

Secondary Cardiac Pleomorphic Rhabdomyosarcoma – A Case Report and Review of Literature

SANDHYA ILANTHODI, ARAVIND PALLIPADY, JAYAPRAKASH K, FRANCIS N P MONTEIRO

ABSTRACT

Pleomorphic rhabdomyosarcoma (PRMS) is a rare and controversial tumour of the skeletal muscle phenotype. Although it has been recognized that aggressive soft tissue sarcomas may give rise to cardiac metastases, these manifestations are usually late and clinically silent, they being the prevailing findings in exceptional cases. This report describes the occurrence of a massive cardiac metastasis which was secondary to the PRMS of the lower limbs, for which the patient had undergone amputation.

This manifestation was the cause of rapidly progressive congestive heart failure and together with the unusual occurrence of autoimmune thrombocytopaenia, this led to a difficult patient care with a significantly negative influence on the outcome.

Key Words: Pleomorphic rhabdomyosarcoma, Cardiac metastasis, Sarcomas, Metastasis

INTRODUCTION

Primary cardiac tumours are rare, with an incidence of 0.0017 to 0.019% [1]. It is important to note that metastatic tumours in the heart are 20 to 30 times commoner than the primary tumours [2]. Approximately 200 sarcomas which primarily involved the myocardium have been recorded, 31 of which were rhabdomyosarcomas [3]. The name 'rhabdomyosarcoma' is derived from the Greek words 'rhabdo', which means rod shape, and myo, which means muscle. Although Weber first described rhabdomyosarcoma in 1854, a clear histological definition was not available until 1946, when Arthur Purdy Stout recognized rhabdomyosarcoma as a distinct entity [4]. Rhabdomyosarcomas are high-grade sarcomas that exhibit varying degrees of skeletal muscle differentiation. Collectively, they have accounted for 2.2% of all soft tissue tumours of the foot in the Memorial Sloan-Kettering series and 3.6% of those that were malignant [5]. Although rhabdomyosarcomas may arise anywhere in the body, they occur predominantly in three regions: the head and neck, the genitourinary tract and the retroperitoneum, and in the upper and lower extremities. The head and neck is the principal location of rhabdomyosarcoma. After the head and neck, the genitourinary tract is the second most common site for rhabdomyosarcoma. Rare rhabdomyosarcomas of virtually all subtypes have also been described in the anterior mediastinum, lung, bone and skin [4]. Rhabdomyosarcoma is rare in adults [6]. The most common subtype of rhabdomyosarcoma which occurs in adults, however, is the pleomorphic type. Other rhabdomyosarcoma subtypes that occur rarely in adults include the predominantly juvenile alveolar and embryonal, the spindle cell subtype of the embryonal, and the rare adult clear cell and sclerosing pseudovascular subtypes [7]. Each of these subtypes occur in characteristic age groups. Because of the few recorded instances and the unusually diffuse nature of the metastasis which we encountered, the following additional case is being reported.

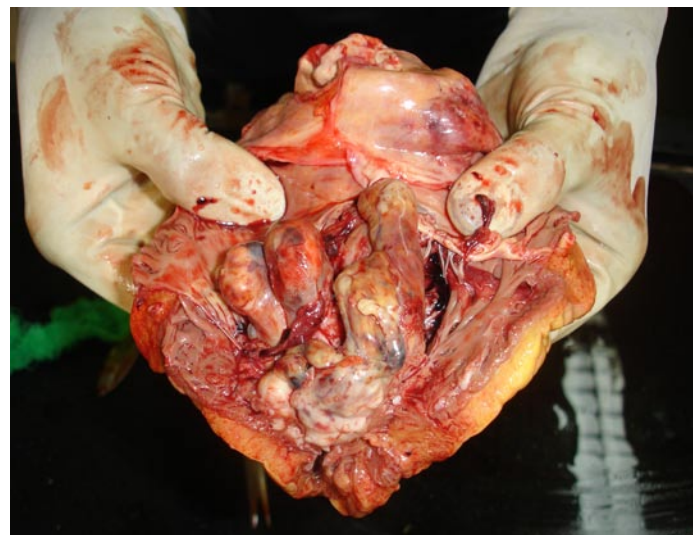
CASE REPORT

A 55 years old man presented with a 3 week history of right-sided pleuritic chest pain, high fever, night sweats and cough with expectoration. He was extremely breathless, with poor oxygenation and his blood tests showed the presence of anaemia and thrombocytopaenia. He had undergone the amputation of the left leg 2 years back for some malignancy, for which he had no hospital records

in his possession.

