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CASE REPORT

PATHOLOGY/BIOLOGY

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A Case of Sudden Infant Death Due to a Primary Cardiac Sarcoma

ABSTRACT: The case reported herein concerns the unexpected death of a 3-month-old female newborn who suddenly collapsed in her mother's arms and was dead on arrival at the hospital. The clinical histories of the baby and her parents were negative for symptoms or signs of illness, even those of cardiovascular origin. Furthermore, no clinical appearance of a pathologic status was noted by pediatricians after the birth until the last emergency recovery. The autopsy excluded external and internal signs of violence but revealed a large primary cardiac tumor arising from the free wall of the left ventricle, which had totally invaded the heart causing mitral valve deformation. Histological examination showed a low-grade sarcoma that completely infiltrated the myocardial tissue. The pathogenesis of this sudden infant death was postulated as being owing to a fatal ventricular fibrillation combined with a tumor-related restrictive cardiomyopathy obstructing left ventricular filling.

KEYWORDS: forensic science, sudden death, cardiac tumor, heart, asymptomatic, malignancy, restrictive cardiomyopathy

Medical investigations into sudden death cases are a challenge for the forensic pathologist, especially when related to infancy and because of exceptional illnesses such as primary cardiac tumors. These are very rare diseases, and, on the basis of a large autopsy series, occur at a frequency of approximately 0.02% (1), of which three-quarters are derived from benign forms and one-quarter from malignant forms (2).

Almost all, malignant primary cardiac tumors are sarcomas derived from the mesenchyme (3), forming a wide variety of histological subtypes that occasionally show a particular site predilection in the heart (4). Extraordinarily, sarcomas originating in the coronary arteries have been observed, causing sudden death (5,6).

Primary cardiac sarcomas may arise at any age and they are distinctly unusual in infants and children (7–9), except for rhabdomyosarcomas and fibrosarcomas, which can also present with ventricular involvement (10,11).

In this paper, we present the case of a sudden infant death owing to a primary cardiac tumor identified as a low-grade sarcoma arising from the left ventricular wall.

Case Report

A 3-month-old female newborn suddenly collapsed in her mother's arms at home after the evening feed and was dead on arrival at the hospital, despite prolonged resuscitation activities, where skin paleness, peripheral cyanosis, fixed mydriasis, and irreversible cardiopulmonary arrest were noted.

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Clinical History

The course of the pregnancy and fetal growth and development were regular, characterized by normal biometric parameters. Fetal two-dimensional echocardiography performed at 28 gestational weeks excluded cardiac anomalies and hemodynamic alterations.

The baby was spontaneously born at 39 weeks of gestation, was healthy, with an APGAR index of 8 at the first minute and 9 at the fifth minute, weighed 4050 g, and was 53 cm in length. Also, the baby's clinical history after birth and the parent's anamnesis were negative for signs or symptoms of illness, even those of cardiovascular or neoplastic origin. Furthermore, no clinical signs of pathologies (including abnormal sounds at cardiac auscultation) and a regular pattern of growth were noted by pediatricians during the baby's planned medical examinations at 1 week, 4 weeks, and 2 months of age. As usual for apparently healthy patients, no radiological or sonographic investigations were made during the 3 months of extrauterine life.

After the second month of life, the baby was also treated with the hexavalent vaccine with no complications. Finally, she died suddenly at the third month of life, as reported previously.

Autopsy Findings

The autopsy confirmed the normal growth and good appearance of the baby except for widespread cyanosis, and external signs of violence and internal injuries were also excluded. On the other hand, the autopsy revealed increased dimensions of the heart by up to 8 cm in length, 7 cm in width, and 90 g in weight, and histological sections (Fig. 1) showed a pale, 5 cm-diameter circular shape, and fasciculate neoplasm arising from and completely infiltrating the muscular layer of the left ventricular wall. The left ventricular chamber appeared to be totally invaded, including mitral valve deformation, and the right cavities and the left atrial auricola appeared reduced in volume while the pulmonary artery was enlarged.

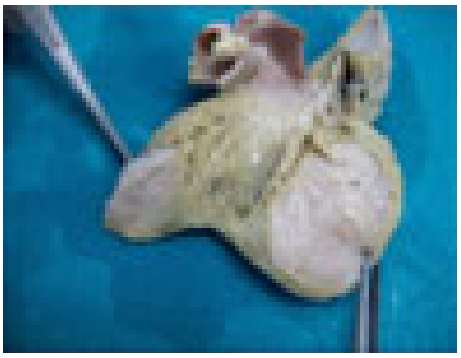

FIG. 1—*The gross photograph of the neoplasm arising within the left ventricle.*

During the autopsy, pulmonary and cerebral congestion and edema were also noted, whereas no signs of illness were found in any of the other organs; lymph node and distant metastases were also excluded.

