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Case Report

Primary pericardial synovial sarcoma: A case report and literature review

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ABSTRACT

Primary pericardial synovial sarcoma is extremely rare, with few published cases in the literature. We report the case of an adolescent aged 13 years with primary pericardial synovial sarcoma discovered during tamponade, confirmed by molecular biology, and for whom treatment combined radiosurgery and adjuvant chemotherapy. The particularity of the case we are reporting stems from the young age of our patient (13 years) as well as the duration of remission, which is quite long (21 months) prior to a superior mediastinal relapse compared to cases reported in the literature.

<**Learning objective:** Synovial sarcoma is difficult to diagnose and has a poor prognosis. Here, a 13-year-old diagnosed with primary pericardial synovial sarcoma was treated with combined radiosurgery and adjuvant chemotherapy leading to continuous remission for 21 months. This regimen could be used to successfully manage future patients. Molecular biology is useful in the diagnosis of synovial sarcoma through the identification of t(X;18) translocation in atypical locations as in the present case.>

Introduction

Synovial sarcoma is a highly malignant mesenchymal tumor that usually affects the deep soft tissues near the large joints of the extremities in adolescents and young adults [1,2]. Other atypical primary localizations have been described: head and neck, heart, pleura, abdomen, kidney, prostate, and vulva [1]. Pericardial localization is extremely rare [3–6]. Only a few well-documented cases have been published [1,5–15]. In this manuscript we report a new case.

Case report

A 13-year-old child, with no medical history, presented for consultation in February 2011 in the emergency department for an exertional dyspnea of sudden onset.

The clinical examination found an orthopnea, tachycardia, and pericardial friction rub on heart auscultation. The chest X-ray showed a cardiomegaly, leading to his hospitalization in the department of cardiovascular surgery.

The echocardiography showed pericardial effusion in the right sub-costal area, as well as a 73 mm × 61 mm right lateral-atrial intra-pericardial mass responsible for diastolic compression of the right ventricle free wall (Fig. 1). Pericardial drainage brought 500 ml of sero-hematic fluid.

The chest computed tomography scan performed subsequently showed an expansive intra-pericardial process in contact with the right auricle and ventricle (Fig. 2a and b). The partial resection of the intrapericardial tumor was performed secondarily to prevent heart failure and to gain a definitive diagnosis. Complete resection of the tumor was impossible because of the intrapericardial localization of the tumor. Histologically, it was a malignant tumor proliferation arranged in bundles. The cells were often spindle-shaped, with poorly defined cytoplasm and elongated nuclei with a fine, dusty chromatin, and mitoses were common (Fig. 3a and b). On immunostaining, cells were positive for epithelial membrane antigen and vimentin but negative for pankeratin AE1/AE3, CD 34, CD 45, and chromogranin. Given these morphological and

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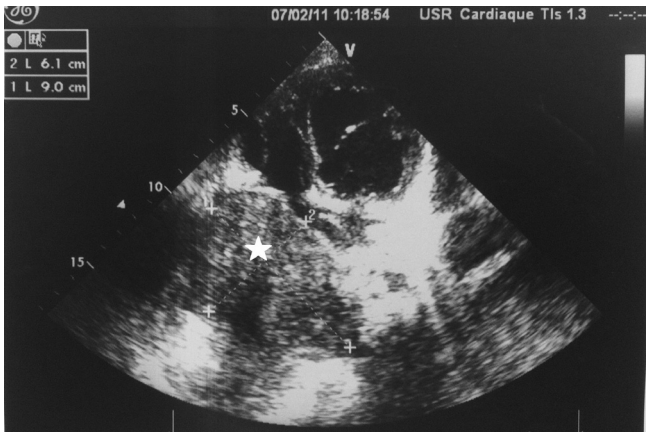

Fig. 1. Echocardiography showing a right lateral atrial intra-pericardial mass (*white star*).

immunophenotypic aspects, a monophasic synovial sarcoma with grade III malignancy according to *the FNCLCC* (*French Fédération Nationale des Centres de Lutte Contre le Cancer*) system is given. The diagnosis was confirmed by molecular cytogenetic examination (fluorescence in situ hybridization; FISH), which showed that 65% of cells showed rearrangement of the SS18 locus molecular equivalent of the characteristic t(X;18) translocation (Fig. 4). The examination for an extra-pericardial localization particularly in the soft tissues came back negative.