His chest X-ray showed haziness in the upper, middle and lower lobes. An ultrasonographical study of the abdomen revealed a large retroperitoneal mass which was associated with other smaller masses in the perirenal region. A trans-thoracic echocardiogram confirmed the presence of a large right ventricular mass filling the entire right ventricle. Ultrasound guided fine needle aspiration of the abdominal mass confirmed it to be a soft tissue sarcoma. Due to extensive metastatic deposits and the poor general condition of the patient, even before further intervention, the patient succumbed to death.

Because of the diffuse nature of the metastasis, the aggrieved relatives wanted a clinical autopsy to be done, to find out the exact type of malignancy. The heart weighed 450 grams and it was occupied by a massive yellow tan-to-white, firm tumour expanding from the right ventricular wall into the cardiac cavity [Table/Fig 1].

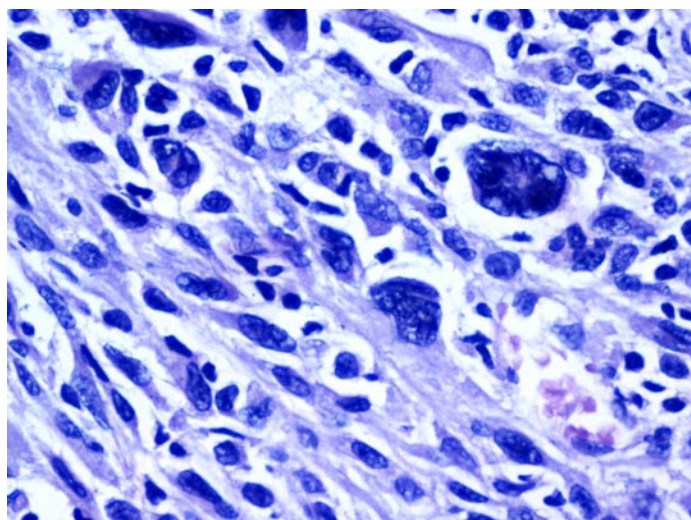


[Table/Fig 1]: Heart revealing pedunculated growth in the right ventricle at autopsy.

The tumour projected into the right ventricle as a multiple pedunculated mass, measuring 2cm x 1.5cm to 3cm x 1cm, over an area of 7cm x 6cm. The myocardium which was uninvolved by the tumour, measured up to 0.5cm in thickness in the right ventricle and 2.0 cm in the left ventricle. The valves and the coronary arteries were normal. The cut surface of the pedunculated mass was fleshy, with necrotic and haemorrhagic areas. There was a retroperitoneal mass with a bosselated surface, measuring 30cm x 15cm x 8cm. The cut surface was fleshy, with areas of necrosis and haemorrhage. The perirenal metastatic deposits measured 7cm x 5cm x 4cm and were similar in appearance, both externally and on the cut surface. The cut surface of the lung showed abundant exudative material oozing out. Grossly, no metastasis was noted in the lung.

