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Hypoplastic left heart syndrome: morphological study of 21 autopsy cases

The term hypoplastic left heart syndrome (HLHS) is used to describe a spectrum of structural cardiac malformations that are characterised by severe underdevelopment of the structures in the left heart-aorta complex (13). The substantial feature of the syndrome is then hemodynamically inefficient left ventricle, which leads to congestive heart failure and cyanosis (11). The syndrome occurs in 0.16 per 1,000 live births (3). It is a fatal condition without surgical intervention, and the mortality within the first month after birth is about 95% (8). HLHS is the fourth most common cause of cardiac death in newborns and infants (7).

The aim of the present study was an analysis of the frequency and morphological features of HLHS, as well as its association with other congenital malformations in autopsy material of our institution.

MATERIALS AND METHODS

The autopsy files of the Department of Clinical Pathomorphology, Medical University of Lublin in the years 1991-2000 were reviewed. Of 1,301 children aged up to 1 year (body weight >500 g), twenty-one cases of HLHS were found. According to Saied et al. (11) the cases with abnormal relations of the great arteries were excluded from the study. The surgical treatment was not performed in any case. Data concerning the age and clinical diagnosis were obtained from the notes based on the case histories and included in the autopsy protocols. Detailed data on congenital malformations that have been found at gross examination came from the autopsy protocols, too. In each case, the heart and great vessels were sectioned according to a standard protocol, and the samples

were taken for microscopic examination. The following staining methods were performed: hematoxylin and eosin (H+E), Selly's, resorcin-fuchsin, and van Gieson's.

RESULTS

The total number of autopsy cases with HLHS was 21. This comprises 4.2% of all cases with congenital malformations and 9.8% of cases with cardiovascular anomalies found in our institution during the period of 10 years. This group consists of 13 males (61.9%) and 8 females (38.1%) with an age ranging from 0 to 21 days (mean 5.7 +/-5.5; median 3 days). Eighteen infants (85.7%) were delivered at term, and 3 (14.3%) before 37th week of gestation. The mean body weight was 3124 g +/– 643.0 with a range between 1250 and 4050 g. Fifteen newborns died during the first week, 3 during the second, and 2 during the third week after birth. One case of stillbirth was also noted. The clinical diagnosis of HLHS was made in 6 cases (28.6%), and the existence of cardiovascular malformations was suspected in additional 9 cases (42.9%).

The mean heart weight was 29.5 g +/– 8.9 with a range between 12.0 and 48.0 g. In all cases gross examination revealed rudimentary left ventricle, as well as hypertrophied and dilated right ventricle and atrium. The left heart valvular abnormalities were as fol-

Fig. 1. Left ventricular fibroelastosis (arrowheads) in hypoplastic left heart syndrome (H+E, 100x)

lows: aortic stenosis with mitral stenosis in 8 cases (38.1%), aortic atresia with mitral stenosis in 7 (33.3%), aortic atresia with mitral atresia in 4 (19.0%), and aortic stenosis with mitral atresia in 2 cases (9.5%). Moreover, patent foramen ovale was found in 17 cases (80.9%), secundum-type atrial septal defect in 4 (19.0%), and ventricular septal defect in 3 cases (14.3%) (one heart showed two defects in ventricular septum). In 9 cases (42.9%) there was an endocardial fibroelastosis of the left ventricle (Fig. 1). The ascending aorta was hypoplastic in all cases, but coarctation of aorta was found in 5 cases (23.8%) (preductal in 4, and postductal in 1 case). The coronary arteries arose from aorta in typical manner. The arterial duct was universally patent.

Coexistence of HLHS with the congenital malformations of other systems was seen in 6 newborns (28.6%). There were both isolated congenital malformations (in 5 cases) i.e. agenesis of the kidney, solitary cyst of the liver, diaphragmatic hernia, intrahepatic biliary atresia, accessory spleen, and multiple ones including microcephaly, hypoplasia of the mandible, polycystic kidney disease and Meckel's diverticulum (in 1 case).

Microscopic examination revealed: recent myocardial necrosis in 8 cases (38.1%) (Fig. 2), interstitial fibrosis in 8 cases (38.1%), and focal mainly subendocardial calcification in 7 cases (33.3%).

