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Sudden Death in Mitral Valve Prolapse

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ABSTRACT: Four cases of sudden death in young females with clinical and pathologic features of mitral valve prolapse are discussed. The approach to postmortem examination of the mitral valve is reviewed and various risk factors are stressed. Because of the sudden nature of these deaths, this entity is more commonly seen in medical examiner's populations than hospital autopsies. A practical approach to the investigation of such cases is given.

KEYWORDS: pathology and biology, death, mitral valve prolapse, sudden death

Mitral valve prolapse is a disease of fairly recent recognition, the first report occurring in 1958 [*1*]. The syndrome has many other names, including floppy mitral valve, myxoid mitral valve, and midsystolic click syndrome. It is an extremely common condition and may be found in 5 to 10% of the general population [*2,3*]. The syndrome is characterized by a constellation of symptoms, signs, electrocardiographic changes, various imaging technique abnormalities, and pathologic changes found in the heart [*4,5*].

Sudden death in mitral valve prolapse occurs in adults where the sole finding on autopsy may be thickening or ballooning or both of the cusps of the mitral valve. The victims may or may not have a history of a midsystolic click on auscultation of the heart and electrocardiographic abnormalities. In the past, this condition has been ignored by pathologists, who did not believe it to be significant [*6*]. There is also evidence that other pathologists have misidentified this entity as rheumatic valvular endocarditis or healed bacterial endocarditis [*6*].

Only 60 cases of sudden death in mitral valve prolapse have been reported in the literature [*7-9*]. This would indicate an incidence of 4 to 5 deaths annually for the entire English-speaking world. A number of authors have indicated that the incidence of sudden death in mitral valve prolapse is probably underreported [*6,10,11*]. We report 4 cases of sudden death in mitral valve prolapse occurring in a 6-month period in Cook County, Illinois.

Case Reports

Case 1

A healthy 28-year-old white female had a seizure in her car while paying a parking attendant. Paramedics brought her to the emergency room at a local hospital within minutes after

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her collapse. Upon arrival at the emergency room, she had a weak pulse and ventricular fibrillation. Despite resuscitative measures, the patient died shortly after her arrival to the emergency room.

At autopsy, the body weighed 59.1 kg (130 lbs) and measured 167 cm (66 in.) in length. The heart weighed 323 g (predicted normal weight 237 g). The mitral valve leaflets billowed up into the left atrium. The valve was thickened and opaque with mild interchordal hooding on both the anterior and posterior leaflets (Fig. 1). The free margins of the valve curved inward toward the ventricle. The chordae tendinae were short and thin except in areas where they were fused. The aortic, tricuspid, and pulmonic valves were normal. The thicknesses of the right and left ventricular walls were normal. The coronary arteries pursued their usual anatomic course and displayed no evidence of atherosclerosis. Other findings at autopsy included a hemorrhagic gastritis and several small hemangiomas of the liver.

Case 2

A 26-year-old white female with a history of mitral valve prolapse was found unresponsive on her living room floor with a paint roller in her hand. Open cans of paint were found in the next room. Paramedics transported her to a local hospital where she was pronounced dead on arrival. At age 21, during hospitalization for an ovarian cyst, mitral valve prolapse was discovered. An echocardiogram revealed marked prolapse of the mitral valve leaflets during systole. Her electrocardiogram was normal. She was placed on propranolol (Inderal®) 20 mg 4 times a day.

At autopsy, the body weighed 56.4 kg (124 lbs) and measured 173 cm (68 in.) in length. The heart weighed 283 g (predicted normal weight 226 g). Viewed from the left atrium, both mitral valve leaflets were large and billowy and bulged into the left atrium (Fig. 2). When the heart was opened, it was noted that the valve leaflets were thickened and opaque with moderate interchordal hooding which was much more pronounced on the posterior leaflet (Fig. 3). The chordae tendinae were elongated, thin, and focally fused. There was concentric left

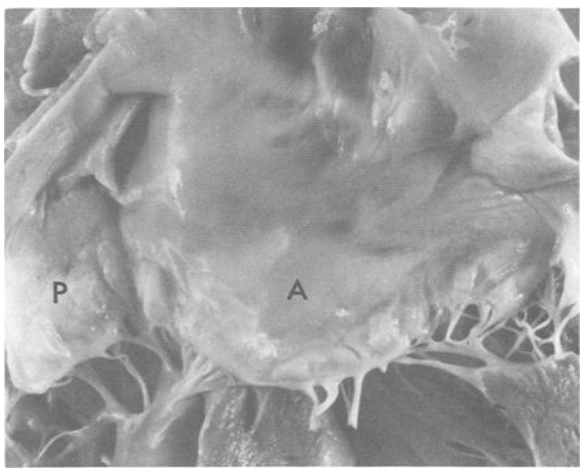

FIG. 1—*Case 1: Mitral valve of heart opened in the conventional manner. The posterior leaflet* (P) *shows diffuse thickening and fibrosis. A gelatinous consistency was noted on the cut edge of the valve. The anterior leaflet* (A) *shows thickening and fibrosis on its free margin except in the region of the posterior commissure, where the leaflet remains thin and translucent. The chordae tendinae are thin and delicate. There is fibrosis on the tips of the papillary muscles.*