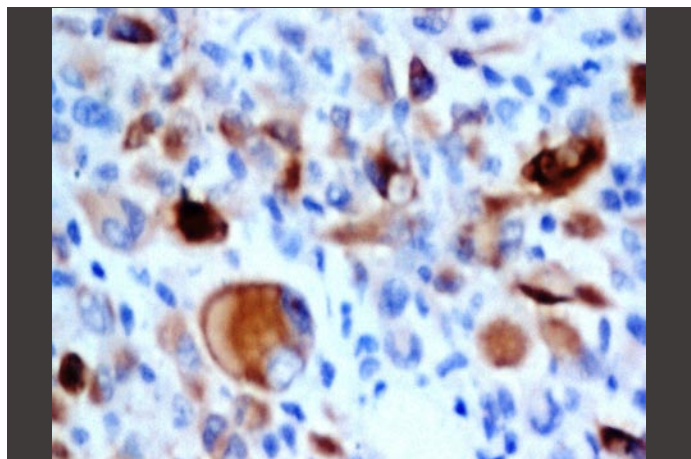
MATERIALS AND METHODOLOGY

After the death of the patient, a clinical autopsy was done. All the organs were inspected thoroughly for metastatic foci. All the metastatic foci were subjected to histopathological examination, with special stains and immunohistochemistry for confirmation. Metastatic deposits were noted in the heart and the retroperitoneum. The lungs were spared of the metastases, but they showed extensive sepsis. A microscopic examination of the tumour revealed a tumour consisting of sheets of loosely arranged, haphazardly oriented, spindle shaped, large, round, pleomorphic cells with eccentric hyperchromatic nuclei and deeply eosinophilic fibrillar cytoplasm. [Table/Fig 2]



[Table/Fig 2]: Microscopy of the tumor showing pleomorphic rhabdomyoblasts (Haematoxylin & Eosin 40X)

Large tad pole and racket shaped rhabdomyoblasts along with large bizarre tumour giant cells were noted. Large bizarre cells with fibrillar cytoplasm and eccentric nuclei showed desmin immunoreactivity, thus suggesting a diagnosis of rhabdomyosarcoma. [Table/Fig 3]



[Table/Fig 3]: Immunohistochemical stain desmin reactivity seen as brown colour in the tumour cells (40X)

The advanced age of the patient and the microscopic features with desmin immunoreactivity, helped us in identifying this tumour as pleomorphic rhabdomyosarcoma. The microscopic features of the retroperitoneal mass and the perirenal masses were similar to that of the cardiac mass. The gross and microscopic examination of the gastrointestinal tract, liver, spleen, pancreas, prostate, testes, thyroid, and the bone marrow showed no additional abnormality. The death was attributed to secondary cardiac pleomorphic rhabdomyosarcoma.

DISCUSSION

The National Cancer Institute classified Rhabdomyosarcoma into three broad categories, which included Embryonal rhabdomyosarcoma, Alveolar rhabdomyosarcoma and Pleomorphic rhabdomyosarcoma. The embryonal subtype of rhabdomyosarcoma accounts for approximately 49% of all the rhabdomyosarcomas [4]. It mostly affects children who are younger than 10 years of age, but it also occurs in adolescents and young adults; it is rare in patients who are older than 40 years of age. This RMS variant arises most commonly in the soft tissue of the head and neck or in the genitourinary system; however, roughly 9% of these rhabdomyosarcomas occur in the skeletal musculature of the extremities [8]. Genetic studies have identified allelic losses in the chromosomal region 11p15 in most cases of embryonal RMS [9].

Histologically, "embryonal rhabdomyosarcoma" bears a close resemblance to various stages in the embryogenesis of the normal skeletal muscle, but its pattern is much more variable, ranging from poorly differentiated tumours that are difficult to diagnose without immunohistochemical or electron microscopic examination, to well differentiated neoplasms that resemble the foetal muscle [4]. Alveolar rhabdomyosarcoma is the second most common subtype, accounting for approximately 31% of all the rhabdomyosarcomas [8]. Unlike embryonal RMS, the alveolar variant is more variable with regards to its sites of predilection. Though this neoplasm may arise in any location, almost 40% of such tumours are located in the extremities [10]. There were 3 alveolar sarcomas which have been described among the 401 soft tissue tumours of the foot, which have been published in the Memorial Sloan-Kettering series [5]. Alveolar RMS demonstrates a higher level of aggressiveness than the embryonal subtype. Most cases of alveolar RMS carry the genetic translocation $t(2;13)$ and less commonly, they show the translocation $t(1;13)$ [11]. Histologically, alveolar rhabdomyosarcoma is composed largely of ill-defined aggregates of poorly differentiated round or oval tumour cells that frequently show the central loss of cellular cohesion and degeneration and necrosis. In rare instances, viable cells are virtually absent, and the tumour consists merely of a coarse sieve-like or honeycomb-like meshwork of thick fibrous trabeculae surrounding small, loosely textured groups of severely degenerated cells with pyknotic nuclei and necrotic cellular debris [4].