Chemotherapy with four courses of ifosfamide and doxorubicin treatment every three weeks was well tolerated. Radiographic evaluation revealed a tumor regression greater than 50%. The patient received postoperative radiotherapy on the heart in total at a dose of 30.6 Gy in 17 fractions with a double exposure on the tumor bed at a dose of 19.6 Gy in 11 fractions. Monitoring by echocardiography and electrocardiography during radiotherapy

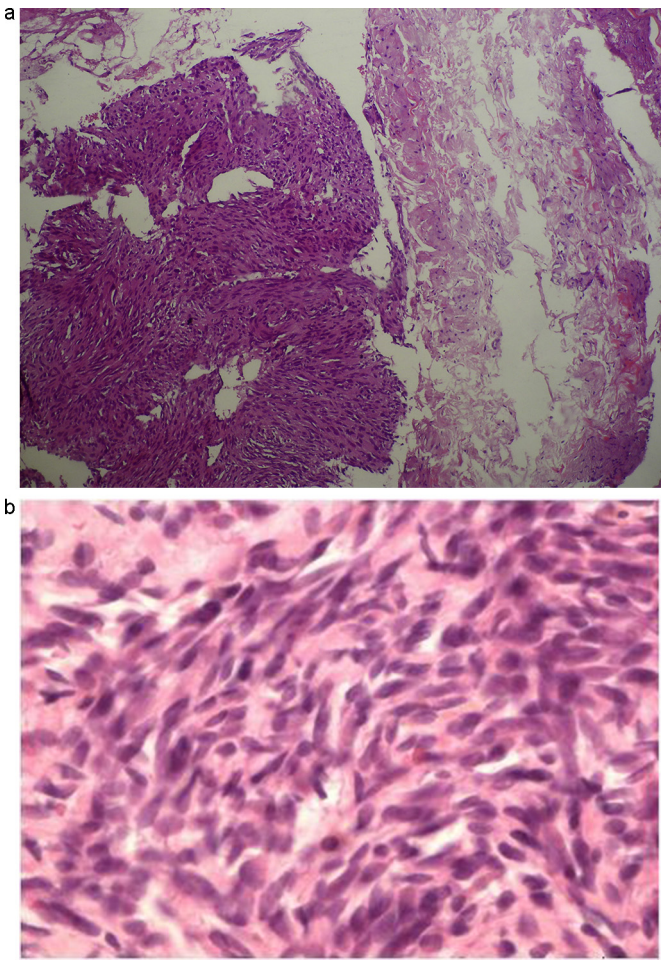

Fig. 3. (a) Overview of spindle cell tumor infiltrating pericardium tissue (hematoxylin–eosin, original 40×). (b) A photomicrograph of the primary pericardial tumor showing fasciculi of the spindle cells (hematoxylin–eosin, original 400×).