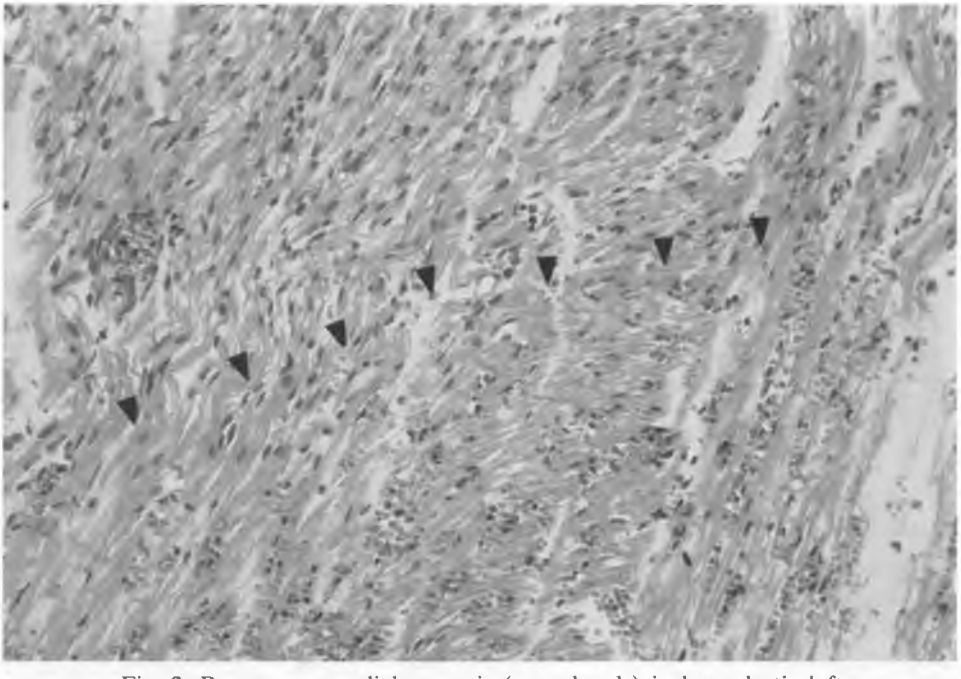

Fig. 2. Recent myocardial necrosis (arrowheads) in hypoplastic left heart syndrome (H+E, 200x)

DISCUSSION

Many different terms were applied for description of cases with dominant underdevelopment of left-sided chambers including hypoplasia of the aortic tract complexes, hypoplastic left ventricle syndrome or the cases were classified according to a few pronounced anomalies e.g. aortic atresia with hypoplasia of the left ventricle, but now the term hypoplastic left heart syndrome is commonly used (11). The severity of malformations encompassed by HLHS varies greatly but all of them cause the obstruction of the left outflow tract (3). Some evidences exist that HLHS results from multiple errors in the early stages of cardiogenesis (2). The congenital anomalies of atrium including premature closure or obliquities of the foramen ovale, anomalous attachment of septum primum, hypoplasia of the eustachian valve, and abnormal orientation of the limbus of the foramen ovale may result in HLHS by reducing inflow to the left side of the heart (9). Either environmental or genetic factors may contribute to the origin of HLHS. Maternal upper respiratory infections during the first trimester of pregnancy are thought to be one of the significant risk factors (14). The association between HLHS and many genetic disorders and chromosomal aneuploidies e.g. trisomy 13, 18 and 21 as well as Turner syndrome was also reported (8).

HLHS seems to be a rare cardiac malformation in our group. The predominance of male infants found in our study is in accordance with other reports (8, 11). Most infants had normal body weight and were delivered at terms and only one case of stillbirth was noted. This suggests that HLHS does not induce preterm delivery and does not interfere with intrauterine development of the foetus. Similar results were obtained by Reis et al. (8), but Rosenthal et al. (10) have found that infants with HLHS were smaller, especially their head volume was disproportionately small in relation to the body weight.

None of the newborns in our series was surgically treated, and none survived longer than one month. This confirms that HLHS is uniformly a fatal condition. The only way for improvement of survival is a staged reconstruction surgery (e.g. modified Norwood procedure), or heart transplantation (2). The current 5-year survival after reconstructive surgery in some specialised medical centres ranged from 58 to 69% (8).