In contrast to the embryonal and alveolar RMS, the pleomorphic variant is found exclusively in adults, most of whom are middle-aged or older [12]. There is a slight male predominance [12]. The most common location for pleomorphic RMS is the deep soft tissue of the lower extremities; however, they may virtually arise anywhere [13]. The tumour arises most commonly in the skeletal muscle of the extremities, particularly in the thigh, though rare tumours arise in the chest wall musculature, in the retro peritoneum, and in the head and neck [12], [13]. PRMS usually presents with a rapidly growing painless mass with a history of several months duration, sometimes with pulmonary metastasis. However, it is interesting to note that in this case, the patient had no metastasis in the lung, when he otherwise had extensive metastasis including those in the heart. The tumours are usually large (> 10 cm), and most are fleshy, well-circumscribed, intramuscular masses with focal haemorrhage and extensive necrosis. Histologically, pleomorphic rhabdomyosarcomas can be distinguished from embryonal and alveolar rhabdomyosarcomas by the association of loosely arranged, haphazardly oriented, large, round or pleomorphic cells with hyperchromatic

nuclei and deeply eosinophilic cytoplasm. The presence of large bizarre tumour cells with deeply eosinophilic cytoplasm is quite helpful in arriving at the diagnosis of the pleomorphic subtype. These cells are classically immunoreactive to desmin. In embryonal rhabdomyosarcomas, there are racket-shaped and tadpole-shaped rhabdomyoblasts, but they are generally larger with more irregular outlines. Cells with cross-striations, with focal pleomorphic features, are commonly found in embryonal rhabdomyosarcomas, but these are rare in adult pleomorphic rhabdomyosarcomas [14].

The popularity of PRMS waxed and waned with the introduction of electron microscopy and the entity of malignant fibrous histiocytoma, respectively [12]. Immunohistochemical antibodies were applied to these tumours in the early 1980s predominantly, by using myoglobin, desmin, creatinine kinase subunit M, and various actins to detect the skeletal muscle differentiation [15]. With the exception of myoglobin, a protein which is found late in the embryonic muscle development and which requires experienced interpretation, all other antibodies were found to be nonspecific for the skeletal muscle phenotype. In the most recent decade, several researchers in their several series of experiments, have used an immunohistochemical approach to identify PRMS [12], [13], [16].

In 1993, fast myosin, a skeletal muscle-specific marker, was added to the repertoire for PRMS [12]. MyoD1, the product of a gene which is activated early in myogenesis was discussed as a skeletal muscle-specific marker, but it was not applied to pleomorphic rhabdomyosarcoma until 1995 [16], [17]. Myf4, a skeletal muscle-specific myogenin, has only been studied on four cases of PRMS in the literature [17].

Metastatic heart involvement is gaining increased attention. It has been recognized that heart metastases are more common (at least 2% of all the disseminated cancers) than it was previously thought. However, secondary heart tumours, especially those arising in the context of the cardiac wall, usually remain silent and rarely gain clinical attention. Nevertheless, the obstruction of the ventricular inflow or the outflow tract may occur, and in exceptional cases, the heart involvement substantially contributes to the mechanism of death, as in our patient.

In this case, the cause for the amputation of the leg may be attributed to the primary PRMS, which had metastasized into the cardiac and the abdominal structures. This case has been presented for its unusual metastatic involvement, along with the use of immunohistochemistry for its confirmation.

