Spontaneous closure of small apical muscular ventricular septal defects

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Between 1993 and 2002, apical muscular ventricular septal defects were identified in 99 cases by echocardiographic examination. Spontaneous closure time was analyzed in 42 cases followed up at least two years, retrospectively. The ages of 42 cases ranged between 1 day and 13 years old. Initial examination was performed in 22 cases within the newborn period, in 8 cases between 1 and 6 months of age and in 12 cases at more than 6 months of age. Spontaneous closure was seen in 24 of 42 cases (57.1%) between 1 and 36 months of age, and it was most commonly recorded during the first 6 months. It was remarkable that spontaneous closure occurred in 20 of 22 cases (90%) diagnosed in the neonatal period. Closure was seen in 4 of 8 cases (50%) whose initial examination was performed between 1 and 6 months and in none of the patients diagnosed at more than 6 months of age.

In conclusion, the frequency of spontaneous closure in cases diagnosed in the neonatal period is higher than previously believed. It is advisable to follow up patients to determine spontaneous closure, especially within the first two years of life.

Key words: apical muscular ventricular septal defects, rate of spontaneous closure.

Most of the apical ventricular septal defects (VSDs) have a fairly good prognosis and do not produce cardiac symptoms except for the presence of a murmur[1]. The rate of spontaneous closure of apical VSDs is not defined very well and may have been underestimated in the past[2-5]. Therefore, we retrospectively analyzed the cases with apical VSDs followed up at least two years to determine the frequency of spontaneous closure and to analyze the effect of age at time of diagnosis on the closure rate. This information would be important to predict the natural course of apical VSDs.

Material and Methods

In the period from 1993 to 2002, apical VSD was identified in 99 cases using color flow Doppler echocardiographic examination. All cases were referred to our department for their murmurs. Forty-five of 99 cases were followed up for a minimum of two years. Among them, the rate of spontaneous closure was retrospectively analyzed in 42 cases with small and single apical VSDs. Cardiac physical examination, growth and developmental assessment, and chest roentgenographic and electrocardiographic examinations were performed in all cases. Echocardiographic examination was performed using commercially available echocardiographic equipment (Hewlett Packard, Model Sonos 5500 cardiac imager, Andover Massachusetts, USA and Diagnostic Ultrasound Equipment Model SSH-140 A, Toshiba, Japan) with available transducers. Two dimensional, CW Doppler and color flow Doppler echocardiographic images were obtained at the standard parasternal long-axis view, classic and modified short-axis views and apical, subcostal four-chamber views. Detection of color flow signals crossing the interventricular septum at the distal portion of the right ventricle below the moderator band indicated the presence of an apical muscular VSD. When color imaging showed interventricular shunting, the diagnosis was confirmed by continuous and/or pulsed Doppler analysis, which indicated the timing

and direction of the flow transversing the interventricular septum. Defect sizes were measured as the maximum thickness of color jet at the level of interventricular septum. The patients were follow-up at intervals of 1, 3, and 6 months and at 1 year. All received prophylaxis for infective endocarditis.

Kaplan-Meier analysis was used to show an exponential curve of closure rate.

Results

The ages of 42 cases who were followed-up at least two years ranged between 1 day and 13 years old (mean ± SD: 25.4 ± 43.7 months) at the time of initial examination. Twenty-two of 42 cases (52.3%) were diagnosed in the neonatal period. In 8 cases, initial echocardiographic examination was performed between 1 and 6 months. Twelve cases were diagnosed beyond the first 6 months. In 6 cases, initial echocardiographic examination was performed between 6 and 60 months. Twenty-six of them were female and 16 male (F/M=1.6). All patients were asymptomatic. All cases had normal chest roentgenographic and electrocardiographic findings. Defects were detected only with color flow Doppler echocardiographic imaging in 39 cases (92%); in 3 cases (7.1%) defects were also visible by 2-D imaging. By color flow Doppler imaging, all cases had a single small defect (diameter of VSD, range: 1 to 4 mm) with a narrow small jet flow (Fig. 1). Three cases also had a small sized secundum atrial septal defect as an associated cardiac defect. One case had an atrial septal aneurysm.

