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CASE REPORT

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Sudden Death in Infancy due to Bicuspid Aortic Valve

ABSTRACT: Symptoms of bicuspid aortic valve usually occur in the age group of 50–70 years, but rarely, it can also lead to sudden unexpected death in infancy and early childhood. The autopsy of a 2-month-old baby boy, found dead in his cot, revealed the heart weight as 25 g, and the macroscopic examination showed the circumference of the aortic valve consisting of two leaflets as 8 mm. The thickness of the left ventricle, right ventricle, and septum was measured as 8, 7, and 10 mm, respectively. Microscopically, the heart revealed hypertrophic changes of myocytes. Subendocardial areas displayed necrosis of myocytes, and severe and diffuse ischemic changes characterized by loss of myofibers and vacuolization. Interstitial pneumonia was identified in the lungs. Death occurred as a result of a congenital bicuspid aortic valve obstructing the left ventricular outflow tract complicated by lung infection. As there are only a few reported cases in infancy, and congenital bicuspid aortic valve can lead to sudden unexpected death, this case is presented to the forensic community.

KEYWORDS: forensic science, forensic pathology, childhood, sudden death, congenital bicuspid aortic valve, myocardial ischemia

Congenital or acquired obstruction of the left ventricular outflow tract can occur at valvular, subvalvular, or supravalvular levels. Aortic valvular stenosis is a common finding in bicuspid aortic valves (1), accompanying 68% of the cases in adults (2). Bicuspid aortic valves, a congenital heart disease, is found in 1–2% of the normal population (3). Symptoms of bicuspid aortic valve usually occur in the age group of 50–70 years, but rarely, it can also display clinical findings or lead to sudden death in infancy or early childhood. The mechanism leading to fusion of leaflets in lesions developing in the intrauterine period is not clear (4).

A case of bicuspid aortic valve obstruction ending in sudden death in an infant is presented. The literature is reviewed, as there are only a few reported cases in infancy, and congenital bicuspid aortic valve can lead to sudden unexpected death, this case is presented to the forensic community.

History

A 2-month-old baby boy with a height of 56 cm and a weight of 3600 g was found dead in his cot. Clinically, rapid respiration, growth retardation, and difficulties in breastfeeding started in the second week after birth were observed.

The echocardiographical examination at 4 weeks of age revealed no atrial septal defect (ASD), ventricular septal defect (VSD), patent ductus arteriosus (PDA), and no coarctation of the aorta. Right ventricular pressure was measured as $80+10=90$ mmHg by Doppler, and the systolic gradient between the left ventricle and the aorta was measured as 74 mmHg by Doppler. The case history displayed clinically diagnosed bicuspid aortic valve, left ventricular outflow obstruction due to aortic valve stenosis, and mitral valve insufficiency. The child was not on any medication. Before the planned surgery could be performed, the mother found the baby dead in his bed in the supine position at around 9 o'clock in the morning. There was no mechanical obstruction with a blanket, the nose area was free, and the bed was medium-hard. Clinically, the baby did not show any findings of infection. Postmortem cultures were negative.

Autopsy Findings

The autopsy was performed at the Morgue Department of the Council of Forensic Medicine. The heart weighed 25 g (expected heart weight for this particular age group: 22–23 g), and the macroscopic examination showed that the aortic valve was formed by two leaflets and that its circumference was 8 mm (Fig. 1). The dimensions of the other valves were normal. The wall thickness of both ventricles and that of the septum were increased. The thickness of the left ventricle, right ventricle, and septum were measured as 8, 7, and 10 mm, respectively. Table 1 compares normal and expected measurements of heart valves and walls in this particular age group with the related measurements in our case (5). Macroscopic examination of the heart revealed white-yellow irregular areas on the free walls of the right and left ventricles and the septum, particularly on the subendocardial area. This case did not show any pathology of the coronary arteries, either macroscopically or microscopically. Cross sections of both lungs were solid, white-yellow, and speckled. The weights of right and left

