

Case Report

Primary pericardial primitive neuroectodermal tumor: a case report and review of literature

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Received January 15, 2018; Accepted February 23, 2018; Epub April 1, 2018; Published April 15, 2018

Abstract: Primitive neuroectodermal tumor (PNET) is a rare, high-grade malignant tumor that most commonly occurs in the peripheral nervous system, bone, and deep soft tissues. It is extremely rare in the pericardium. To the best of our knowledge, only two patients with primary PNET of the pericardium have been reported so far in the literature. We report a case of PNET of the pericardium in a 13-year-old female patient, who was referred to our hospital for dyspnea and edema of lower extremities. Computer tomography (CT) scanning revealed a soft tissue mass in the pericardium which was surgically removed. The diagnosis of PNET was confirmed by histology, immunohistochemistry and molecular study. The patient was alive and well at follow up 8 months after surgery.

Keywords: Pericardium, primitive neuroectodermal tumor, CD99, EWSR-1

Introduction

Primary malignant tumors of the heart and pericardium are extremely rare with prevalence of about 0.001%-0.3% [1, 2]. Among these rare malignancies, primitive neuroectodermal tumor (PNET) is even more infrequent. PNET is a group of rare, aggressive and highly malignant neoplasms thought to be derived from neuroectodermal cells through a balanced reciprocal translocation t(11;22) involving the EWSR1 and FL1-1 genes and most commonly occur in the peripheral nervous system, bone, and deep soft tissues [3, 4]. PNETs can occur in numerous solid organs such as the kidney [5], pancreas [6], thymus [7], and lung [8]. Primary PNET in the pericardium is extremely rare, with only two prior cases reported in the literature [13, 14]. We report another primary PNET arising in the pericardium of a 13-year-old female.

Case report

A 13-year-old female was admitted to the emergency department because of a 2-week history of shortness of breath, cough, and lower extremities edema. Treatment for an upper

respiratory tract infection failed to improve her symptoms. Past medical history and routine laboratory investigations were unremarkable. An echocardiogram revealed a 3.3 × 2.6 × 4.4 cm hypoechoic solid mass at the left coronary sulcus within the pericardial cavity (**Figure 1**). CT scan of the chest demonstrated a large mass in the pericardial cavity featuring mild to moderate heterogeneous enhancement measuring 3 × 4 cm (**Figure 2A, 2B**). Abdominal and brain CT scans and bone scintigraphy were normal, with no evidence of primary tumor elsewhere. Pericardiocentesis yielded fluid which contained only red blood cells and neutrophils. The patient was subjected to surgery and a mass was detected in the pericardium which protruded into the pericardium cavity. Adjuvant chemotherapy was given post-operatively. At follow-up 8 months after surgery, there was no clinical or radiological evidence of tumor recurrence or metastasis.

Pathological examination

Gross examination revealed a solitary, well-circumscribed mass measuring 7 cm × 3 cm × 2.5 cm, which featured fleshy homogeneous

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Figure 1. Echocardiography showing a large solid mass of hypoechoic texture filling the pericardial cavity.

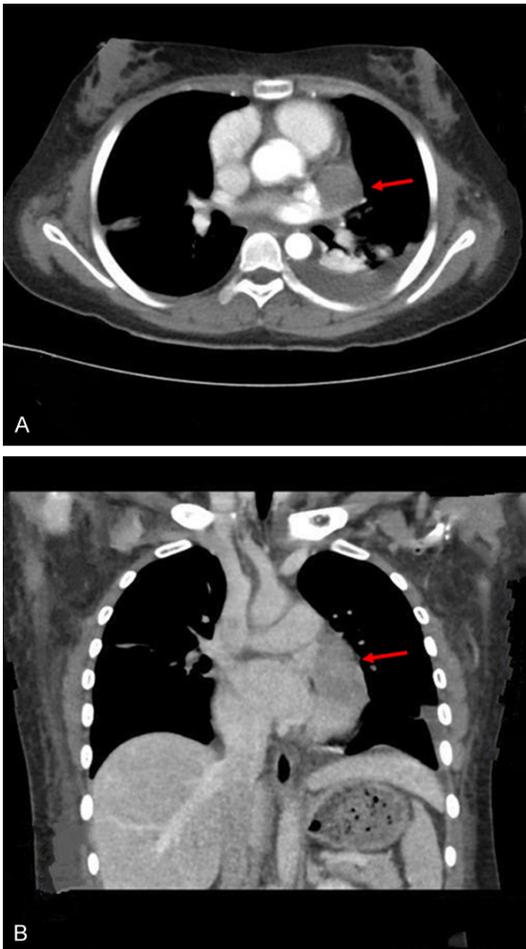


Figure 2. A, B: CT findings revealed a solid mass with heterogeneous enhancement measuring 3 × 4 cm in the pericardial cavity.

