Cerebral metastasis of a primary heart sarcoma

Przerzut pierwotnego mięsaka serca do mózgu

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Abstract

Primary cardiac sarcomas are exceptionally rare tumours. A brain metastasis of a primary cardiac sarcoma has never been reported before. Although we know lots of primary malignomas spreading to the brain, we never observed cerebral metastases of an atrial spindle cell sarcoma. Cardiac sarcomas are more likely to haematogenously metastasize to the lung or the liver. Here, we describe the case of a young man, who suffered from a cerebral metastasis of a spindle cell sarcoma in the left heart atrium nine years ago. Postoperative whole brain irradiation with 30 Gy was performed. Later on, the patient experienced a local recurrence within the left atrium accompanied by cardiac arrhythmia and mitral valve insufficiency. This case is the very first description of a true cerebral metastasis from a primary heart sarcoma. Therefore, clear treatment paradigms are not established. Further case illustrations and the publication of larger patient series are mandatory, whenever possible.

Key words: primary cardiac sarcoma, brain metastasis, mitral valve insufficiency, neoadjuvant chemotherapy, adjuvant chemotherapy.

Streszczenie


W pracy opisano przypadek młodego mężczyzny, u którego 9 lat wcześniej wystąpił guz przerzutowy mózgu, którego źródłem był mięsak wrzecionowatokomórkowy lewego przedsionka. Po leczeniu chirurgicznym przeprowadzono napromienianie całego mózgowia dawką 30 Gy. W późniejszym czasie u chorego wystąpiła miejscowa wznoswa guza lewego przedsionka, której towarzyszyło migotanie przedsionków i niedomykalność zastawki dwudzielnej.


Słowa kluczowe: pierwotny mięsak serca, przerzut do mózgu, niedomykalność zastawki dwudzielnej, chemioterapia neoadjuwantowa, chemioterapia adjuwantowa.
Introduction

Primary cardiac malignomas are exceptionally rare tumours with a low prevalence of 0.002-0.28% [1]. A few institutions report of small groups [4-6] or even single cases [8-16]. In particular, spindle cell sarcomas and leiomyosarcomas of cardiovascular origin are extremely rare. About half of all cardiac sarcomas are situated in the left atrium [8,9,12,13]. Due to the extreme rareness of cardiac spindle cell sarcomas, there is no general experience in their management [5,11,12]. Nevertheless, sarcomas are the most common primary cardiac tumours and include leiomyosarcomas, rhabdomyosarcomas, myxosarcomas, angiosarcomas, liposarcomas, fibrosarcomas, osteosarcomas, neurofibrosarcomas, spindle cell sarcomas, malignant fibrous histiocytomas, synovial sarcomas, and undifferentiated sarcomas [1-6,12,16,17].

A few reports describe Ebstein-Barr virus-associated leiomyosarcomas of the heart in immunosuppressed patients [18,19,21]. The typical symptoms of heart tumours include intracardiac obstruction, signs of systemic embolization, and systemic or constitutional symptoms. Serious complications are ischaemic stroke, myocardial infarction and even sudden death [1,5,6,14,21]. Despite surgical tumour resection of heart sarcomas and subsequent adjuvant treatment, the prognosis of malignant cardiac tumours remains poor, with a median survival of about 25 months [5,6,9,12,17]. Still, the knowledge about primary cardiac sarcomas remains very restricted.

Brain metastases are known to occur in a lot of malignant tumours. Although we can readily imagine cardiac sarcomas as frequently spreading to the brain, central metastases have never been reported except for one case illustration describing a central metastasis of a histiosarcoma [10]. Here, we report the first case of a young man with a highly malignant primary cardiac spindle cell sarcoma and subsequent cerebral metastasis.

Case report

A young man experienced an intermittent absolute cardiac arrhythmia in November 1996. Starting in October 1998, the patient repeatedly suffered from visual deficits, headache, vertigo, sensory deficits in his face and upper and lower extremities, a reduced productivity, generalized weakness, and fever up to 39.5°C. In the blood test, an enhanced erythrocyte sedimentation rate was found. Echocardiography revealed a globular tumour within the left atrium that was confirmed by electrocardiogram-triggered magnetic resonance imaging (MRI) of the heart (Fig. 1, part A). The tumour was surgically removed in December 1998 by means of a partial septectomy within healthy tissue margins as a so-called R0 resection.