REFERENCES:

- [1] Shanmugam G. Primary cardiac sarcoma. *Eur J Cardiothorac Surg* 2006; 29:925 - 932.
- [2] Devbhondari MP, Meraj S, Jones MJ, Kadir I, Bridgewater B. Primary cardiac sarcoma: reports of two cases and a review of current literature. *J Cardiothorac Surg* 2007; 2:34.
- [3] Fine G. Neoplasms of the pericardium and heart. In *Pathology of the Heart and Blood Vessels*. 3rd Edition. Canada: Charles C Thomas; 1968; 851-883
- [4] Weiss SW, Goldblum JR, Enzinger FM. *Enzinger and Weiss's soft tissue tumors*. 4th ed. Missouri: Mosby Inc.; 2001: pp 785-836.
- [5] Bakotic BW, Borkowski P. Primary soft-tissue neoplasms of the foot: The clinicopathologic features of 401 cases. *J Foot Ankle Surg* 2001; 40:28-35.
- [6] Yang GCH, Tao LC. *Transabdominal fine-needle aspiration biopsy: a colour atlas and monograph*. 2nd Edition. Singapore: World Scientific Publishing Co. 2007. 234-285
- [7] Miettinen M. Rhabdomyosarcoma in patients older than 40 years of age. *Cancer* 1988; 62:2060-2065
- [8] Newton WA Jr, Soule EH, Hamoudi AB, Reiman HM, Shimada H, Beltangady M, et al. Histopathology of childhood sarcomas, Intergroup Rhabdomyosarcoma. Studies I and II: clinicopathologic correlation. *J Clin Oncol* 1988; 6: 67-75.
- [9] Koufos A, Hansen MF, Copeland NG, Jenkins NA, Lampkin BC, Cavenee WK: Loss of heterozygosity in three embryonal tumours suggests a common pathogenetic mechanism. *Nature* 1985; 316:330-334.
- [10] Harms D. Alveolar rhabdomyosarcoma: a prognostically unfavorable rhabdomyosarcoma type and its necessary distinction from embryonal rhabdomyosarcoma. *Curr Top Pathol* 1995; 89:273-296.
- [11] Barr FG. Molecular genetics and pathogenesis of rhabdomyosarcoma. *J Pediatr Hematol Oncol* 1997; 19:483-491.
- [12] Gaffney EF, Devan PA, Fletcher CDM. Pleomorphic rhabdomyosarcoma in adulthood: analysis of 11 cases with definition of diagnostic criteria. *Am J Surg Pathol* 1993;17:601-607.
- [13] Schurch W, Begin LR, Seemayer TA, Legace R, Boivin JC, Lamoureux C, et al. Pleomorphic soft tissue myogenic sarcomas of adulthood. A reappraisal in the mid-1990's. *Am J Surg Pathol* 1996;20(2):131-147.
- [14] Kodet R, Newton WA Jr, Hamoudi AB, Asmar L, Jacobs DL, Maurer HM. Childhood rhabdomyosarcoma with anaplastic (pleomorphic) features: a report of the Intergroup Rhabdomyosarcoma Study. *Am J Surg Pathol* 1993;17(5):443-53.
- [15] Enzinger PM, Shiraki M. Alveolar rhabdomyosarcoma: an analysis of 110 cases. *Cancer* 1969; 24:18-31.
- [16] Wesche WA, Fletcher CDM, Dias P, Houghton PJ, Parham DM. Immunohistochemistry of myoD1 in adult pleomorphic soft tissue sarcomas. *Am J Surg Pathol* 1995;19(3):261-269.
- [17] Dias P, Parham DM, Shapiro DN, Tapscott ST, Houghton PJ. Monoclonal antibodies to the myogenic regulatory protein myoD1: epitope mapping a diagnostic utility. *Cancer Research* 1992;52:6431-6439.

AUTHORS:

1. Dr. SANDHYA ILANTHODI
2. Dr. ARAVIND PALLIPADY
3. Dr. JAYAPRAKASH K
4. Dr. FRANCIS N P MONTEIRO

NAME OF DEPARTMENT(S) / INSTITUTION(S) TO WHICH THE WORK IS ATTRIBUTED:

Dept of Pathology, A.J. Institute of Medical Sciences, Mangalore, India.

Dept of Forensic Medicine and Toxicology, A.J. Institute of Medical Sciences, Mangalore, India.

NAME, ADDRESS, PHONE, E-MAIL ID OF THE CORRESPONDING AUTHOR:

Dr. Sandhya Ilanthodi, Faculty, Dept of Pathology, A.J. Institute of Medical Sciences, Mangalore-575004, India.

Email: drsandhyai@rediffmail.com, Phone: +91-9611873871

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