whitish-tan to brown tissue with foci of hemorrhage and necrosis (**Figure 3A**). Histologically,

the tumor consisted of solid sheets of cells divided into irregular nests by fibrovascular septae. The tumor cells were uniformly small with round to oval nuclei containing fine chromatin, scanty clear or eosinophilic cytoplasm, indistinct cytoplasmic membranes, and brisk mitotic activity (**Figure 3B**). A few Homer Wright rosettes with a central core of neuropil were formed (**Figure 3C**). Immunohistochemically, the tumor cells showed strong and consistent membranous expression of CD99 (**Figure 3D**), cytoplasmic staining for synaptophysin (**Figure 3E**) and neuron-specific enolase. Fluorescence *in situ* hybridization (FISH) showed a clear separation of red and green signals within a single cell in most tumor cells, which demonstrated the presence of the EWSR1 rearrangement (**Figure 3F**). The histological, immunophenotypic and molecular findings, confirmed the diagnosis of primary PNET of the pericardium.

Discussion

Primary and secondary tumors of the heart are rare, and primary pericardium tumors are even more infrequent. According to the review by Meng et al. [9] and Patel et al. [10], primary pericardial tumors accounts for only 6% to 12% of all primary tumors arising in the heart and pericardium. PNET belongs to the Ewing's sarcoma family and occurs mostly in extremities and soft tissue. Although secondary involvement of the pericardium by PNET elsewhere have been reported [11, 12], primary PNET of the pericardium remains exceptionally rare. To the best of our knowledge, only two cases of primary PNET of the pericardium have been reported [13, 14]. Our case represents the third case in the English literature. The previously reported cases with our case are summarized in **Table 1**. The ages of patients range from 13-51 years (average, 27.3 years), with a predilection for younger patients. In contrast to PNET of other sites, which is slightly male predominant, primary PNET of the pericardium appears to show female predominance (2 females and 1 male). Two tumors were located in pericardial cavity position as polypoid and presented with early clinical symptoms induced by cardiac tamponade, such as dyspnea, edema of lower extremity cough and chest discomfort. The excised lesions ranged in size from 5 to 6.4 cm (average, 5.4 cm).

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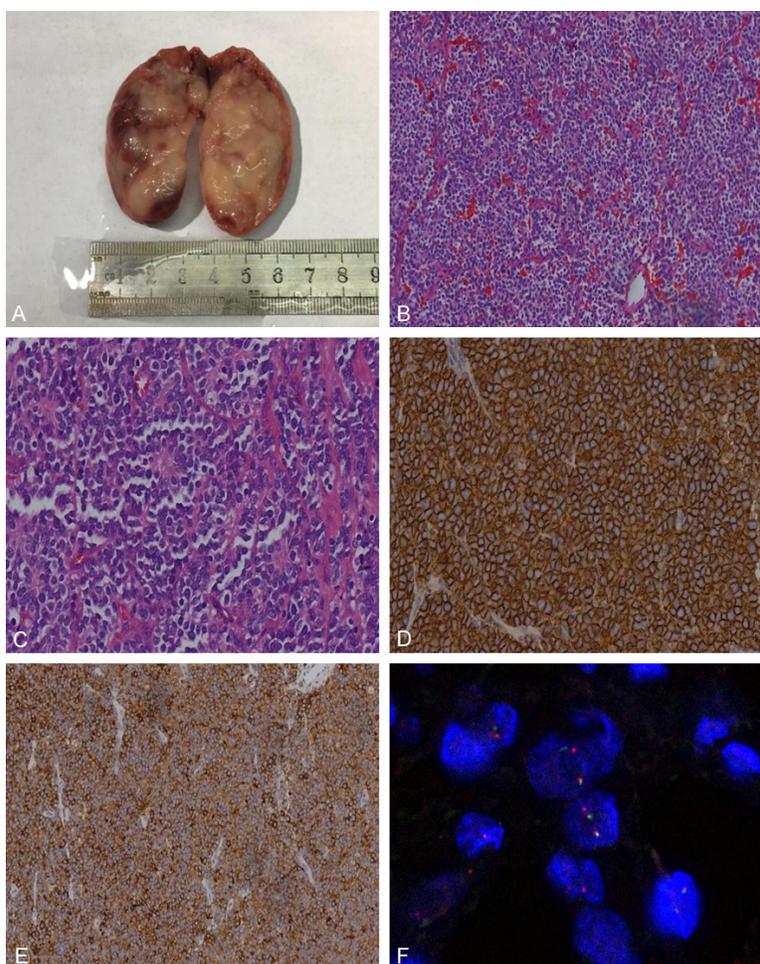


