Congenital rhabdomyoma of the heart

Case report, immunohistochemical observations and review of literature

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A case of congenital rhabdomyoma of the heart in a newborn who died immediately after delivery is presented. The tumour occupied almost all the cavity of the left ventricle. Histological appearance of the lesion was that typical of rhabdomyoma. There was no family history or autopsy findings indicative of tuberous sclerosis.

Immunohistochemistry study of the tumour showed positive staining with myoglobin, with no reactions using antisera developed against S-100 protein, actin, desmin and vimentin.

The incidence, location, clinical presentation, diagnostic procedures, therapy, histogenesis and the nature of this rare tumour are reviwed.

Key words: congenital rhabdomyoma, heart, immunohistochemistry

In general, congenital rhabdomyomas of the heart are considered to be rare tumours. These lesions, however, are usually associated with tuberous sclerosis complex. The term »rhabdomyoma« hae been the most widely used one, but it is misleading, since the lesion is probably not a true neoplasm. Rhabdomyomas are still rarely diagnosed before autopsy. We are reviewing our first case of rhabdomyoma of the heart in a stillborn who died immediately after delivery. Clinicians suspected the congenital heart disease, and autopsy revealed rhabdomyoma of the left ventricle. The term »tumours« is used in the paper to describe this entity, and not in the sense of neoplasmal growth.

CASE REPORT

The mother of the patient was a 20-year-old primipara. The prenatal and past histories were non-contributory. There was no family history of the tuberous sclerosis. She spontaneously delivered an apparently normal full-term boy, weighing 3290 grams, 53 cm in length.

The infant was quite flaccid immediately after delivery and did not respond to any stimuli. Respirations were delayed, respiratory movements were weak due to diaphragmal contractions only. The heart rate was that of bradycardia. The newborn suddenly began to show generalised cyanosis. Oxygen was given with no results, as was confirmed by blood gases data. In spite of assisted respiration, the infant died two hour and 40 minutes after delivery. Clinicians suspected a congenital heart disease.

The autopsy was performed 17 hours after the patient died. The body was that of a moderately well developed, white, male infant, weighing 3140 grams and measuring 53 cm in length. A moderate post-mortem lividity over the dependent portions, as well as generalised cyanosis of the skin were seen. No external anomalies were noted.

About 50 ml of serous fluid was present in the peritoneal cavity. Abdominal organs were placed normally, showing no abnormalities. Diaphragm was displaced lower – in the projection of the 6th rib on the left side, and in the level of the 6th intercostal space on the right side. Cardiomegaly was easy to notice (figure 1.). Only a small portion of the right lung was visible.

Pericardial cavity contained about 80 ml of serous fluid. The heart measured 7 cm in its transverse and 5 cm in its longitudinal diameter, with a marked distortion of the left ventricle. A few small, raised, rounded nodules were seen beneath the epicardinum in the walls of the left venticle, and one more beneath the epicardium in the front wall of the right ventricle. The positions of the large blood vessels were normal, as was the appearance of the valve leaflets. The ductus arteriosus, measuring 3 mm in diameter, connected the pulmonary

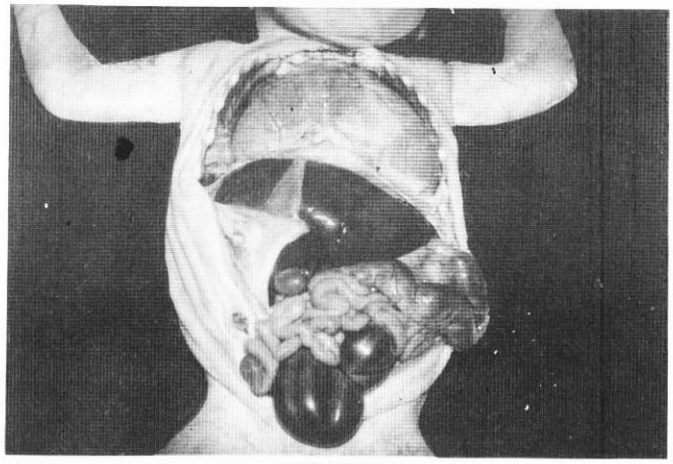

FIGURE 1.
Cardiomegaly duo to congenital rhabdomyoma of the left ventricle wall was clearly visible at autopsy
SLIKA 1.
Na obdukciji uočeno povećanje srca zbog prirođenog rabdomioma stijenke lijeve srčane komore