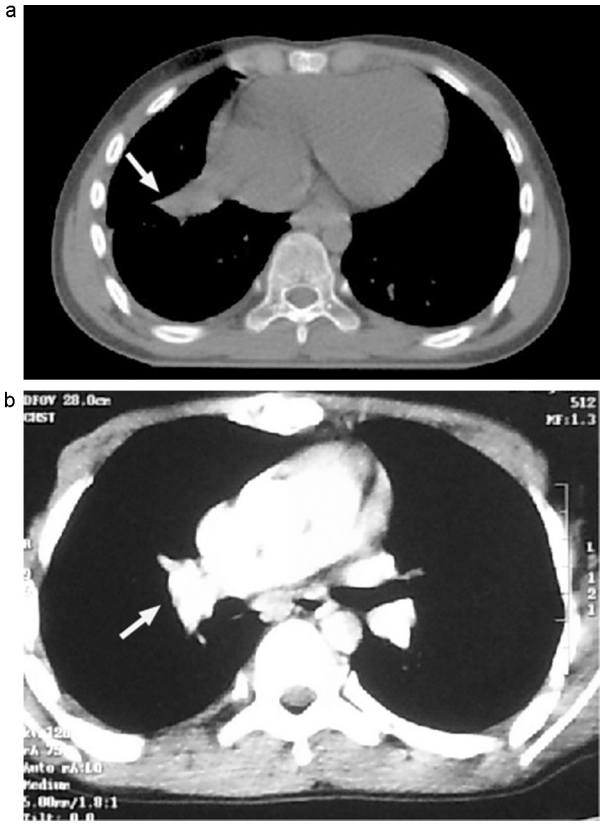

Fig. 2. Chest computed tomography (CT) findings. (a) Plain and (b) contrast-enhanced CT image. Intra-pericardial tumor in contact with the right atrium and right ventricle (*arrow*).

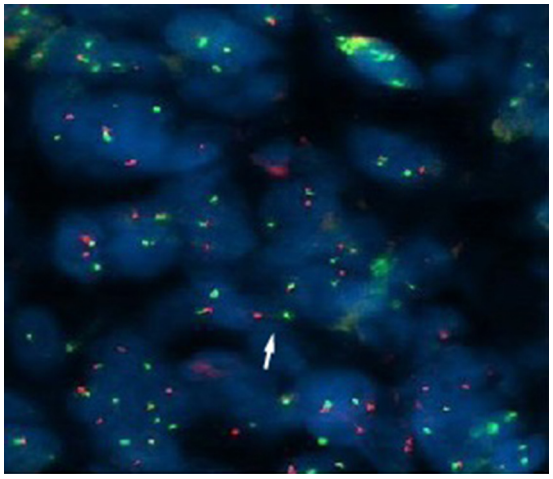

Fig. 4. Fluorescence in situ hybridization analysis of the tumor (FISH): bi-color DNA probe, Breakapart, SS18 locus rearrangement in 18q11.2 molecular equivalent of the t(X;18) translocation (*arrow*).

did not objectify specific abnormalities. The patient remained in continuous remission for 21 months and the pericardial tumor remained stable. The evolution was marked by an anterior superior mediastinal relapse for which the child is receiving second-line chemotherapy combining ifosfamide, carboplatin, and etoposide. After four cycles, the tumor response was less than 50%. The general condition of the patient is currently under re-evaluation by a team of supportive care.

Discussion

Pericardial tumors are extremely rare with an incidence of 0.001–0.28% in some autopsy sets [5]. Metastatic lesions are more common than primary lesions [16]. These are dominated by mesothelioma while primitive pericardial synovial sarcoma is extremely rare [3–6] with only 17 cases reported to date in the English literature (Table 1) [1,3,5–15]. Malignant spindle cell tumors, pericardial cysts, liposarcomas, lipomas, and teratomas are other less common varieties of primitive pericardial tumors [14]. It is assumed that there is no direct relationship between the synovial tissue and synovial sarcoma, the tumor derived from a synovial differentiated pluripotent mesenchymal cell [17]. There is a discreet male predominance, the sex ratio being 2.5/1 [1], with a higher incidence in the 3rd and 4th decade [3]. The average age of patients at diagnosis is 39 years [1]. Our patient was 13 years old at diagnosis, the youngest among all cases reported in the literature. Clinically, the symptoms are attributed to tamponade [1]. Dyspnea is by far the most common symptom. Other symptoms include chest pain, cough, and orthopnea [1,5]. The diagnosis is usually established by trans-thoracic or trans-esophageal echocardiography, computed tomography, magnetic resonance imaging, cytological examination of pericardial effusion, and pericardial biopsy [5]. It is well established that magnetic resonance imaging allows for a better assessment of heart and pericardial tumors and distinguishes between benign and malignant tumors [5,18]. It is effective in post-treatment monitoring [6,7]. Generally, a pericardial mass associated with a pericardial effusion shows up. Tumors vary in size from 6 to 15 cm (mean 10.6 cm) [1].