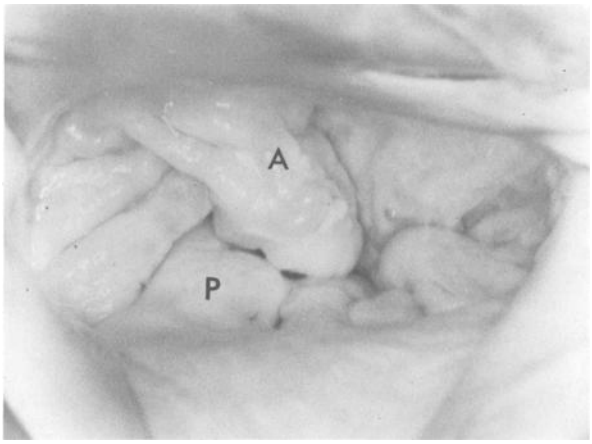

FIG. 2—*Case 2: Mitral valve of heart viewed from left atrium shows markedly enlarged billowy anterior* (A) *and posterior* (P) *valve leaflets with moderate interchordal hooding bulging into the left atrium.*

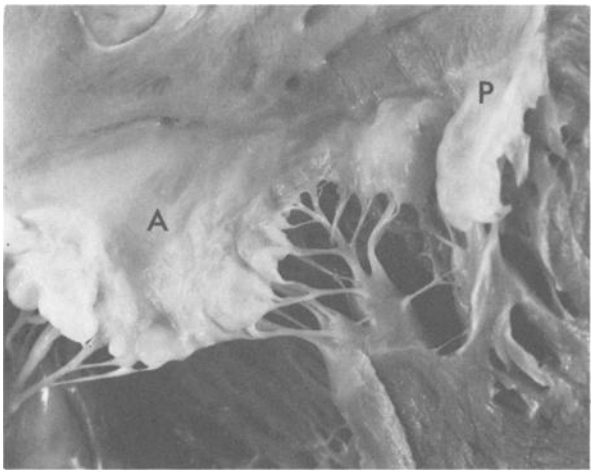

FIG. 3—*Case 2: Mitral valve of heart opened in the conventional manner. The posterior leaflet* (P) *shows diffuse thickening, fibrosis, and interchordal hooding. Note the thickness of the leaflet's cut edge. The anterior leaflet* (A) *shows thickening, fibrosis, and interchordal hooding on its free margin. The valve leaflet in the region of the commissure is thin and translucent. The chordae tendinae are thin and delicate.*

ventricular hypertrophy measuring 2.0 cm in thickness. The right ventricle was normal. The aortic, tricuspid, and pulmonic valves were normal. The coronary arteries pursued their usual anatomic course and displayed no evidence of atherosclerosis. A cortical retention cyst was found in the right kidney. A postmortem propranolol (Inderal) level was 14 ng/mL, which was subtherapeutic.

Case 3

A 40-year-old white female was found dead on the living room sofa. She had complained of chest pains the previous day and had been feeling ill for the week before her death. During a routine employee physical 2 years prior to death, she was found to have asymptomatic multiple premature ventricular contractions with bigeminy and trigeminy, and she was referred to a cardiologist for evaluation. Auscultation of the heart revealed only a midsystolic click without murmur. She had a normal electrocardiogram and treadmill test. Her ejection fraction was 40 to 50%. Holter monitoring confirmed tachycardia with numerous premature ventricular contractions. She was prescribed propranolol (Inderal) 40 mg twice a day, which improved the tachycardia.

At autopsy, the body weighed 76.8 kg (169 lbs) and measured 170 cm (67 in.) in length. The heart weighed 435 g (predicted normal weight 308 g). The mitral valve showed extensive billowing of the leaflets. The valve was thickened and opaque with intermittent areas of translucence (Fig. 4). There was marked interchordal hooding of both valve leaflets. The chordae tendinae were short and delicate except in the area where they were fused. The thicknesses of the right and left ventricles were normal. The coronary arteries pursued their usual anatomic course and displayed no atherosclerosis.