Histopathologically, the diagnosis of a primary highly malignant spindle cell sarcoma of the left atrium was made. The additional oncological screening did not show any further tumour manifestations in the patient's body.

Only 14 months later, the patient suffered from focal epileptic seizures, headache, and a sensory loss in the left lower extremity. In addition, muscle stretch reflexes of the left lower extremity were weaker than on the right side. Cranial imaging with computed tomography (CT) revealed bleeding in the right central region of the brain. MRI with the intravenous administration of gadolinium-DTPA demonstrated a right-sided lesion within the central cerebral region with an irregular gadolinium enhancement at the lesion's margins, a hypointense centre of the lesion, and a perifocal brain oedema (Fig. 1, parts B-D). The cerebral angiography demonstrated a high vascularization of the lesion (Fig. 1, part E). This high vascularization was pronounced in the vicinity of the superior sagittal sinus. Screening for a cardiac tumour recurrence or distant metastases using transoesophageal sonography, thoracic CT, and selective proximal angiography of the heart and the pulmonary vessels did not reveal any further tumour lesions.

Intracranial tumour bulk removal was performed in April 2000 with the aid of a multiplanar neuronavigation system and by the use of continuous intraoperative neuromonitoring with direct cortical stimulation to localize the central region by phase inversion (Fig. 2). Postoperatively, the patient received percutaneous whole brain irradiation with a total dose of 30 Gy until May 2000. In November 2000, the patient developed new cardiac arrhythmia. The consecutive imaging demonstrated a new tumour mass within the left atrium and local lymph node metastases within the mediastinum (Fig. 1, part H). This time, surgical resection was performed including a reconstruction of the cardiac septum between both atria by the use of a pericardial patch. Following surgery of this local tumour recurrence, percutaneous irradiation of the left atrium including the proximal pulmonary artery was performed up to a total dose of 50 Gy. Later on, the patient developed slight
insufficiency of the aortic valve and insufficiency of the mitral valve, cardiac fibrillation, and dyspnoea during daily life activities according to the NYHA grades II–III. The progressive insufficiency of the mitral valve made a biological replacement necessary that was performed in March 2007 and was followed by implantation of a pacemaker because of a postoperative atrioventricular block grade III. A postoperative haematothorax in May 2007 was treated by repeated thoracotomies. Currently, the patient is in a stabilized condition and shows no signs of recurrent tumour or any distant metastases.

**Histopathological evaluation**

Brain tumour material was fixed with 6% paraformaldehyde. Tumour tissue slices were established at a thickness of 4 μm. Histopathological workup was performed with H&E staining and subsequent immunohistochemistry. Primary antibodies were used to label Ki67, vimentin, desmin, ASMA, S100, HHF-35, MNF, and CD31.

Histopathological workup of brain metastasis material revealed a highly cellular and vascularized tumour with about 5% to 10% mitoses per high power field (Fig. 3, parts A-D). Tumour cell invasion into the surrounding brain parenchyma was visible in some areas (Fig. 3, part A) in contrast to a sharp tumour-brain border in other areas (Fig. 3, part B). Tumour necroses were not observed. In the resected tumour material, pleomorphic and partly vesicularly transformed cell nuclei could clearly be seen. Furthermore, atypical mitoses were visible. The tumour cells themselves were of a spindle cell type and only partly of a polygonal shape. The tumour tissue showed older and fresh bleeding. Tumour cell staining was negative for HHF-35, ASMA, MNF, and desmin. Immunopositivity was only detected for vimentin (Fig. 3, part F). The proliferative activity, evaluated by the Ki67 positivity of the metastasis, was estimated between 5% and 10% (Fig. 3, part E).