Histologically, synovial sarcomas are classified as biphasic, monophasic, or poorly differentiated [1,6,14]. The biphasic variant appears to be more common in the pericardial localization compared to the other synovial sarcoma sites [1]. Most tumors carry a characteristic t(X;18) translocation, which involves the genes SSX1 or SSX2 from the chromosome X (Xp11) and the gene SYT from the chromosome 18 (18q11) [3]. More than 90% of patients with synovial sarcoma have a t(X;18) translocation, which is not associated with other sarcomas [1].

In the case we are reporting, cytogenetics confirmed the macroscopic and microscopic findings. The molecular diagnosis is therefore essential especially when histological diagnosis is difficult. In addition to the case we are reporting, 12 other cases of primary pericardial synovial sarcomas reported in the literature were confirmed either by reverse transcription – polymerase chain reaction (RT-PCR), or by FISH, or by both [1,2,7,9–13]. The FISH technique has better sensitivity in the detection of the t(X;18) translocation than RT-PCR, while the latter has the advantage of identifying gene fusion transcripts [1]. The differential diagnosis arises mainly with pericardial mesothelioma, which is usually associated with a history of asbestos exposure and with a diffuse infiltration of the pericardium. On the other hand, the synovial

Table 1
Primary pericardial synovial sarcoma: summary of published studies.

Authors	Sex/age (y)	Tumor size (cm)	Histological subtype	Symptoms	Molecular biology	Treatment	Evolution
Al-Rajhi et al. (1999) [7]	M/19	10	Biphasic	Difficulty breathing	t(X,18)	Surgery, RT	In remission for 12 months
Kojima et al. (1999) [9]	F/35	11	Monophasic	Chest pain, nausea, dyspnea	t(X,18)	NA	NA
Oizumi et al. (1999) [12]	F/19	14	Biphasic	Dyspnea, asthenia	t(X,18)	Surgery	Deceased after 7 months
Anand et al. (2003) [8]	M/29	8.5	Monophasic	Difficulty breathing	Not performed	Surgery–RT–CT	In remission for 13 months
Van Der Mieren et al. (2004) [10]	M/26	NA	Biphasic	Tamponade	t(X,18)	Surgery–CT–RT	In remission for 14 years
Bégueret et al. (2005) [11]	M/59	15	NA	NA	t(X,18)	NA	NA
Schumann et al. (2007) [18]	F/64	NA	NA	Difficulty breathing, tachycardia	Not performed	Surgery	NA
Hing et al. (2007) [13]	M/15	NA	Biphasic	Cough, tachypnea, weight loss	t(X,18)	CT–surgery	Deceased after 31 months
Korula et al. (2009) [15]	M/49	13	Monophasic	Dyspnea, chest pain	Not performed	Supportive care	NA
Katakura et al. (2009) [2]	F/70	13	NA	Cough, dyspnea	t(X,18)	Surgery, palliative care	Deceased after 79 days
Moorjani et al. (2009) [3]	M/61	6	Biphasic	Dyspnea, peripheral edema	Not performed	Surgery–CT	In remission after 2 months
Rangreze et al. (2011) [5]	M/19	15	Monophasic	Cough, dyspnea, orthopnea	Not performed	Surgery–palliative CT	In progress
Akerström et al. (2011) [6]	F/54	11	Biphasic	Malaise, fever, chest pain	t(X,18)	Surgery–CT–RT	In remission for 22 months
Cheng et al. (2012) [1]	M/31	10	Biphasic	Fever, cough	t(X,18)	CT–surgery	In remission for 12 months
	M/31	8	Monophasic	Fever, night sweats, tachypnea, chest pain	t(X,18)	Surgery–CT	Deceased after 27 months
	M/38	8	Monophasic	Chest pain, difficulty breathing	t(X,18)	Waiting for a heart transplant	In remission for 2 months
Kodikara et al. (2012) [14]	M/61	5	Biphasic	Discovered at autopsy death/hypertensive disease	t(X,18)	–	–
Our case	M/13	7.3	Monophasic	Dyspnea, orthopnea, tachycardia	t(X,18)	Surgery–CT–RT	In remission for 21 months anterior superior mediastinal relapse