Figure 3. A: Gross examination shows a well-circumscribed mass, with pale and glistening or gelatinous cut surface, areas of hemorrhage, and necrosis. B: Sheets of primitive, small, round cells are separated by fibrous septae. Some tumor cells have clear cytoplasm (H and E, $\times 20$). C: Homer Wright rosettes with a central core of neuropil are formed (H and E, $\times 40$). D: Positive CD99 membranous staining of tumor cells (EnVision, $\times 20$). E: Positive expression of synaptophysin (EnVision, $\times 20$). F: Dual color interphase fluorescence in situ hybridisation utilizing the EWSR1 break-apart probe. Split red and green signals within a single cell demonstrated the presence EWSR1 rearrangement.

Primary PNET of the pericardium have morphological appearance similar to those arising in other locations. The tumor was composed of uniform small round cells with round to oval nuclei containing fine chromatin, scanty clear or eosinophilic cytoplasm, and some areas featuring Homer Wright rosettes. PNET is derived from neural crest cells exhibiting neuroectodermal differentiation, as confirmed by the expression of CD99, synaptophysin, and CD56. The differential diagnoses include malignant mesothelioma, rhabdomyosarcoma [15] and synovial sarcoma [16, 17]. The latter two tumors were

also CD99 positive, and may cause diagnostic confusion. PNET shows the specific for t(12;22) translocation, which is not present in these other tumors.

Treatment of Primary PNET of the pericardium requires a combination of surgery, chemotherapy, and radiotherapy. Chemotherapy includes a standard regimen of doxorubicin, vincristine, cyclophosphamide, and dactinomycin alternating with courses of ifosfamide and etoposide [18]. Compared with surgical excision alone, combination of chemotherapy, radiotherapy, and surgery improves 2-year survival rate from 23%-44% to 59%-67% and decreases the rate of distant metastasis from 46%-65% to 12%-32% [19]. Radiotherapy is strongly recommended in surgically inoperable tumors. According to our review, among the two patients with primary PNET of the pericardium reported in the literature, there was one patient who received surgery and chemotherapy and was alive at 24 months of follow-up [14] and the other died shortly. Our case as well as the cases reported in the literature showed that the growth pattern of PNET was related to the prognosis. The

prognosis of PNET in the pattern of intrapericardial polypoid growth was better than that of in the pattern of intrapericardial diffuse growth. However, more cases of this rare tumor need to be collected and studied for prognosis and further development of effective therapeutic protocol.

In conclusion, primary pericardial PNET is an exceedingly rare tumor. This report illustrates that the pericardium is a possible site for primary PNET. Immunophenotypic and molecular studies are important in arriving at an accurate

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Table 1. The clinical and pathologic features of primary PNET of the pericardium in three patients

Case	Sex	Age (Years)	Symptoms	Location	Size	Microscopy	Immunophenotype	Follow Up
1 [13]	F	18	Anasarca, tachycardia, tachypnoea, hemorrhagic pericardial effusion.	The pericardium was greatly thickened by tumor, and tightly encasing the whole heart and the root of great vessels.	5 cm	Monotonous population of small round cells.	CK, LCA, EMA, and VIM negative.	Died shortly after diagnosis.
2 [14]	M	51	Cardiac tamponade	Pericardial mass that invaded into the entire pulmonary artery and the right and left ventricles.	6.4 cm	Monotonous small, blue, round, uniform tumor cells with vesicular nuclei and scanty cytoplasm.	Strong staining with CD99, CK, CK7, CK20, SYN, CGA, CD56, CD45, TTF-1, S100 protein. Myo D1, and DES were negative. FISH showed a split signal pattern signifying rearrangement of EWSR-1.	NED (24 months)
3 present case	F	13	Dyspnea, edema of both lower limbs	Pericardial mass which protruded into the pericardium cavity.	5 cm	Monotonous small round cells with scanty clear cytoplasm and brisk mitosis. Homer Wright rosettes	CD99, SYN, CD56, NSE positive, CK, CGA, LCA, Myo D1, CR negative. FISH showed a split signal pattern signifying rearrangement of EWSR-1.	NED (8 months)

Abbreviations: M, male; F, female; NED, no evidence of disease; NA, not available; NSE, neurone specific enolase; VIM, vimentin; SYN, synaptophysin; DES, desmin; CGA, chromogranine; CK, Cytokeratin; LCA, leukocyte common antigen; EMA, epithelial membrane antigen; SMA, smooth muscle actin; CR, calretinin; FISH, fluorescent in situ hybridization.

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diagnosis. A multimodality treatment approach including surgery, chemotherapy, and radiotherapy is required.

Disclosure of conflict of interest

None.

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