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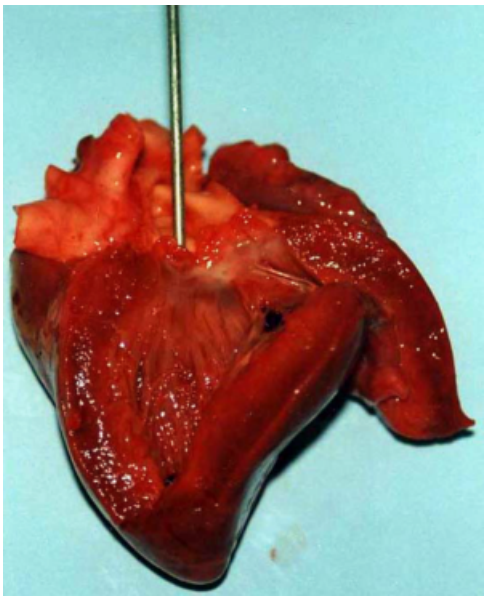

FIG. 1—*Gross heart examination showing two leaflets of the aortic valve at the tip of the pointer. Note: accidental incision of leaflets during autopsy performance.*

lung were 50 and 40 g (normal weights of lungs were 45.5 g for the right lung and 39.5 g for the left lung in this age group) (5).

Histological Findings

Microscopically, the heart revealed hypertrophic changes of the myocytes (Fig. 2). The subendocardial area displayed necrosis of myocytes with severe and diffuse ischemic changes characterized by loss of myofibrils of adjacent myocytes, accompanied by numerous vacuoles in the cytoplasm of these cells (Figs. 3 and 4). In the lungs, there was an interstitial inflammatory reaction, characterized by widened alveolar septa and mononuclear inflammatory infiltration (Fig. 5). There were intraalveolar histiocytes, rare giant cells, and alveolar epithelial cells. Pathological diagnosis of the lungs was interstitial pneumonia. Besides hyperemia, no macroscopic or microscopic pathological changes were observed within other visceral organs.

Toxicological Examination

Barbiturates, salicylates, phenothiazines, benzodiazepines, tricyclic antidepressants, and organophosphates were analyzed in visceral organs, blood, and urine samples. Cocaine, opiates, and cannabis were analyzed in blood and urine samples.

TABLE 1—*Expected heart valve and wall measurements of a 2-month-old baby and the measurements of the presented case.*

	Case (mm)	Normal (mm)
AV	8	21 ± 3 (SD)
PV	24	25 ± 3 (SD)
MV	35	34 ± 5 (SD)
TV	40	40 ± 5 (SD)
RV	7	28 ± 0.8 (SD)
LV	8	6.3 ± 1.5 (SD)

AV, aortic valve circumference; PV, pulmonary valve circumference; MV, mitral valve circumference; TV, tricuspid valve circumference; RV, right ventricle wall thickness; LV, left ventricle wall thickness.

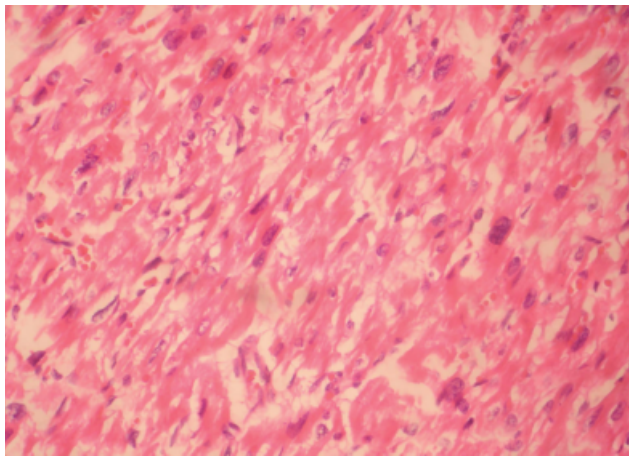

FIG. 2—*Myocardial hypertrophy (H.EX400).*

No toxic substances were identified by postmortem toxicological examination.

The cause of death was determined to be left ventricular outflow obstruction resulting from a bicuspid aortic valve, and interstitial pneumonia.

Discussion

Bicuspid aortic valve abnormality is one of the causes of adult sudden cardiac deaths, but symptoms of bicuspid aortic obstruction are unusual in early childhood (2,4). Sudden and unexpected deaths due to aortic stenosis in childhood are reported in the literature (6–9). However, there is no similar case of sudden death due to aortic stenosis acompanied by bicuspid aortic valve in pediatric age groups.

Aortic obstruction due to a bicuspid aortic valve leads to a pressure gradient of 75–100 mmHg at systole. The increased gradient is the major factor responsible for the high mortality in these cases (2,3). The incidence of sudden death is significantly increased in cases with a gradient higher than 50 mmHg (4,9). In our case, a 74 mmHg systolic gradient was measured between the left ventricle and the aorta by Doppler.

