

Asplenia in children with congenital heart disease as a cause of poor outcome

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Abstract

The absence of a spleen is a well-known risk factor for severe bacterial infections, especially due to encapsulated bacteria. Congenital asplenia can be part of multiple congenital abnormalities as in heterotaxy including Ivemark syndrome with congenital anomalies of the heart or great vessels, or it can be isolated, which is extremely rare. In these cases, asplenia is an important factor effecting mortality. In this report, the clinical courses of five children with asplenia and concomitant minor or complex cardiac anomalies are presented. The ages of the children ranged between 1.5 and 17 months at the time of diagnosis. All of the cases had had a history of hospitalisation for infectious diseases before the diagnosis. The patient who was diagnosed at 17 months old had a history pneumonia, urinary tract infection, and bacterial meningitis beginning at five months old. Three children had complex cardiac anomalies, one child had ventricular septal defect, and one child had atrial septal defect. Howell-Jolly bodies were determined in peripheral blood smear in all of the patients. The diagnoses of asplenia were confirmed with spleen scintigraphy. One of the patients with complex cardiac anomalies died a short time after diagnosis, because of cardiac failure. The rest of the four patients were vaccinated for encapsulated bacteria and were taken under antibiotic prophylaxis. These children did not need hospitalisation for infectious diseases during the follow-up period (5-40 months). In asplenic children, early diagnosis, antibiotic prophylaxis, and immunisation for encapsulated bacteria can decrease the risk of morbidity and mortality.

Key words: asplenia, child, cardiac anomalies, heterotaxy syndrome, infection, immunisation.

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Introduction

Congenital asplenia may occur in isolation. However, it is usually part of a syndrome and is accompanied by abnormalities in other organ systems, especially cardiac abnormalities. Heterotaxy syndrome with asplenia and right atrial isomerism is the most frequent one of these syndromes, occurring approximately in 1 in 10,000-40,000 births. Both isolated and syndromic asplenia are associated with increased incidence of life-threatening invasive infections. In cases with heterotaxy, heart disease is the most common cause of mortality, especially in the first year of life, but fatal infections have also been reported. In these patients, asplenia is an important factor effecting mortality. Early diagnosis and treatment of asplenia in children with cardiac malformations can decrease the additional risk of mortality and morbidity. In this report we present the clinical courses of five children with asplenia and concomitant minor or complex cardiac anomalies.

Case report

The ages of the children ranged between 1.5 and 17 months at the time of diagnosis. Three of the patients were male and two of them were female. All of the cases had a history of hospitalisation for infectious diseases before the diagnosis. The patient who was diagnosed at 17 months old had a history of pneumonia, urinary tract infection, and bacterial meningitis beginning at five months old. Three children had complex cardiac anomalies, one child had ventricular septal defect, and one child had atrial septal defect. One of the children (case 4) with complex cardiac defects had additional anomalies such as unilateral renal agenesis and syndactyly. Howell-Jolly bodies were determined in peripheral blood smear in all of the patients. The diagnoses of asplenia were confirmed with spleen scintigraphy. One of the patients with complex cardiac anomalies (dextrocardia, total anomalous pulmonary venous return, right atrial isomerism, atrioventricular septal defect, transposition of great arteries, pulmonary stenosis)

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Table 1. Clinical and laboratory data of the patients

LABORATORY DATA									
CASE	Age at the time of diagnosis (months)	Duration of follow-up (months)	Gender	Infections before diagnosis	Physical examination	Cardiac manifestations	Peripheral blood smear	USG	Other imaging methods
Case 1 E.K.	1.5	5	F	Pneumonia at 1 months old	Cyanosis, auscultation of heart sounds from right hemithorax, grade 3/6 systolic murmur at the right sternal border	Dextrocardia, AVSD, Secundum ASD, PS, single atrioventricular valve regurgitation, right arcus	Howell-Jolly bodies were seen	Spleen could not be visualised	Absence of spleen in scintigraphy
Case 2 S.T.Y.	4	40	M	Pneumonia at 4 months old	Grade 3/6 systolic murmur at the left sternal border, rhonchi in lung auscultation	AVSD, DORV, grade 1-2 LAVV regurgitation, PA, left MBTT shunt	Howell-Jolly bodies were seen	Spleen could not be visualised	Absence of spleen in scintigraphy
Case 3 S.T.	17	19	F	Pneumonia at 5 and 17 months old Meningitis and pyelonephritis at 8 months old	Failure to thrive, crackles in lung auscultation, grade 2/6 systolic murmur at the mesocardiac area	VSD	Howell-Jolly bodies were seen (Fig. 1)	Spleen could not be visualised	Absence of spleen in scintigraphy
Case 4 K.C.G.	11	16	M	Pneumonia at 4 months old	Failure to thrive, micrognathia, low-set ears, syndactyly of II-III fingers feet, grade 2/6 systolic murmur at the left sternal border	Atrial septal defect	Howell-Jolly bodies were seen	Spleen and left kidney could not be visualised	Absence of spleen and left kidney in abdominal CT and absence of spleen in scintigraphy (Figs. 2, 3)
Case 5 M.A.	1.5	Died because of cardiac failure one week after diagnosis	M	Pneumonia at 4 months old	Auscultation of heart sounds from right hemithorax, grade 3/6 systolic murmur at the right sternal border	Dextrocardia, TAPVD, right atrial isomerism, AVSD, TGA, PS	Howell-Jolly bodies were seen	Spleen could not be visualised	Absence of spleen in scintigraphy (Fig. 4)