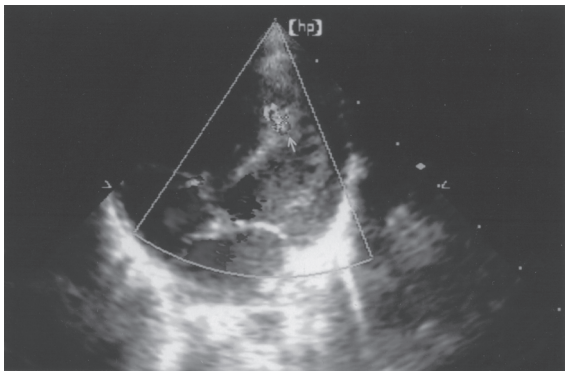

Fig. 1. Color flow signals crossing the interventricular septum at the distal portion of the right ventricle below the moderator band show the presence of a small apical muscular ventricular septal defect (arrows) on an apical four-chamber view.

Patients were followed up to a minimum of 2 years of age and a maximum of 17 years of age, and the duration of follow-up ranged from 1 to 96 months (mean ± SD: 23.5± 25.1 months). Spontaneous closure occurred in 24 of 42 cases (57.1%) who were followed up at least two years. The time of spontaneous closure ranged from 1 to 36 months and it was most commonly recorded during the first 6 months after birth. At the 6th month, the 1st year and at the 18th month, spontaneous closure occurred in 16 (38%), 18 (42%) and 23 (54%) cases, respectively. It was seen in all cases except 1 within the first 18 months; the other defect closed at the 36th month (Table I). It was remarkable that spontaneous closure was seen in 20 of 22 cases (90%) diagnosed in the neonatal period. It was seen in 4 of 8 cases (50%) whose initial examination was performed between 1 and 6 months of ages and in none of the patients diagnosed at more than 6 months of age. The rate of spontaneous closure appears to follow an exponential curve (Fig. 2). There was no record of infective endocarditis in any of the cases.

Table I. Time of Spontaneous Closure During Follow-up Period

Time of the spontaneous closure (months)	Number of patients	Ratio (%)	Cumulative ratio (%)
≤1	2	8.3	8.3
1–≤3	5	20.8	29.1
3–≤6	9	37.5	66.6
6–≤12	2	8.3	75.0
12–≤18	5	20.8	95.8
18–≤36	1	4.1	100
Total	24	100	–

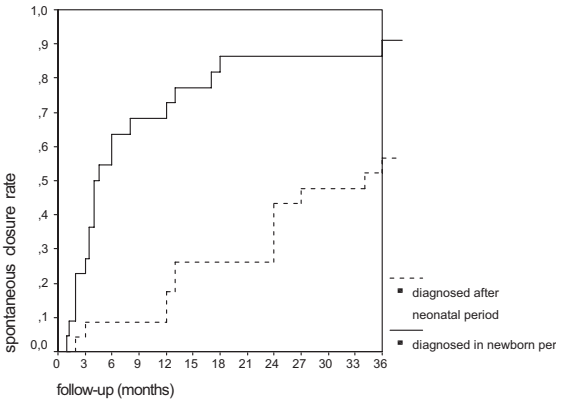

Fig. 2: A Kaplan-Meier exponential curve of spontaneous closure rate.

Discussion

Spontaneous closure of muscular VSDs is a well-known phenomenon and is believed to occur in the majority of cases within the first few years of life[1-10]. In previous clinical studies, the rate of spontaneous closure of muscular VSD has been reported between 24% and 96%. These rates are quite different, but as a common result, most of the small defects close within the few months after birth[6-10]. Some investigators suggested that small defects are not a malformation and that early spontaneous closure of these defects is a normal developmental process[5,11].