Other findings at autopsy included enlargement of the uterine corpus, a boggy bluish cervix, and dilatation of the fallopian tubes. These findings were suggestive of an intrauterine pregnancy; however, no microscopic evidence of chorionic villi was found, and a postmortem serum human chorionic gonadotropin (beta subunit) determination was negative. A postmortem propranolol (Inderal) level was 302 ng/mL which was slightly above the therapeutic level.

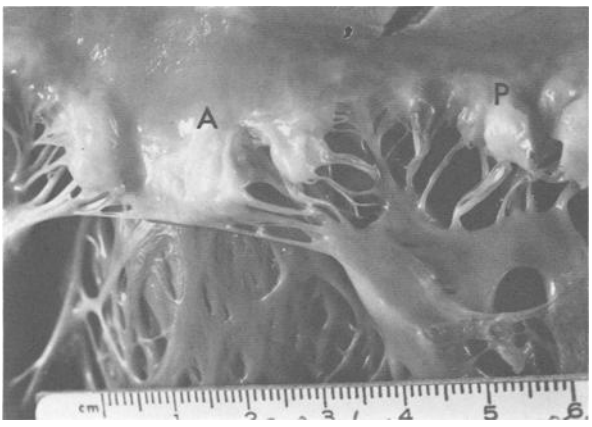

FIG. 4—*Case 3: Mitral valve of heart opened in the conventional manner. The posterior leaflet* (P) *shows diffuse thickening and fibrosis with marked interchordal hooding. The anterior* (A) *leaflet shows areas of thickening, fibrosis, and interchordal hooding on its free margin. Note the thin translucent valve leaflet in the region of the posterior commissure. The chordae tendinae are thin and delicate but show focal areas of fusion.*

Case 4

A 34-year-old white female, in her eighth month of pregnancy, was found lying face down on the kitchen floor by her husband. Two years before death she had seen a cardiologist for chest pains and palpitations. On auscultation of the heart he noted a mid-systolic click. An electrocardiogram showed premature ventricular contractions. An ML mode echocardiogram revealed late systolic prolapse of the posterior mitral leaflet. Holter monitoring for 24 h disclosed numerous ventricular ectopic beats of multifocal origin, some appearing in couples. The patient was placed on propranolol (Inderal) 10 mg three times a day; however, this was discontinued when she became pregnant. During her pregnancy, the patient gained 13.6 kg (30 lbs).

At autopsy, the deceased weighed 80 kg (176 lbs) and measured 178 cm (70 in.) in length. Petechial hemorrhages were noted on the right forehead, right face, the sclerae of both eyes, and the mucosa of the trachea beneath the vocal cords. The heart weighed 398 g (predicted normal weight 266 g). There was a thin, membranous, probe-patent foramen ovale. The left ventricle was dilated. The mitral valve leaflets showed only early changes of mitral prolapse including thickening and opacification (Fig. 5). Retrograde infusion of water into the left ventricle through the aorta showed the posterior mitral valve leaflet to balloon into the left atrium and leak water. There was mild subendocardial fibrosis of the tips of the papillary muscles and of the interventricular septum beneath the anterior mitral leaflet. The aortic, tricuspid, and pulmonic valves were normal. The coronary arteries pursued their usual anatomic course and displayed no evidence of atherosclerosis.

The lungs weighed 1520 g and were markedly edematous. The liver weighed 2290 g; the spleen 460 g. Both organs were congested. The uterine fundus was 32 cm (12.5 in.) above the pubic symphysis. The uterus contained a male fetus weighing 2180 g. A postmortem propranolol (Inderal) determination was negative.

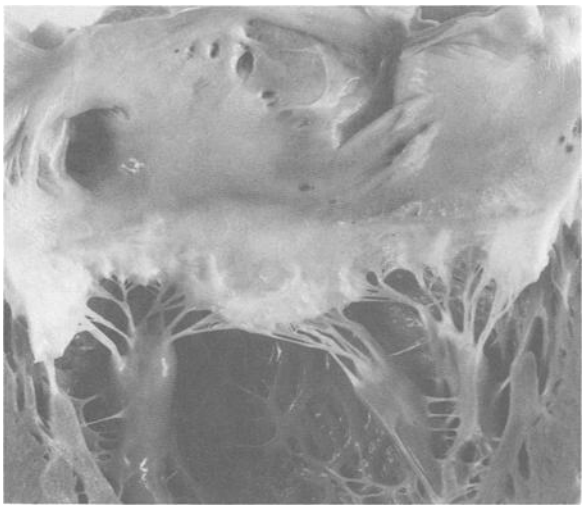

FIG. 5—*Case 4: Mitral valve of the heart opened in the conventional manner. Both mitral leaflets show only early changes of prolapse including thickening and opacification. No interchordal hooding is seen.*

Discussion

Clinical Features of Mitral Valve Prolapse

The majority of people with mitral valve prolapse are asymptomatic and never seek medical attention [*12*]. A family history of mitral valve prolapse or sudden death or both may be helpful in suspecting the entity. There is a wide constellation of signs and symptoms related to the mitral valve prolapse syndrome: these include light-headedness, syncope, chest pain, palpitations, dyspnea, and tachycardia [*12, 13*].