In 15 infants in our study the cardiovascular malformations were diagnosed or suspected clinically, including 6 children with correct diagnosis of HLHS. To our knowledge, in all cases the diagnosis was made during postnatal period on the basis of physical and X-ray examinations, electrocardiograms and echocardiography. At present, the role of early, especially antenatal diagnosis of HLHS made by obstetric ultrasonography followed by foetal echocardiography is emphasised due to its favourable impact on therapeutic option, preoperative condition of neonates or survival after palliative surgery (8, 15).

The most common anatomic subtype of HLHS in our study was aortic stenosis with mitral stenosis (38.1%), however some authors reported the predominance of aortic atresia with mitral atresia among patients with HLHS (4, 5). This discrepancy is difficult to be explained. The clinical evaluation of anatomic subtype of HLHS may be helpful in

the selection of the management options. It seems that patients with aortic atresia and mitral atresia are least likely to do well with reconstructive surgery, and therefore should be directed to transplantation, whereas patients with aortic stenosis and mitral stenosis have better late outcome with reconstruction (5).

Like Aiello et al. (1) in their study based mainly on detailed gross examination of 102 hearts with HLHS, we have also found the coexistence of ventricular septal defects (3 cases) with aortic atresia (in 2 of them) and endocardial fibroelastosis (9 cases) with patent mitral valve (in all of them). We have also observed aortic coarctation in 5 cases, mainly preductal type (in 4 of 5 cases).

We have revealed the coexistence of HLHS with extracardiac congenital malformations in 28.6% of cases. The frequency presented by others ranged between 12 and 37% (8). The discrepancies may result from the selection of the evaluation method (clinical vs. morphological). Reported malformations concerned mainly gastrointestinal and genitourinary tract (8).

At microscopic examination of heart samples we found fresh myocardial necrosis, focal interstitial fibrosis and calcification in total number of 15 cases. These histological findings were also described by others (1, 6, 12). Furthermore, Sugiyama et al. (12) revealed that histological anomalies pointed above were more frequent in cases with mitral stenosis, which is consistent with our observations (in 12 of 15 cases). Some authors suggested that myocardial necrosis especially right ventricular subendocardial infarction, is an important cause of death in children with HLHS, much more significant than constriction of the arterial duct (6). The ischemic lesions may be either the consequence of the deficient coronary arterial perfusion, or the massive administration of vasoactive drugs (1). We have revealed myocardial necrosis in 8 cases only, but our study was based on a small number of samples taken routinely from each heart, and not on serial sections of the whole organ.

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SUMMARY

Hypoplastic left heart syndrome is a group of relatively rare congenital malformations associated with severe obstruction of the left outflow tract. Twenty-one cases of Clinical with the syndrome were found in the autopsy files of the Department of Pathomorphology, Medical University of Lublin in the years 1991-2000. Most children were males, delivered at term, with normal body weight. None of them was surgically treated nor survived longer than one month. The most common subtype of valvular malformations included in the syndrome was aortic stenosis with mitral stenosis. In 15 cases microscopic examination revealed: recent myocardial necrosis, interstitial fibrosis and focal calcification. In 6 cases the syndrome coexisted with the congenital malformations of other systems.

Zespół hipoplazji lewego serca: badanie morfologiczne 21 przypadków autopsyjnych

Zespół hipoplazji lewego serca stanowi grupę stosunkowo rzadkich wad wrodzonych związanych z wybitnym zwężeniem drogi odpływu lewej komory. W materiale autopsyjnym Katedry i Zakładu Patomorfologii Klinicznej AM w Lublinie z lat 1991-2000 stwierdzono 21 przypadków tego zespołu. W większości dotyczył on noworodków płci męskiej, urodzonych o czasie, z prawidłową urodzeniową masą ciała. Żadne z dzieci nie było leczone operacyjnie i nie przeżyło miesiąca. Najczęściej występującym podtypem wad zastawkowych wchodzącym w skład zespołu hipoplazji lewego serca było zwężenie zastawki aortalnej ze zwężeniem zastawki dwudzielnej. W 15 przypadkach w badaniu mikroskopowym stwierdzono wczesną martwicę, włóknienie śródmiąższowe lub ogniskowe zwapnienia. W 6 przypadkach zespół współistniał z zaburzeniami rozwojowymi innych układów.