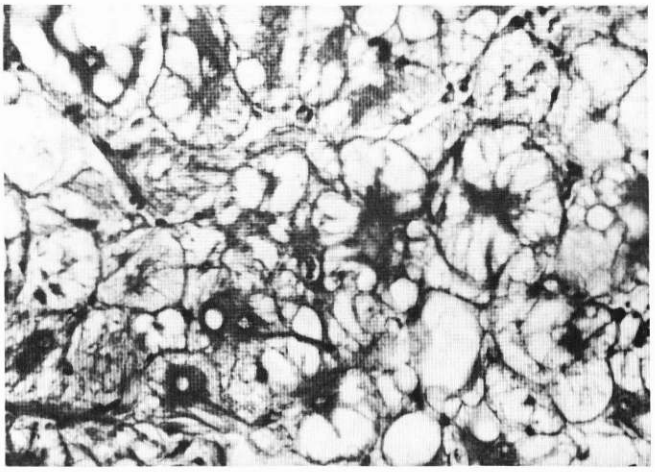

FIGURE 2.
Typical vacuolated appearance of the rhabdomyoma. Numerous »spider cells« are visible within the tumour tissue. Haematoxylin-eosin, 25X
SLIKA 2.
Uobičajeni vakuolizirani izgled tumora. Vide se i brojne stanice nalik na pauka. Hematoksilin-eozin, 25X

artery with the aorta. A homogeneous, well-circuscribed, grayish-pink tumour nodule was observed in the left ventricle myocardium, occupying almost all the cavity of the left ventricle. The septum and the anterior papillary muscle were free of tumour. A nodule in the right ventricle myocardium was of the same appearance, measuring 9 mm in diameter.

The lungs, histologically atelectatic and congested, were compressed by the enlarged heart. Intraalveolar haemorrhages were also noted. The other organs, including the brain, appeared normal on gross inspection. Acute passive congestion was the only finding revealed by histological examination.

Representative blocks of the tumour tissue were placed in a 10% formaldehyde solution, embedded in paraffin and stained with haematoxylin-eosin (HE) and with phosphotungstic acid-haematoxylin (PTAH). Sections of the nodules stained with HE presented typical well-circumscribed, non-incapsulated vacuolated macro and micronodules described in the literature (figure 2). Numerous »spider-cells« were observed within the tumour tissue (figure 3). On both, HE and PTAH stained sections, cross-striations were easi to identify. There were no signs of mitotic activity. The boundaries of the nodules were sharp, shawing no areas of a gradual transition from normal cardiac fibres to the vacuolated cells.

Immunohistochemistry analysis were performed on the formalin-fixed material by application of the PAP tehnique with antibodies directed against the following antigens: S-100 protein, vimentin, desmin and myoglobin. Myoglobin showed strong positive spots in the cells with clearly visible cross-striations. The tumour cells were negative for other antisera used.

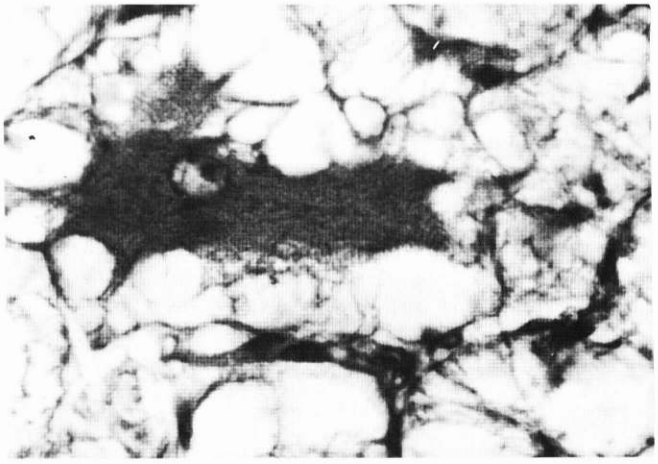

FIGURE 3.
Cross-striations within the cytoplasm of one tumour cell are identified even with haematoxylin-eosin stain. 100X
SLIKA 3.
Poprečna ispruganost citoplazme jedne od tumorskih stanica vidi se i na rutinskom bojenju hematoksilinom i eozinom. 100X

DISCUSSION

Primary tumours of the heart are exceedingly rare. Metastatic tumours of the heart occur with approximately 16 to 40 times the frequency of primary growths, almost exclusively in adults (28,32). Autopsy statistics show primary tumours of the heart to have an incidence of 0,01% to 0,0017% (2,6) 80% of which are benign. Rhabdomyoma is reported to be the commonest space-occupying lesion of the heart in the neonatal period, and during infancy or childhood (6). The youngest subject reported was a 6-month-old fetus and the oldest was 45 years old (20). Most of the cases were associated with tuberous sclerosis complex (12,13,15,16,22,26,27,29, 30,35,38) (31-56%), and sometimes with renal lesions (cystic disease, angiomyolipoma) (4,12,15,38) or tetralogy of Fallot (15). Some authors noticed approximately a 2:1 to a 3:2 predominance of male over female patients (3,12,13,22).