NA: not available; CT: chemotherapy; RT: radiotherapy; t: translocation; M: male; F: female.

sarcoma is usually a solitary mass and not associated with a history of asbestos exposure [3]. Immunohistochemical and molecular cytogenetic studies confirm the diagnosis in cases of doubt [1].

Given its rarity, synovial sarcoma of the pericardium is difficult to diagnose, its primary character difficult to confirm. A secondary pericardial lesion of soft tissue synovial sarcoma should be excluded prior to maintaining its primary character [16]. In our case, the absence of an extra-pericardial tumor localization at diagnosis and after 21 months of follow-up confirms the primary character of the tumor. Because of the rarity of pericardial synovial sarcomas, there is no standard therapy. Treatment, as in all soft tissue sarcomas, is multimodal combining surgery and radiochemotherapy.

Complete surgery remains the primary treatment option [10,15]. External beam radiation therapy is given in the event of incomplete surgical excision, providing better local control [7,8,10]. Chemotherapy is indicated in the event of unresectable tumors because of its spread or metastases [10]. The use of doxorubicin can be limited due to its cardiotoxicity. In our case, the combination of radio-surgery and chemotherapy allowed for loco-regional control with a follow-up of 21 months. Pazopanib, a multi-targeted tyrosine kinase inhibitor, is a new treatment option for patients with non-adipocytic, metastatic soft-tissue sarcoma after failure of standard chemotherapy [19].

Primary pericardial synovial sarcoma has a poor prognosis especially when complete surgical resection is not possible [8,18]. This is explained by the large size of the lesions and the difficulty achieving complete resection because of the anatomical position [1]. Overall, survival is short. The only exception is the case reported by Van der Mieren of a 26-year-old patient, operated on for a biphasic pericardial synovial sarcoma with microscopically healthy surgical resection margins, having received adjuvant radiotherapy and chemotherapy, and with a survival of 14 years [10]. In conclusion, primary pericardial synovial sarcoma is an extremely rare and aggressive tumor, with difficult diagnosis and poor prognosis. The discovery of a pericardial lesion must first eliminate a secondary location. Molecular biology examination by searching for the t(X,18) translocation characteristic contributes significantly to the diagnosis. The particularities of our observation stem from the young age of our patient (13 years), while the average age of reported cases is 39 years, and the relatively long duration of remission of 21 months, following treatment combining surgery, chemotherapy, and radiotherapy.

Conflict of interest

Authors declare no conflict of interest.

