# Ivemark syndrome: asplenia with kidney collecting duct cysts and polysplenia with cerebellar cyst

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Two newborns, one male and one female, from two different families, with Ivemark syndrome proven at autopsy are reported. One of them had asplenia and another had polysplenia. Both newborns had complex cardiac defects with isomerism of the lungs. The newborn with asplenia had dextrocardia, transposition of the great vessels, stenosis of the pulmonary artery, common atrioventricular canal and patent ductus arteriosus. The newborn with polysplenia had a common atrium, hypoplastic left ventricle and patent ductus arteriosus. The patient with asplenia had cystic dilated collecting ducts of the kidney and the patient with polysplenia had cerebellar cyst. These associate malformations have not been reported previously. Both cases were sporadic.

*Key words: cerebellar cyst, dextrocardia, Ivemark syndrome, kidney collecting duct cysts, transposition of great vessels.*

Ivemark syndrome is a severe congenital malformation characterized by visceral heterotaxia, and cardiovascular and bronchopulmonary malformations[1]. This syndrome has been known by many names including asplenia/polysplenia syndrome, isomerism sequence, situs ambiguous and laterality sequence[2]. The etiology is not clearly defined yet, but exogenous factors between the 31st and 38th day of gestation are suggested as the main cause[3].

Ivemark syndrome results from bilateral right- or left-sidedness[2]. Bilaterally placed organs are identical, and unilateral organs may be duplicated or absent. Asplenia has been termed bilateral right-sidedness or right-isomerism. Hypoplasia of the spleen is sometimes the finding rather than aplasia. Asplenia is usually associated with severe atrioventricular canal malformations and marked deficiency of the interventricular septum, with bilaterally trilobed lungs, together with short eparterial bronchi and a heart with two right atrial appendages[2]. The liver remains in central position. The gallbladder is situated to the left near the obliterated umbilical vein. The stomach is tubular in shape and lies medially. The mesentery is aligned vertically rather than diagonally, with the result that malrotation of the bowel is common[4]. Other gastrointestinal malformations have often been described in association with congenital asplenia[5].

Polysplenia has been called bilateral left-sidedness or left isomerism. The atrioventricular defect associated with polysplenia is usually less severe and there are greater abnormalities of the interatrial septum[6]. Each lung has two lobes, there are two long hyparterial bronchi with distal branching and two atria with left atrial appendages[2]. The liver forms centrally and occasionally the gallbladder is absent[7].

Most cases are sporadic, but affected sibs are also reported[8]. The prognosis depends on the degree of the malformation of the heart, but other anomalies and sepsis complicate the clinical course.

## Case Reports

Two cases of Ivemark syndrome are reported. In both, the syndrome was proven at autopsy. Both cases were sporadic.

*Case 1*

A ten-day-old male newborn was admitted to hospital because of severe cyanosis. He was born after an uneventful pregnancy with a birth weight of 3800 g. Parents were unrelated with no similar disorders in their families.

On examination the child had a systolic heart murmur. Echocardiography showed dextrocardia, transposition of the great vessels, stenosis of the pulmonary artery, common atrioventricular canal and patent ductus arteriosus. Acute omphalitis and bilateral pneumonia had developed. He died on the 13$^{th}$ day of life.

The autopsy documented dextroposition of the heart with cardiac defect, asplenia and bilateral trilobed lungs (Figs. 1 and 2). The liver was in a central position (Fig. 3). Histopathological finding of the liver was normal. There were no gastrointestinal malformations. The kidneys were of normal size and shape, with distinct border between cortex and medulla. Collecting system had no visible malformation or obstruction. Histological examination of the kidneys revealed some cystic-like dilated collecting ducts at the cortico medullary border and isolated dilated Bowman capsules (Fig. 4). Mildly dilated collecting ducts were lined by cuboidal epithelium (Fig. 5).

