities. The importance in diagnosis lies in the potential clinical consequences of polysplenia/ heterotaxy syndrome and agenesis of the dorsal pancreas, including late-onset diabetes mellitus, pancreatitis, and intestinal volvulus.

INTRODUCTION

Polysplenia/heterotaxy syndrome is a relatively rare disorder often involving multiple cardiac and gastrointestinal structural abnormalities with possible effects on normal physiology. Patients with polysplenia often present with atrioventricular septal defects and may have anomalous inferior vena caval flow or other gastrointestinal structural abnormalities including partial or complete agenesis of the dorsal pancreas. These findings may have clinical relevance with a possible increased risk for intestinal volvulus, diabetes mellitus or pancreatitis.

We report a unique case of agenesis of the dorsal pancreas in association with polysplenia/heterotaxy syndrome incidentally identified in an otherwise asymptomatic patient with a prior diagnosis of aortic coarctation.

CASE REPORT

A 25-year-old asymptomatic male with a surgically repaired coarctation of the aorta and hemodynamically insignificant pulmonary stenosis presented to the pancreas clinic via the adult congenital heart disease clinic following an incidental thoracic CT finding of polysplenia with multiple accessory splenules in conjunction with the absence of identifiable pancreatic tissue. His medical history was unremarkable for polyuria, polydipsia, weight loss, steatorrhea, or pancreatitis. Physical

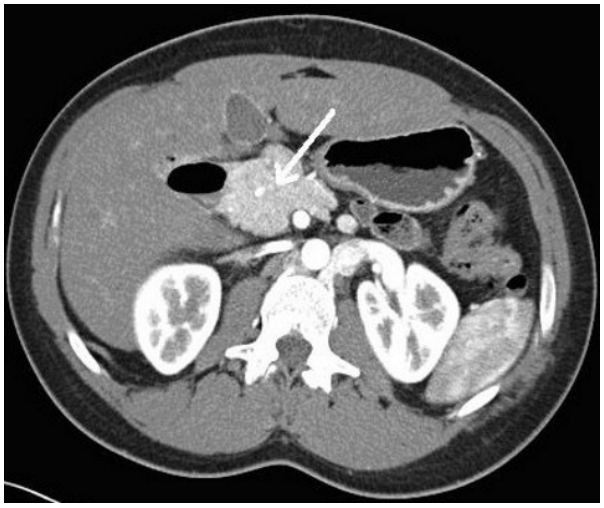

Figure 1. A prominent pancreatic head with associated absence of body and tail of the pancreas (arrow). The mild prominence of the pancreatic head may be due to some compensatory hypertrophy.

exam demonstrated a non-tender, non-distended abdomen without notable hepatomegaly, splenomegaly, palpable masses, or audible bruits. Laboratory values revealed normal pancreatic and liver biochemistry, fasting glucose and lipid profile.

A pancreas protocol CT scan verified complete agenesis of the dorsal pancreas in addition to findings of polysplenia and prominence of the azygous vein with absence of the suprarenal inferior vena cava (Figures 1 and 2). The pancreatic head was prominent in size representing some mild compensatory hypertrophy. In the absence of clinical endocrine or exocrine pancreatic dysfunction no further invasive studies were performed.

DISCUSSION

The incidental findings in our patient are consistent with that of polysplenia/heterotaxy syndrome, which belongs to a spectrum of cardiosplenic syndromes. Studies suggest that up to 2.2% of patients with congenital heart defects may have an underlying splenic abnormality [1]. There is a further significant association between developmental splenic abnormalities and malformation of the gastroenterologic system, including, but not limited to, the abdominal vasculature, in particular the inferior vena cava, pancreas, small intestine, and liver [2].

Symmetry is a characteristic of the mammalian phenotype, although much of the internal anatomy is asymmetric. This is particularly true in the cardiovascular, pulmonary, and gastrointestinal systems. These organs form and evolve around the embryonic midline. The normal arrangement of the asymmetric organs is called *situs solitus*. In extreme cases, all of the midline structures may be rotated around the midline, resulting in a mirror image of the normal anatomy, termed *situs inversus*. Intermediate states of malrotation are termed *situs ambiguus*.

Grouping of patients with *situs ambiguus* is based on whether the right or the left sided structures predominate [3]. Patients with left-sided symmetry are characterized as having polysplenia, which includes either a segmented spleen or multiple splenules that may or may not be functional. Asplenia is

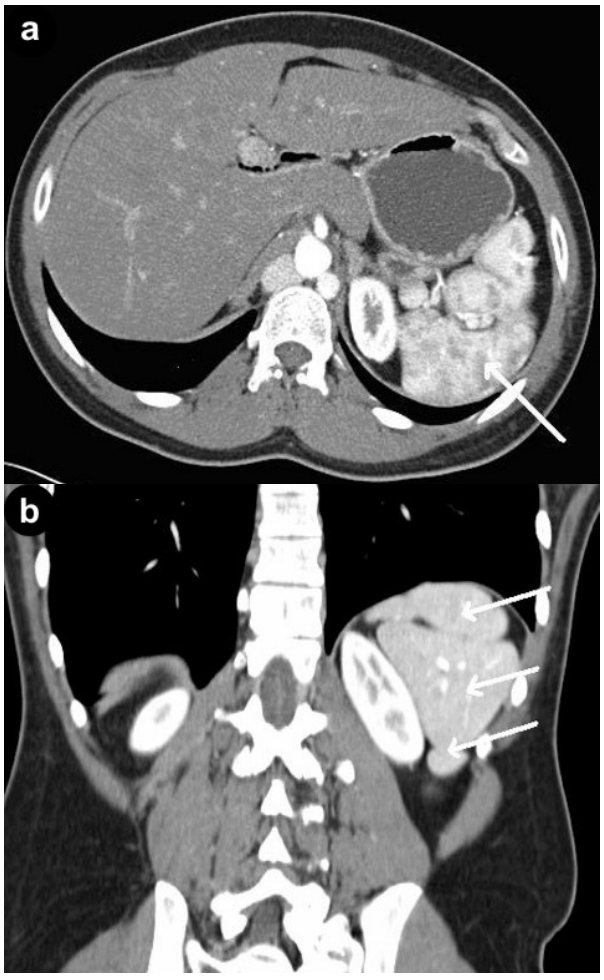

Figure 2. Extensively septated spleen and splenules consistent with polysplenia (arrows).