Auscultatory findings usually reveal a characteristic midsystolic click. Other changes reported include a late systolic murmur or pansystolic murmur [*4, 11–13*].

Electrocardiographically documented arrhythmias are primarily ventricular premature complexes with bigeminy or trigeminy. Atrial fibrillation or flutter, ST-T abnormalities, prolongation of the QT interval, atrial or ventricular tachycardia, and ventricular fibrillation have all been reported [*12*].

Holter monitoring, portable electrocardiogram recording, is used to document frequency and occurrence of arrhythmias and whether or not they are exercise related. Some cardiologists use Holter monitoring to check the response of the arrhythmias to medication.

Treadmill exercise testing may show depression of the ST-T segments which indicates myocardial ischemia. Angiography may be necessary in these cases to document the absence or coronary artery disease. Some cardiologists recommend treadmill testing as a routine screening test in patients suspected of mitral valve prolapse to determine whether arrhythmias develop under exercise induced stress.

Echocardiography is a noninvasive procedure used to track the motion of the atrial and ventricular walls and the cardiac valves. The usual finding in mitral valve prolapse is an abrupt, mid-systolic billowing motion of the mitral valve in which the leaflets separate.

Another method for diagnosis of mitral valve prolapse is invasive left ventricular cineangiography, which can show any portion of the mitral leaflets billowing into the mitral valve orifice. There is, however, no generally accepted qualitative criteria for the angiographic diagnosis of mitral valve prolapse [*3, 12*].

Pathology

The underlying pathologic process in mitral valve prolapse is myxomatous proliferation in the spongiosa layer of the involved leaflet that invades and disrupts the fibrosa layer. In the early stage of mitral prolapse, the valve leaflets are delicate, transparent, and sometimes appear gelatinous [*3, 6, 14*]. Later the affected cusps become opaque and white with marked increase in surface area [*3, 14–16*]. The leaflets become more fibrotic and thickened especially on their atrial surfaces [*4, 6, 14*]. As the process continues, aneurysmal dilatation of the leaflet areas between the chordae tendinae occurs [*6, 16*]. This process is known as interchordal hooding and gives the valve a parachute appearance [*3, 6*]. Thickening and fusion of the chordae tendinae may be seen [*3*]. All of these changes may occur on either leaflet, but they are usually more evident on the posterior leaflet [*3, 6*]. Mitral valve prolapse may be differentiated from rheumatic valvular disease because the valve commissures are not involved and there is no inflammatory neovascularization of the cusps [*3*]. In the advanced stages, complications include mitral regurgitation, calcification of the mitral annulus, rupture of chordae tendinae, and infective endocarditis [*4*]. Sudden death may occur in any stage [*7, 14*].

Examination of the Heart

The diagnosis of mitral valve prolapse may be made on the basis of a consistent medical history, the gross pathologic changes seen in the heart, and the exclusion of other causes of

death. Retrograde infusion of water by hose through the aorta into the left ventricle is a simple way of demonstrating mitral valve prolapse at autopsy [*14*]. Pressure fixation of the heart with formalin and examination of the cardiac conducting system, while desirable, are not necessary for establishing the diagnosis. Microscopic examination should confirm the myxoid proliferation in the spongiosa and disruption of the fibrosa of the affected valve leaflet [*3,4,15,17*].

Incidence of Sudden Death

The incidence of sudden death in mitral valve prolapse syndrome varies from 0 to 12.5% in long-term studies [*17–21*]. Young adult white females appear to be at high risk for sudden death in mitral valve prolapse [*18,19*]. Other risk factors include frequent premature ventricular contractions of multifocal origin, ST-T changes on electrocardiogram, marked prolapse on echocardiography, mitral regurgitation, family history of sudden death, and a late systolic or holosystolic murmur [*7,17–20*]. The mechanism of death in these cases is felt to be ventricular arrhythmias [*3,11,13*].

Conclusion

Mitral valve prolapse syndrome is a significant and probably underdiagnosed cause of sudden death, especially in young adult females. Because of the sudden, unexpected nature of these deaths, many will come to the attention of forensic pathologists. It is important that forensic pathologists maintain a high index of suspicion that mitral valve prolapse may be a possibility and that they diligently search for the pathologic changes found in this entity [*6,10*].

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