Bicuspid valves usually exhibit normal function at birth and during early life. The symptoms occur usually in elderly ages or

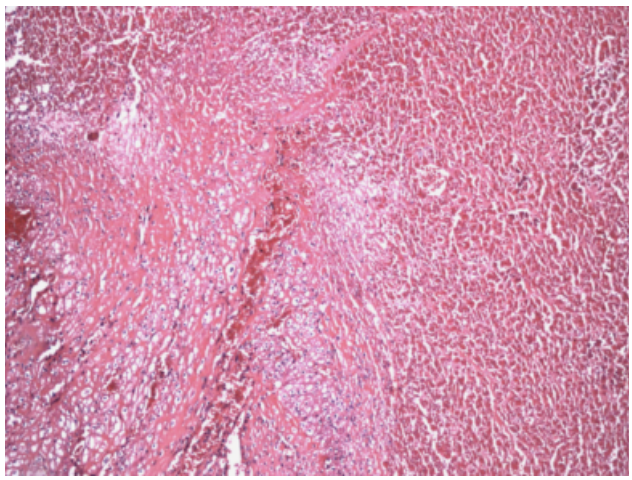

FIG. 3—*Subendocardial myocyte necrosis (H.EX200).*

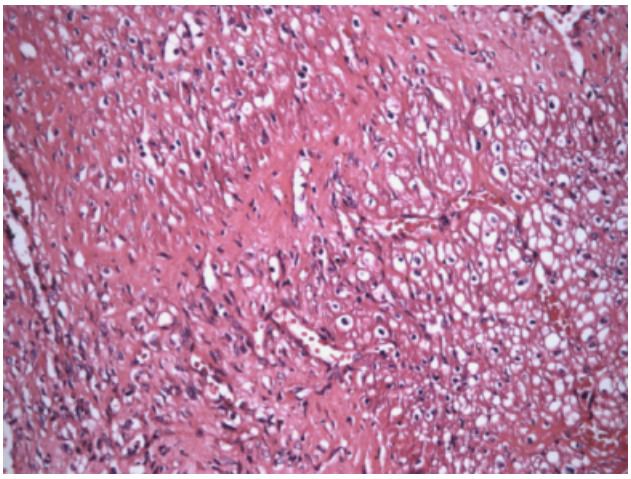

FIG. 4—*Severe ischemic changes characterized by loss of myofibrils of adjacent myocytes and vacuolization (H.EX400).*

under conditions of increased volume load, such as in pregnancy. If it is not diagnosed clinically, deaths due to such congenital heart abnormalities can sometimes imitate sudden suspicious deaths (9). The age of this case and its similarity to sudden infant death syndrome (SIDS) cases is compatible with the cases in the relevant literature. Considering both the clinically and pathologically proven cardiac abnormalities, the accompanying lung infection in this case, SIDS was excluded.

Bicuspid aortic valves may become stenotic (68%) but become regurgitant (19%), or both (13%) (2,3). The expected aortic valve circumference was 21 ± 3 mm for this particular age group, compared with 8 mm in our case. Although the leaflets were equal in size, there was an accompanying stenosis of the aortic valve. The thickness of the left and right ventricular walls was measured as 8 and 7 mm. These findings were demonstrated by echocardiography and autopsy. The mechanism of sudden death in valvular aortic stenosis is believed to be primarily caused by arrhythmias resulting from left ventricular hypertrophy and subendocardial ischemia. Sudden changes in pressure and volume from hypoperfusion based on congenital heart abnormalities in children can lead to ischemic necrosis of the myocardium (1–4). Ischemic myocardial necrosis occurs in patients at any age, primarily in the papillary muscles and subendocardium as they are nourished by the terminal ends of coronary circulation (2,4). Myocardial ischemia can effect both ventricles equally (4). Obstruction of ventricular outflow may worsen gradually and stimulates progressive concentric ventricular hypertrophy. The marked hypertrophy may cause compression of coronary arteries, especially the left anterior descending branch, with resultant myocardial ischemia. Ischemia of the myocardium may give rise to fibrosis along with ventricular arryhthmias and finally sudden death of the patient (2). In our case, both the microscopic and gross examination supported the presence of septal and ventricular hypertrophy simultaneously in Figs. 1 and 2. Left ventricular outflow obstruction and biventricular hypertrophy caused by bicuspid aortic valve obstruction may lead to severe myocardial necrosis of the subendocardial region. In addition, lung infection contributed to death by worsening respiratory failure (1,10,11). In pediatric age groups, coronary artery abnormalities are considered one of the most important causes of severe myocardial ischemia (4), but our case did not show any pathology of the coronary arteries, either macroscopically or microscopically.