ASD – atrial septal defect; PS – pulmonary stenosis; AVSD – atrioventricular septal defect; DORV – double outlet right ventricle; LAVV – left atrioventricular valve; PA – pulmonary atresia; MBTT – modified Blalock-Taussig; TAPVD – total anomalous pulmonary venous return; TGA – transposition of great arteries; USG – ultrasonography; CT – computerized tomography

died one week after diagnosis, because of cardiac failure. The remaining four patients were vaccinated for encapsulated bacteria and were taken under antibiotic prophylaxis. These children did not need hospitalisation for infectious diseases during the follow-up period (5-40 months). Clinical and laboratory data of the patients are given in Table 1.

Discussion

Asplenia may be acquired (after trauma and surgery), functional (sickle cell anaemia), or congenital. Congenital asplenia is a rare but life-threatening condition. It may arise as a part of situs abnormalities or it may be isolated. Isolated congenital asplenia is a very rare condition, and the mode of inheritance is usually autosomal dominant. Some sporadic cases have also been reported [1]. Heterotaxy syndrome-asplenia and polysplenia is more common. Patients with heterotaxy syndrome often present with congenital heart disease but 5-10% of the patients do not have major cardiac malformations. It is difficult to diagnose when an asplenic patient does not have any concomitant anomalies, and diagnosed cases post mortem have been reported [2, 3]. In heterotaxy syndromes mutations in connexin 43 and ZIC3 genes have been demonstrated. In isolated congenital asplenia, ribosomal protein SA haploinsufficiency has been detected [4]. In our series of five patients, three cases had complex cardiac malformations, one patient had ventricular septal defect, and one patient had atrial septal defect.

The spleen is an important organ in phagocytosis of encapsulated bacteria and immunoglobulin production against these agents [2]. In asplenic patients, the risk of death from septicaemia is 200 times higher than in patients with a spleen. The bacteria causing septicaemia are predominantly pneumococci (50-80% of identified infections) and meningococci, *Haemophilus* sp., and other capsulated

bacteria [2, 5, 6]. In the literature, the youngest congenital asplenic patient was diagnosed with meningitis by *Escherichia coli* occurred for days after birth [2]. Congenital asplenia detected in a 60-year-old woman with septicaemia by streptococcus pneumonia was also reported [7]. However, some patients may be asymptomatic. These data show the variations in the clinical course among patients, even in members of the same family [1]. Asplenia may be a cause of sudden, unexpected death. Kanthan *et al.* presented a previously healthy four-year-old girl with sudden death who had sporadic, isolated congenital asplenia complicated by pneumococcus sepsis and bilateral adrenal haemorrhage diagnosed at autopsy [8]. In a French multicentre study 293 children with sudden death were investigated at autopsy. Four cases of asplenia were identified, three of which were with syndromic asplenia and one of which was with isolated congenital asplenia [9]. In asplenic patients, meningitis, septicaemia, and purpura fulminans are encountered as severe invasive infections. The rate of invasive bacterial infections, mortality, and major sequelae have been reported as 69%, 64%, and 7%, respectively [2]. Heterotaxy with asplenia leads to a high morbidity and mortality [10]. Mikate *et al.* evaluated 8923 cases operated due to congenital heart disease. Asplenia has been shown to be one of the postoperative risk factors influencing mortality when operated due to congenital heart disease, while with heterotaxy, morbidity and mortality increases [11]. In all of our patients there was a history of hospitalisation because of lower respiratory infection before the diagnosis of asplenia. One patient had a history of urinary tract infection and acute bacterial meningitis additionally.

The presence of Howell-Jolly bodies in peripheral blood smear is an important sign of congenital or functional asplenia [7]. Therefore, careful examination of peripheral blood smear is important in children with congenital heart disease. When Howell-Jolly bodies are present in peripheral blood smear, the diagnosis of asplenia must be confirmed by ultrasonography, computerised tomography, magnetic resonance imaging, or spleen scintigraphy [9]. In all of our cases, the spleen could not be imaged by ultrasonography. The diagnosis of asplenia was confirmed by computerised tomography in one of the cases, and by spleen scintigraphy in four of the cases.