Histological Examination

Histological samples were obtained by resection of the invaded left ventricular wall and the central portion. First, the tissue sections were routinely stained with hematoxylin and eosin and showed a conspicuous tumoral stroma constituting of a rich vasculature, abundant myxoid matrix-containing stellate cells, and solid areas composed of cellular fascicles of spindle cells (spindle-shaped nuclei, chromatin spread, and rare cytoplasm) mixed with deteriorated myocardial cells (Figs 2 and 3).

Immunohistochemical data were positive for vimentin (fibroblasts), smooth muscle actin (smooth muscle cells), and myoglobin (muscle cells) markers.

A histological diagnosis of low-grade, primary cardiac sarcoma was finally made by combining both the morphological features and the immunoprofile of the tumor, according to the current literature on this topic (12–15).

Discussion

Primary cardiac sarcomas, known as malignant neoplasms of mesenchymal origin, are extremely rare, especially during infancy, whereas under 1 year of age, rhabdomyomas and teratomas, which are benign, comprise about 75% of all primary cardiac neoplasms (3,7–11).

Among the primary cardiac sarcomas, the majority were found to be angiosarcomas followed by undifferentiated sarcomas, except in the pediatric population where rhabdomyosarcomas were the second most prevalent subtype followed at the same level by fibrosarcomas, leiomyosarcomas, and undifferentiated sarcomas (4,7,14).

Defining the pathology and differentiation (vascular, nervous, or muscular) of cardiac sarcomas with confidence, which has been difficult in the past, is now possible with the use of antibodies. Histologic patterns and immunohistochemical studies can in fact aid the categorization of different subtypes, although a high proportion of cardiac sarcomas defy precise classification: the incidence of unclassifiable sarcomas varies from 0% to 50%, depending on the series (15).

The modes of clinical presentation, as well as the pathogenesis of fatal events (7,14), are quite variable and more closely depend on the anatomical site involved and on the size of the neoplasm combined with the effects on the surrounding structures.

Angiosarcomas and liposarcomas are usually found to involve the right side of the heart and the pericardium, causing features of right heart failure and/or cardiac tamponade; undifferentiated sarcomas, osteosarcomas, fibrosarcomas, and leiomyosarcomas most commonly involve the left atrium, and the latter one also involves the pulmonary vessels, the aorta, and the cavae, causing congestive cardiac failure; rhabdomyosarcomas usually involve the myocardium with nonspecific systemic symptoms.

The involvement of the left ventricle by a sarcoma is much rarer than the other locations (14,16). Furthermore, ventricular tumors, which are predominantly intramural, may be asymptomatic. They can affect diastolic function by mimicking a restrictive cardiomyopathy or systolic function by mimicking a dilatative cardiomyopathy. Tumors located within the ventricular myocardium can also cause premature ventricular beats, ventricular tachycardia, ventricular fibrillation, and sudden cardiac death, even if these are very extraordinary events, possibly caused by benign or malignant neoplasms invading the conduction system or impeding blood flow (17).

In our case, clinical anamnesis combined with the autopsy evidence revealed that the death of the baby was completely unexpected and lacked premonitory clinical signs, suggesting that death was owing to a final ventricular fibrillation caused by a tumor-related restrictive cardiomyopathy with total obstruction of filling of the left ventricle.

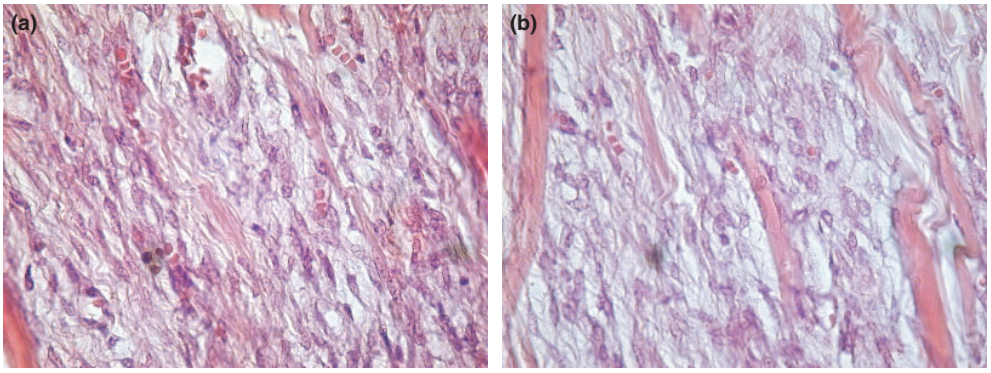

FIG. 2—*The tumoral stroma mixed with deteriorated myocardial cells (hematoxylin and eosin stain). Note the abundant myxoid matrix-containing stellate cells and solid areas composed of cellular fascicles of spindle cells.*