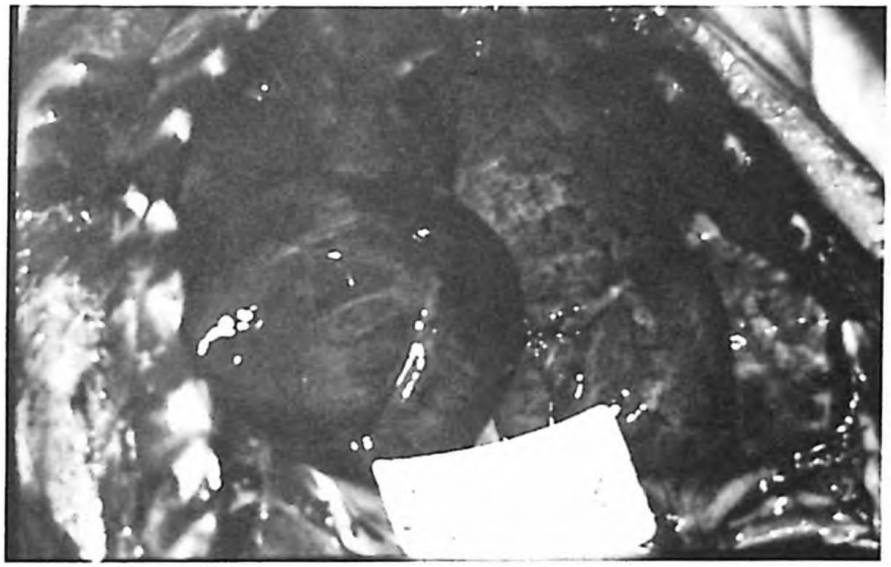

Fig. 1. Dextroposition of the heart (H) and trilobed left lung (LL).

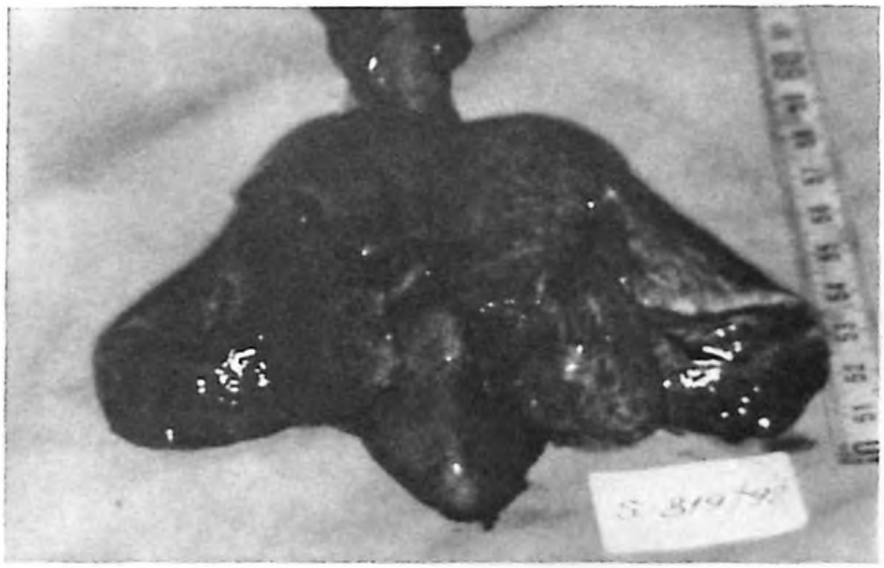

Fig. 2. Bilateral trilobed lungs (RL: right lung; LL: left lung).