There are quite a few clinical reports related to the rate of closure of apical muscular VSDs[1-5,12]. Ramaciotti et al.[2] reported that the rate of closure for muscular VSDs and apical muscular VSDs was 24% and 23%, respectively. They emphasized that spontaneous closure of muscular VSDs was most commonly seen in the first 18 months of life. They also observed that the natural history of single muscular VSD is not influenced by location in the muscular septum. Since a significant percentage of patients were lost to follow-up, this study probably underestimates the true closure rate. Hornberger et al.[3] did not observe closure in patients with apical muscular VSDs. They emphasized that VSDs smaller than 4 mm in size more likely closed spontaneously but apical muscular VSDs tended to persist in their patency. Hiraishi et al.[4] reported that most of the muscular VSDs diagnosed in the neonatal period by color flow Doppler echocardiograpic imaging closed or diminished in size during infancy. They observed that the rate of spontaneous closure during the first 12 months was 76% for all muscular VSDs but 45% for apical muscular VSDs. They mentioned that spontaneous closure most commonly occurred during the first months of life and that the rate was much lower after the first 6 months. They also reported that the frequency of closure was not related to the morphologic features and initial size of the defects. Du et al.[5] screened full-term neonates with color flow Doppler imaging for muscular VSDs. The rate of closure at the end of the first year was found as 84.8%, but only one-fourth of defects were located in the apical region. They found that defects localized in the apical region and defects of >4 mm in size remain patent more than VSDs located elsewhere.

As a developmental process depending on size and location of defects, spontaneous closure of VSDs begins in intrauterine life and continues during the postnatal period, most prominently during the first few months[12-15]. In studies of chick embryo hearts, it was shown that muscular ventricular septum consisted of multiple interventricular channels which were diminished in size or closed progressively during intrauterine life[13,14]. Orie et al.[15] reported that isolated VSDs diagnosed in utero with fetal echocardiographic examination closed in 74% of cases either in the intrauterine period or in the postnatal period. As an important external influencing factor, mechanical pressure produced by contraction may enhance the myocardial growth[16]. Jet flow with high velocity between two ventricles can make up a stimulating factor which produces endothelial thickness, growth and hypertrophy of the muscular septum around the defect[17,18]. Because of the hemiovoid shape of the left ventricle, these effects are observed the least at the apex[16]. Depending on these processes and clinical investigations, it was proposed that the possibility of spontaneous closure of defects located in the apical region can be expected to be lower than observed in other locations[2-5,16].

In contrast to other reports, Sapin et al.[12] and Meberg et al.[19] found high closure rates (75% and 77%) for apical VSDs. Although Sapin et al.[12] did not cite age at first examination, all infants in Meberg et al.'s[19] study with apical muscular VSD were diagnosed in the neonatal period. In our previous study, we observed that spontaneous closure occurred in 10 of 23 apical muscular VSD cases (43.5%) who were followed-up between 3 months and 3.5 years; remarkably 7 of them were diagnosed in the neonatal period[1].

As mentioned in our previous study, and in the studies of Meberg et al.[19] and Sapin et al.[12], we also found in this present study a high closure rate for apical muscular VSDs diagnosed in the neonatal period. It was remarkable that spontaneous closure was seen in 20 of 22 cases (90%) diagnosed in the neonatal period. Closure occurred in 4 of 8 cases whose initial examination was performed between 1 and 6 months and in none of the patients diagnosed at more than 6 months of age. Since few infants were diagnosed after 6 months of age, we could not compare the closure rate in

different age groups. In a previous animal study, it was shown that myocardial cells increase remarkably during the second and fourth weeks after birth and thereafter increase at a much slower rate until 4 months of age[20]. This report and other clinical reports emphasizing that closure of VSDs commonly occurs within the first 6 months may explain why we did not observe closure in cases diagnosed at more than 6 months of age.

In conclusion, the frequency of spontaneous closure of apical muscular VSDs in cases diagnosed in the neonatal period is higher than previously believed. Diagnosing even a small VSD is important because of the risk of infective endocarditis. It is necessary to follow up patients to determine the spontaneous closure, especially within the first two years of life. Because of the high closure rate of apical VSDs diagnosed in the neonatal period and the absence of increased morbidity, parental anxiety should be minimized.

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