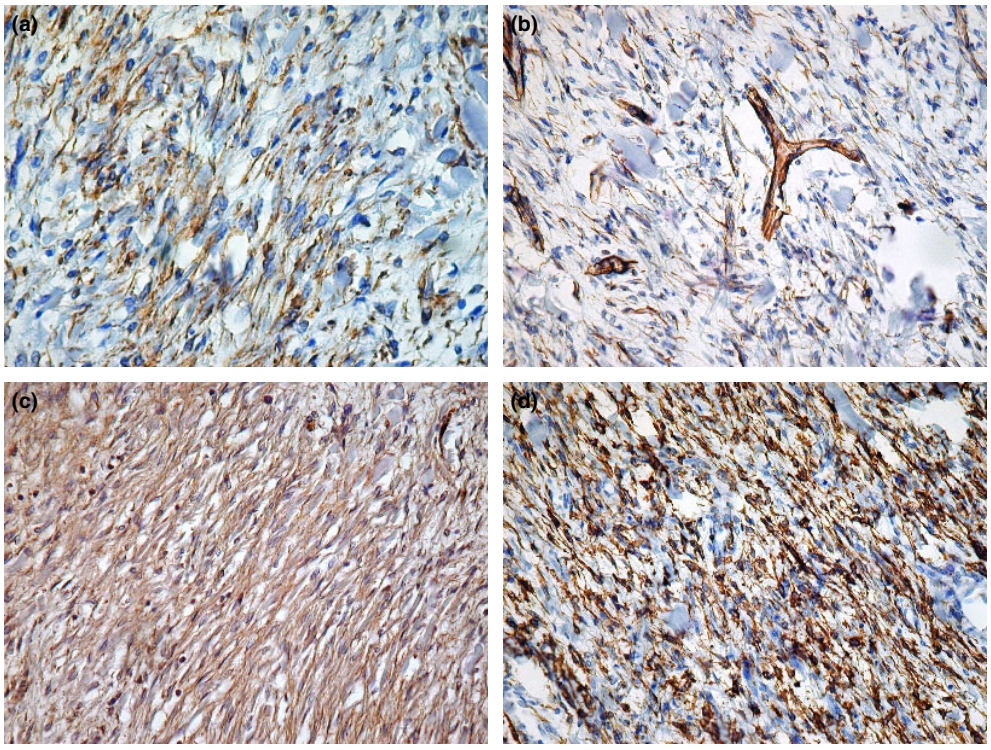

FIG. 3—*Immunohistochemical results showing reactivity to (a,b) vimentin markers (fibroblasts), (c) smooth muscle actin markers (smooth muscle cells), and (d) myoglobin markers (muscle cells).*

The histological pattern and immunohistochemical results allowed us to recognize a low-grade sarcoma, despite the conspicuous dimensions reached in the few months of the newborn's life. Also, considering the fact that the fetal echocardiography, performed at the 28th gestational week, excluded the presence of the neoplasm as well as of other anomalies, the rapid development of the low-grade malignant tumor could be explained by the activity of growth factors able to stimulate cardiomyocyte proliferation (18).

Furthermore, in this case, despite the well-defined malignant nature, we could not identify a specific subtype of sarcoma because the neoplasm had features of fibroblastic cells (positive for vimentin), smooth muscle cells (positive for smooth muscle actin), and muscle cells (positive for myoglobin). This aspect supports the evidence that a high proportion of cardiac sarcomas defy classification despite exhaustive immunohistochemical and ultrastructural analyses because antigenic expression and ultrastructural findings are not specific for a given sarcoma (12,19).

Thus, a nosographic classification of primary cardiac sarcoma may be difficult. Also, performing immunohistochemical analyses as well as a clinical diagnosis could be very difficult considering the variability of the symptoms at clinical presentation until an extremely rare, sudden death, as presented in this case.

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