Rhabdomyomas may occur as solitary, multiple or diffuse lesions of the myocardium, usually well demarcated from the surrounding heart muscle fibres, but non-incapsulated. The lesions are almost always multiple (up to 92%), although in some instances multiplicity can only be detected microscopically (1,12,13,22). Cases of diffuse involvement are rarely reported (3,21,40). The tumours may be subepicardial, intramural or subendocardial, and may involve almost every portion of the heart, including the valves (3,6,13,28,30). The typical localisation is, however, the left ventricle wall (6,13).

The cells constituting these lesions tend to be larger than the surrounding myocardial fibres and appear vacuolated, having small nuclei uniform in size. Within the vacuolated areas the »spider cells« may be observed as many-processed cells, characterised by a centrally located mass of finely granular cytoplasm with thin, elongated projections and slender myofibrils extending to periphery. Occasional cells are smaller and have an eosinophilic granular cytoplasm. The cells are filled with a mucopolysacharide (stains positive with PAS reaction) which is considered to be glycogen (3,26).

The clinical presentation of cardiac rhabdomyomas can be explained on the basis of obstruction of blood flow in the right or left side of the heart, myocardial involvement and disturbance of cardiac rhythm. Intramural tumours may be silent or may give conduction aberrations due to infiltration of conduction tissue. Intracavitary tumours by their spece-occupying nature may be responsible for inflow or outflow obstruction (more than 50% of cases) (12,35).

Obstruction of the left ventricular outflow may simulate subaortic stenosis. (2,16,30,31,32) Obstruction of the outflow tract of the right ventricle can give rise to the features of pulmonary stenosis. (2,15) Obstruction of the tricuspidal valve may give rise to shunt reversal and central cyanosis if oval foramen is patent (17,27,30). Mitral valve obstruction hae also been reported (2,37,38). Congestive heart failure due to myocardial involvement is a rather common complication of rhabdomyomas of the heart (16,17,30). Among cardiac arrhythmias, the commonest are paroxysmal atrial tachycardia and atrioventricular block (15,16,17,29,30,35). Occasionally, as in our case, a mild pericardial effusion has been reported (6,10).

When faced with a cyanotic newborn infant, congenital heart disease is often first incriminated as a cause of cyanosis (17,27,38).

Other causes usually include pulycythaemia, sepsis, hypoglycaemia, shock, central nervous system disease, cooling and pulmonary disease (17,27).

Accurate antemortem diagnosis of cardiac tumours is often difficult, especially when tuberous sclerosis symptoms are dominant. Echocardiographic study of the heart is therefore recommended in the routine evaluation of infants and children wiht tuberous sclerosis (8). The diagnosis may be suspected on clinical grounds substantiated by radiology (cardiomegaly), ECG, echocardiography and, when necessary, by angiocardiography (4,8,27,29,30,32,35,38).

Despite its biological benignity, rhabdomyoma has a rather poor prognosis. Between 40% and 53% of the patients are dead at six months of age, and 60-78% by the end of one year (4,13,30). Cases of sudden, unexpected death due to rhabdomyoma of the heart have been described (2,6,40). On the other hand, a few cases of probably spontaneous regression of this non-proliferating tumour were also reported (36,38). Operative removal of the lesion may well result in a cure (2,16,21). The main object of surgery should be to free the outflow tract obstruction, and not to insist on complete eradication of the tumour (35).