By antibiotic prophylaxis and immunisation for pneumococcal infections and haemophilus influenzae type b, protection from invasive infections is possible [2, 12, 13]. Although conjugated vaccines increase protection from pneumococcal infections, 19% of the patients are prone to infections by serotypes out of the content of heptavalent pneumococcal vaccine. Moreover, vaccine induced immunity may be defective in asplenic patients. Therefore, fever of unknown origin must be evaluated carefully in asplenic patients [2, 5, 13]. The four of our cases were taken under antibiotic prophylaxis and were vaccinated for encapsulated bacteria. These children did not necessitate

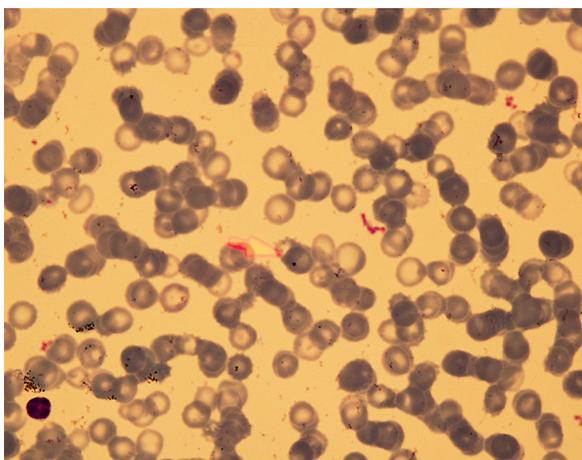


Fig. 1. Howell-Jolly bodies in the peripheral blood smear (case 3)

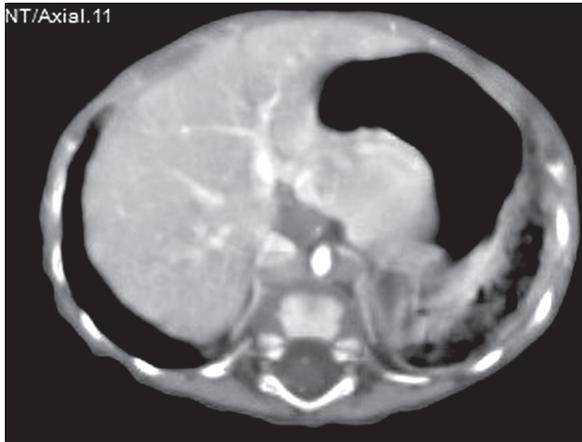


Fig. 2. Absence of spleen in abdominal computerised tomography (case 4)

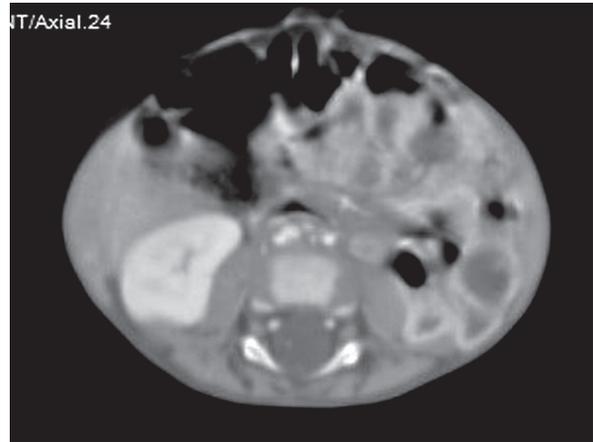


Fig. 3. Absence of left kidney in abdominal computerised tomography (case 4)

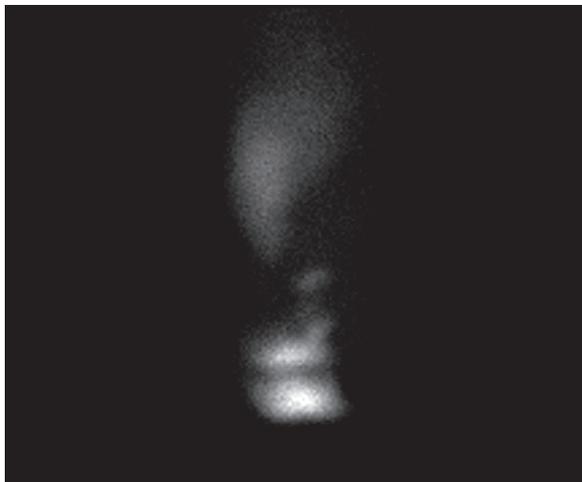


Fig. 4. Absence of spleen in scintigraphy (case 5)

hospitalization for infection diseases during the follow-up period (5-40 months). One of our cases, who had complex cardiac malformations, was lost owing to heart failure on the seventh day after diagnosis.

Conclusions

Asplenia can be accompanied by major or minor cardiac anomalies. The existence of Howel-Jolly bodies in peripheral blood smear is useful for determining asplenia in patients with cardiac anomalies. In asplenic children, early diagnosis, antibiotic prophylaxis, and immunisation for encapsulated bacteria, can decrease the risk of morbidity and mortality due to invasive infections.

The authors declare no conflict of interest.

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