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References

[1] Cheng Y, Sheng W, Zhou X, Wang J. Pericardial synovial sarcoma, a potential for misdiagnosis: clinicopathologic and molecular cytogenetic analysis of three cases with literature review. Am J Clin Pathol 2012;137:142–9.
[2] Katakura H, Fukuse T, Shiraishi I, Hayatsu E, Nishijo K, Toguchida J, Nakashima Y, Wada H. Mediastinal synovial sarcoma. Thorac Cardiovasc Surg 2009;57:183–5.
[3] Moorjani N, Peebles C, Gallagher P, Tsang G. Pericardial synovial sarcoma. J Card Surg 2009;24:349–51.
[4] Karn CM, Socinski MA, Fletcher JA, Corson JM, Craighead JE. Cardiac synovial sarcoma with translocation (X: 18) associated with asbestos exposure. Cancer 1994;73:74–8.
[5] Rangreze I, Banday Manzoor A, Sheikh Aejaz A, Bhat S, Mohammad Latif C. Primary synovial sarcoma of pericardium: a case report. Chinese-German J Clin Oncol 2011;10:428–9.
[6] Akerström F, Santos B, Alguacil AM, Orradre JL, Lima P, Zapardiel S. Pericardial synovial sarcoma. Thorac Cardiovasc Surg 2011;59:175–7.
[7] Al-Rajhi N, Husain S, Coupland R, McNamee C, Jha N. Primary pericardial synovial sarcoma: a case report and literature review. J Surg Oncol 1999;70:194–8.
[8] Anand AK, Khanna A, Sinha SK, Mukherjee U, Walia JS, Singh AN. Pericardial synovial sarcoma. Clin Oncol (R Coll Radiol) 2003;15:186–8.
[9] Kojima KY, Koslin DB, Primack SL, Kettler MD. Synovial sarcoma arising from the pericardium: radiographic and CT findings. AJR Am J Roentgenol 1999;173:246–7.
[10] Van der Mieren G, Willems S, Sciot R, Dumez H, Van Oosterom A, Flameng W, Herijgers P. Pericardial synovial sarcoma: 14-year survival with multimodality therapy. Ann Thorac Surg 2004;78:e41–2.
[11] Bégueret H, Galateau-Salle F, Guillou L, Chetaille B, Brambilla E, Vignaud JM, Terrier P, Groussard O, Coindre JM. Primary intrathoracic synovial sarcoma: a clinicopathologic study of 40 t (X;18)-positive cases from the French Sarcoma Group and the Mesopath Group. Am J Surg Pathol 2005;29:339–46.
[12] Oizumi S, Igarashi K, Takenaka T, Yamashiro K, Hiraga H, Fujino T, Horimoto M. Primary pericardial synovial sarcoma with detection of the chimeric transcript SYTSSX. Jpn Circ J 1999;63:330–2.
[13] Hing SN, Marshall L, Al-Saadi R, Hargrave D. Primary pericardial synovial sarcoma confirmed by molecular genetic studies: a case report. J Pediatr Hematol Oncol 2007;29:492–5.
[14] Kodikara S. Pericardium: an exceedingly rare site for a primary biphasic synovial sarcoma. Indian J Pathol Microbiol 2012;55:227–9.
[15] Korula A, Shah A, Philip MA, Kuruvila K, Pradhip J, Pai MC, Chacko RT. Primary mediastinal synovial sarcoma with transdiaphragmatic extension presenting as a pericardial effusion. Singapore Med J 2009;50:e26–8.
[16] Dawson WB, Mayo JR, Muller NL. Computed tomography of cardiac and pericardial tumors. Can Assoc Radiol J 1990;41:270–5.
[17] Bui-Mansfield LT, Kaplan KJ, Boardman J. Radiologic-pathologic conference of Keller Army Community Hospital at West Point, the United States Military Academy: synovial sarcoma of the chest wall. AJR Am J Roentgenol 2002;179:880.
[18] Schumann C, Kunze M, Kochs M, Hombach V, Rasche V. Pericardial synovial sarcoma mimicking pericarditis in findings of cardiac magnetic resonance imaging. Int J Cardiol 2007;118:e83–4.
[19] Van der Graaf WT, Blay JY, Chawla SP, Kim DW, Bui-Nguyen B, Casali PG, Schöffski P, Aglietta M, Staddon AP, Beppu Y, Le Cesne A, Gelderblom H, Judson IR, Araki N, Ouali M, et al. Pazopanib for metastatic soft-tissue sarcoma (PALETTE): a randomised, double-blind, placebo-controlled phase 3 trial. Lancet 2012;379:1879–86.