The histogenesis of rhabdomyoma is yet an enigma which remains to be cleared. On light microscopy, rhabdomyoma cells remind one of enlarged Purkinje fibres and it has been postulated that the tumour arises from them (9,36). On the other hand, cross-striations, detectable in every rhabdomyoma, as well as the high glycogen content, would appear to be merely a characteristic of embryonal rhabdomyoblast (14). Recent ultrastructural studies have failed to solve this problem. Features common to both, Purkinje and myocardial cells are reported, i.e. sarcomeres, glycogen granules, desmosomes, intercalated discs and bundles of myofibrils (19, 33,34). The present consensus that rhabdomyoma is derived from primitive embryonal cardiac muscle cell is based on ultrastructural findings (7,13,14) and some immunohistochemical features of rhabdomyoma cells i. e. desmin and vimentin, rarely myoglobin positive reaction (5,18). To our knowledge, immunohistochemistry is reported to be performed only in the cases of

extracardiac rhabdomyomas. We can add our observation that cardiac congenital rhabdomyoma stains positively with myoglobin, and do not react with actin, desmin, vimentin and S-100 protein.

The preponderance of multiple as opposed to solitary cardiac rhabdomyomas and their most frequent occurence in infants suggests that the cardiac rhabdomyoma is a hamartoma or malformation (4,12,13,14,28,34) rather than a true neoplasm (12) or a from of glycogen storage defect (9,15,19,22,26). Indeed, the clinical behaviour and the microscopic appearance of these tumours suggest that rhabdomyoma cells lose their mitotic activity, and the lesion may even regress, as was stated earlier. The fact that a rhabdomyoma frequently occurs concurrently with a number of different malformations speaks in favour of hamartomatous nature.

Extracardiac rhabdomyomas occur at wo general locations: orocervical and vulvovaginal (11). Intracranial (41), mediastinal (25), and retroperitoneal (39) lesions are also reported. Whether the cardiac and axtracardiac rhabdomyomas are identical cannot be answered (24). However, some differences are already found on the ultrastructural level (19,23,18), and – as well previously stated – in immunohistochemical expression. Extracardiac rhabdomyomas, furthermore, are not associated with tuberous sclerosis or any known syndrome.

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Sažetak

PRIRODENI RABDOMIOMI SRCA
Prikaz bolesnika, imunohistokemijska analiza i pregled literature

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Odjel za patologiju, Opća bolnica Osijek

Prikazan je slučaj novorođenčeta koje je umrlo neposredno poslije rođenja pod kliničkom sumnjom na prirođenu srčanu grešku. Na obdukciji je pronađeno povećano srce koje je komprimiralo tkivo oba plućna krila. Na ostalim organima ni mikroskopski niti histološki nisu pronađene patološke pojave. Srčani mišić lijeve komore bio je prožet tumorskim tkivom koje je gotovo u cijelosti ispunilo šupljinu lijeve komore. Histološki, tumor je bio građen od dobro ograničenih, neočahurenih čvorova s tipičnim vakuoliziranim stanicama i tzv. stanicama nalik na pauka. U citoplazmama pojedinih stanica opažena je dobro izražena poprečna ispruganost. Mitoza u tumorskom tkivu nije bilo. Nakon provedene imunohistokemijske analize PAP metodom uz primjenu antitijela na S-100 protein, vimentin, desmin i mioglobin, očitana je jasno pozitivna reakcija samo nakon primjene antitijela na mioglobin, upravo u stanicama s izraženom poprečnom ispruganošću.

Rabdomiomi u srcu pojavljuju se kao solitarne, multiple ili katkad i difuzne lezije srčanog mišića, a najčešće su udružene s tuberkuloznom sklerozom, dok se nešto rjeđe pojavljuju uz lezije bubrega ili tetralogiju Fallot. Klinički, rabdomiom srca može biti i asimptomatski, ali se češće prikazuje ili kao lezija koja opstruira protok krvi kroz srce ili izaziva različite poremećaje srčanog ritma. Zbog česte povezanosti s tuberkuloznom sklerozom u ovih se bolesnika preporučuje ultrazvučni pregled srca. Usprkos biološkoj benignosti ove lezije, do navršene prve godine života umire 60-78% oboljelih.

Prema izgledu i podrijetlu, rabdomiomi srca razlikuju se od rabdomioma koji se pojavljuju na drugim lokalizacijama. Dok se za ekstrakardijalne rabdomiome sa sigurnošću može tvrditi da su tumorske proliferacije, srčani rabdomiomi mogli bi spadati u skupinu hamartoma. Histogenetsko podrijetlo srčanih rabdomioma još nije poznato. Dio autora smatra da tumor potječe od Purkineovih stanica, dok većina tvrdi da je embrionalni rabdomioblast ishodišna stanica.

Ključne riječi: imunohistokemija, srce, prirođeni rabdomiom

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