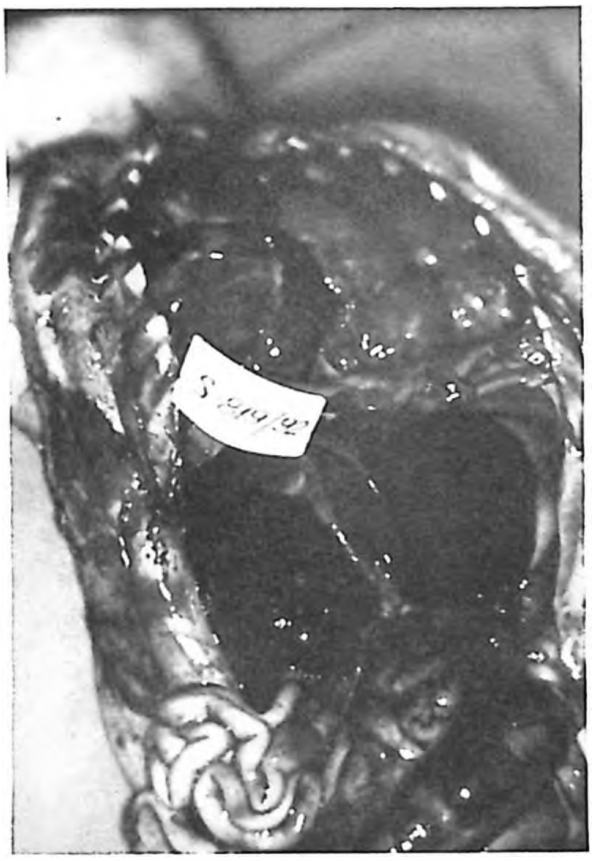

Fig. 3. Centrally situated liver associated with asplenia (a).

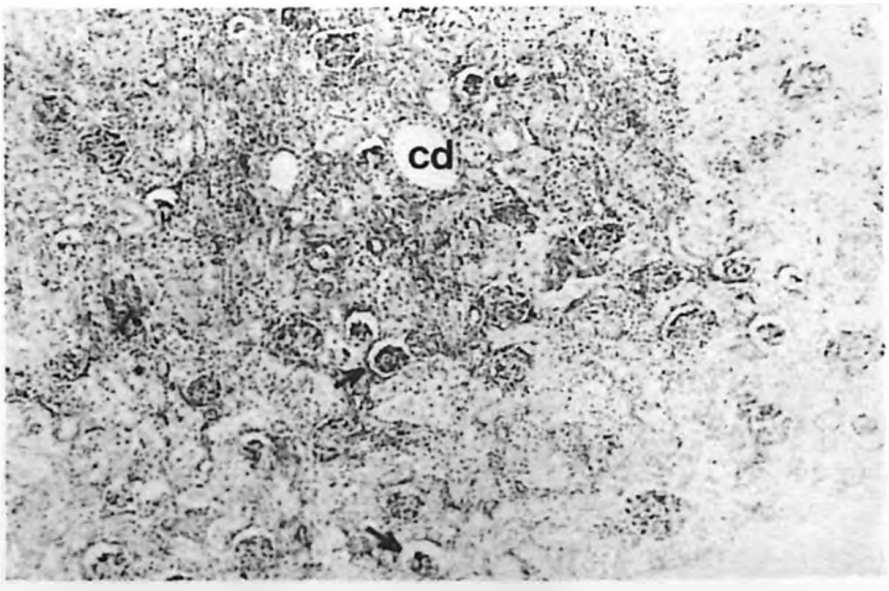


Fig. 4. Slightly dilated Bowman's capsules (arrow) and a few collecting ducts (cd) in the renal cortex (x 40).

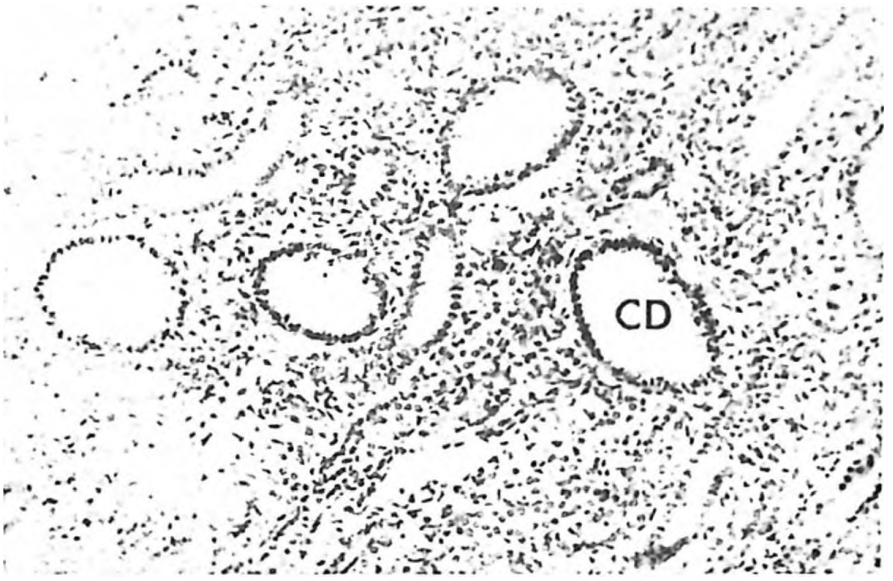


Fig. 5. Cystically dilated collecting ducts (CD) in the renal medulla are lined by cuboidal epithelium (x 200).