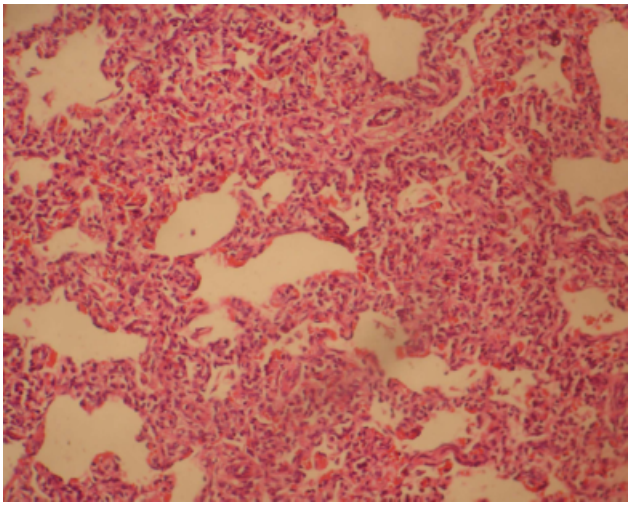

FIG. 5—*Interstitial pneumonia in the lung (H.EX200).*

All infants with congenital aortic and pulmonary outflow obstruction may have a wide range of acute or healed myocardial lesions, including infarcts, fibrotic scars, and dystrophic calcification (4). Coagulation necrosis, contraction band necrosis, myocytolysis (vacuolar degeneration), and wavy appearance of muscle fibers are seen in myocardial damage related to ischemia (1,4). Wavy appearance of muscle fibers may be the initial finding of ischemic damage. Vacuolar degeneration reflects the progressive loss of myofibers (4). This finding is seen in acute or chronic myocardial ischemia, cardiomyopathy, myocarditis, and endocarditis (4). Dystrophic calcification is a common finding of myocardial damage seen in the perinatal period particularly in cases with trisomy 13 and 21. Massive myocardial calcification can also develop in babies exposed to severe prolonged hypoxic ischemia (4). Although myocyte vacuolization was quite evident in our case, no calcification, coagulation necrosis, contraction band necrosis, and wavy muscle fibers were detected. However, fibrotic thickening of the valve was seen on microscopic examination.

Although a bicuspid aortic valves is usually an isolated lesion, it may occasionally be associated with other congenital cardiovascular abnormalities, particularly coarctation of the aorta, aortic hypoplasia, and VSD (2,4). Bicuspid aortic valves and coarctation of the aorta are frequently seen together. It is believed that these malformations result from a single developmental diathesis (12). Cardiovascular malformations, especially coarctation of the aorta and bicuspid aortic valves, are common in patients with Turner's syndrome (13). Liang et al. (14) reported a case of Larsen syndrome accompanying multiple cardiovascular abnormalities such as elongation of the aorta, bicuspid aortic valves, subaortic stenosis, mitral valve prolapse with mitral regurgitation, ASD of the secundum type, and a PDA. Causes of sudden death in children related to bicuspid aortic valves are demonstrated in Table 2.

TABLE 2—*Causes of sudden death in children related to bicuspid aortic valves.*

Coronary artery abnormality
Coarctation of aorta
Aortic root dilatation
Aneurysms of the ascending aorta
Other cardiovascular malformations and complications in various syndromes (Turner syndrome, etc.)

Besides bicuspid aortic valve, aortic stenosis, and mitral insufficiency, no other abnormalities of the heart and main vessels were determined in our case.

Bicuspid aortic valve abnormality usually presents in adults. The present case represents a rare case of sudden death of an infant caused by this cardiac pathology. Like other groups of congenital heart abnormalities, bicuspid aortic valve provides a basis for probable fatal infections including pulmonary infection in children (4). However, intersititial pneumonia in children may develop without any congenital heart abnormalities, e.g., as a result of viruses, leading to respiratory insufficiency. The presence of interstitial pneumonia in this case is considered as the primary cause of death.

Postmortem macroscopic and microscopic examinations are the major requirements to confirm the cause of death in cases of congenital heart disease. In pediatric autopsies, detailed disection will reveal all probable abnormalities and elucidate the underlying cause of cardiac ischemia.

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