associated with right-sided symmetry. More recently, this spectrum of abnormalities has been termed polysplenia syndrome to denote the continuum of possible midline derangements seen in this population.

Abnormalities in this population result from an inability during embryogenesis to fully define laterality, thus resulting in maldevelopment of the asymmetric organs, sparing the symmetric structures. This inability to define laterality is most often sporadic but has been suggested to have possible autosomal and X-linked inheritance patterns. Mouse models have suggested a number of possibly involved genetic mutations, including that of the transforming growth factor beta pathway, though relationship to humans remains to be defined [4]. Unfortunately, the ultimate disposition of organs in this syndrome is largely random, and the defined right or left sided tendency is just that - a tendency - explaining the terming of polysplenia syndrome.

Most commonly, patients present due to symptomatic cardiac abnormalities at birth, as in the case of our patient. However, in some cases, patients may present later in life [5, 6]. The most common anatomic anomaly that points towards a diagnosis of polysplenia syndrome is inferior vena cava interruption with azygous or hemiazygous continuation, though this finding is not necessarily specific for polysplenia [7]. One study suggested that this anatomic finding, in combination with cardiac or situs abnormalities, should suggest a specific diagnosis of a cardiosplenic syndrome, in particular polysplenia [8].

Cardiac anomalies in these patients may include atrioventricular valvular abnormalities, total anomalous pulmonary venous connection, rotation of the heart about its axis, presence of a single atria, or aortic outflow obstruction at the level of the subaortic outflow tract or at the level of the valve [9]. Patients with polysplenia will often have no notable cardiac defect. If there is an abnormality present, it is most commonly an atrioventricular septal defect. One case series involving thirteen patients suggested that the most common findings are atrioventricular channel and great vessel anomalies [10]. In our patient, there was never an atrioventricular septal defect noted but rather aortic coarctation and pulmonary stenosis, though the latter was not considered to be hemodynamically significant. Coarctation of the aorta is not an uncommon finding and often will not present until older age. Due to this, other congenital malformations that may coexist with coarctation may go undiagnosed even after finding a coarctation, as in our patient. The spectrum of findings involving the diagnosis of polysplenia/heterotaxy syndrome in association with an isolated coarctation of the aorta has never been reported to our knowledge in the English literature.

Gastrointestinal abnormalities may include a midline liver and gallbladder, right-sided stomach and spleen, small bowel and colon rotational abnormalities, truncation of the pancreas, extrahepatic biliary malformations and ipsilateral location of the aorta and inferior vena cava [11]. If the child survives the potential cardiovascular effects of the syndrome, gastrointestinal abnormalities have the potential to cause significant problems, including bile flow abnormalities, intestinal volvulus later in life, and diabetes mellitus or pancreatitis related to maldevelopment. In neonates, there is a significant association between biliary atresia and polysplenia, with a further association with anomalous portal venous connections that may be clinically relevant in the context of planned surgical intervention [12].

Agenesis of the dorsal pancreas has been previously described in polysplenia [13]. The clinical significance of this finding relates to a possible relationship to early or late onset diabetes mellitus [14, 15] or the increased incidence of pancreatitis [16, 17]. Computed tomography scanning and ERCP are useful in identifying this finding [18], although the findings must be distinguished between distal pancreas fat replacement and agenesis [19]. On imaging, fat replacement will be distinguished by abundant fat tissue seen anterior to the splenic vein, whereas agenesis of the dorsal pancreas will be characterized by

filling of the distal pancreatic bed with stomach and intestines, as in the case of our patient. However, in order to differentiate complete versus partial agenesis of the dorsal pancreas, ERCP is necessary in order to define absence of the dorsal ductal system, the accessory duct, and the minor papilla [20]. Complete agenesis is actually quite rare, with a total of fifteen cases being reported between 1913 and 2005 [21, 22, 23]. The increased likelihood of pancreatitis in this patient population with dorsal agenesis has been proposed to be due to either sphincter of Oddi dysfunction [24] or higher intrapancreatic duct pressures due to hypertrophy of the ventral gland [25]. Diagnosis may be achieved by a combination of computed tomography or MRI scanning and ERCP. Endoscopic ultrasound has also been proposed as an alternative diagnostic modality [26].

To conclude, the association between dorsal pancreas agenesis, features of polysplenia/ heterotaxy syndrome, and coarctation of the aorta is an interesting collection of findings that has potential clinical correlation related to a possible but as of yet not completely clear propensity for the development of diabetes mellitus or pancreatitis later in life.

Received March 21st, 2007- Accepted April 16th, 2007

Keywords Aortic Coarctation; Embryonic Development; Heart Defects, Congenital; Pancreas

Conflict of interest The authors have no potential conflicts of interest

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Document URL: http://www.joplink.net/prev/200707/02.html

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