*Case 2*

Male newborn, 2900 g weight, with systolic heart murmur was admitted at the Intensive Care Unit. He was born after an uneventful pregnancy, from healthy and unrelated parents with unremarkable family histories.

Echocardiography revealed a common atrium, hypoplastic left ventricle and patent ductus arteriosus. Echosonography of the cerebellum showed one unilocular cyst, 2.5 cm in diameter. The cerebellum was smaller, with atrophic gyri. The patient became septic, developed heart failure and died at the age of 35 days.

The autopsy confirmed the described cardiac defects and a cerebellar cyst filled with clear liquid. The spleen was normal, but close to its hilus there were two smaller accessory spleens. Both lungs were bilobed. Histopathological findings of other organs were normal.

## Discussion

Situs inversus is well described in humans and may be associated with defective cilia in Kartagener's syndrome. In just over one in 10,000 people situs inversus is present with no impairment of function[2]. Ivemark syndrome may be considered an example of damage to a polytopic morphogenetic field in the dorsal mesogastrium where the asymmetry center and the splenic anlage are located[9].

Ivemark also described a quite different syndrome of familial dysplasia of the kidneys, liver and pancreas. Renal-hepatic-pancreatic dysplasia (RHPD) also bears Ivemark's name, at the risk of being confused with asplenic-cardiac anomaly[10]. Ivemark reviewed RHPD four years later than asplenia/polysplenia syndrome[11].

Crawfurd[12] described two sibs with a disorder that appeared to combine features of the two Ivemark syndromes. Both had enlarged polycystic kidneys, a nodular and cystic pancreas associated with absence or hypoplasia of the spleen and cardiac anomalies. A similar case with pancreatic fibrosis, situs inversus, renal dysplasia and cardiovascular anomalies was also reported[13].

A new syndrome with situs inversus totalis, and a cystic dysplastic kidney and pancreas in two sib fetuses was recently reported[14].

Frequencies of the Ivemark syndrome in pediatric autopsies range from 0.02 to 0.38 percent. The male: female ratio is 5:4[9]. Most of cases are diagnosed for the first time at autopsy, as with both patients reported in this study.

Improvements in cardiac surgical techniques can lead to successful repair in some cases, if early cardiac surgery is done[15]. The case of a nine-year-old girl has been described[16].

Up to now there have been only a few reports about an involvement of the kidney[16]. Horseshoe kidney, hydronephrosis, urethral valves, renal hypoplasia, double collecting system, nephroptosis and polycystic kidneys have been reported[17]. A patient with Ivemark syndrome, horseshoe kidney and biliary atresia was also described[18]. The first case of this study had bilateral cystic collecting ducts at the kidney

corticomedullary border. There was no recent report of this kind of cyst associated with asplenia syndrome.

Abnormalities of the central nervous system have been reported in association with asplenia[17]. On the contrary, cerebellar cyst and cerebellar atrophy were associated with polysplenia in this study.

Polymalformation syndromes often include cystic changes. Asplenia syndrome with bilateral cystic collecting ducts at the kidney corticomedullary border and polysplenia syndrome with cerebellar cyst could be an isolated entity or a final pathway of response of these organs to a variety of developmental disturbances.

A sonographic examination of the abdomen should be done in any case of complex cardiac defect in order to diagnose possible asplenia or polysplenia. Similarly, in cases of malrotation of the intestines, special attention should be paid to the heart and spleen. We consider that such an approach could increase the number of cases with Ivemark syndrome diagnosed during their lifetime.

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