Histopathological workup of local recurrence of the primary cardiac spindle cell sarcoma showed S100 negativity (Fig. 4, part A) and CD31 negativity of the...
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tumour cells (Fig. 4, part C). Furthermore, tumour cells were negative for desmin. In contrast to the brain metastasis, tumour cells of the cardiac recurrence were positive for the smooth muscle actin ASMA (Fig. 4, part B). The Ki67 labelling index was evaluated to be about 5% to 10% (Fig. 4, part D).

Discussion

Malignant primary cardiac tumours and even sarcomas of the heart are significantly less common than metastatic tumour disease to the heart [5,17,22]. Especially pulmonary and uterine leiomyosarcomas were reported to spread to the heart [16,23], but carcinomas spread significantly more often into the cardiac region than sarcomas do [23]. Among cardiac sarcomas, angiosarcomas and unclassified sarcomas most often grow within the heart muscle itself [5]. In a series of 1429 sarcoma patients, only 14 patients suffered from a cardiac sarcoma [6]. These 14 patients were characterized by their young age and a poor prognosis of only a few months after the initial diagnosis [6].

Echocardiography and angiography are the essential diagnostic tools for cardiac sarcomas. Technical improvements in the performance of CT and MRI (Fig. 1) have enhanced their impact in the diagnostic approach within the last decade [17]. Whenever possible, total surgical resection is performed [2]. Despite local tumour surgery, subsequent irradiation, adjuvant chemotherapy, and even cardiac transplantation, the prognosis for the affected patients generally remains extremely poor [6]. The benefit of adjuvant chemotherapy was controversially discussed during the last years [2,3,7,14,19,22,26,31,35]. Whereas chemotherapy was not performed in early years, current treatment strategies include surgery, irradiation, and chemotherapy. Only a few reports describe an unclear effect of adjuvant chemotherapy [31,35]. Some authors even report
that the adjuvant chemotherapy and irradiation have no effect on long-term survival [31]. In principle, primary cardiac sarcomas are uniformly associated with poor long-term survival. According to the current point of view, cardiac sarcomas should be treated by extensive surgical excision followed by adjuvant radiation and chemotherapy. This strategy may improve survival with a good quality of life. Even heart transplantation is
a therapeutic option in primary cardiac sarcomas without metastatic disease.

The extent of resection has the main impact on survival, but adjuvant therapy can improve patients’ outcome significantly [3,7,19,31,35]. There were no local recurrences observed in patients with R0 resection [2]. Neoadjuvant chemotherapy can be performed prior to surgery [7]. This simplifies the subsequent surgery significantly [3,7].

The most often used chemotherapeutics are doxorubicin, ifosfamide, and gemcitabine [2,14,19]. In some cases, docetaxel and mesran are included in the chemotherapeutic regimen [14,19]. Although our case presents only the second real cerebral metastasis of a primary cardiac sarcoma, one could imagine brain metastases to display a greater incidence. Neoadjuvant or adjuvant chemotherapy could help to avoid this usually fatal complication.

Metastases of cardiac leiomyosarcomas have been described to occur within the lung, the local lymph nodes and more distantly within the liver [5]. Metastases of malignant cardiac spindle cell sarcomas have been reported within the gastrointestinal tract and local lymph nodes [4,5,12], but not in the brain. Additionally, sarcomas of other organs rarely metastasize to the brain [23-25,27-30,32-34,36]. The current biomedical literature contains 11 publications reporting 14 cases of non-cardiac leiomyosarcomas that metastasized to the brain [23-25,27-30,32-34,36]. In only one case did the brain metastasis originate from a malignant cardiac myxoma [23-25,27-30,32-34,36,37]. A malignant primary cardiac spindle cell sarcoma, metastatic to the brain, has never been described before. The primary sites of the above-mentioned non-cardiac malignant sarcomas metastatic to the brain were the uterus in 13 females and the gastrointestinal tract in one male patient [23-25,27-30,32-34,36,37]. All of them were described to be leiomyosarcomas. The reported cases of uterine leiomyosarcoma metastases to the brain were characterized by a poor prognosis, with survival no longer than
2.5 years [33]. Taken together, cerebral metastases of primary cardiac sarcoma were described in only one more case.

We have described a young man with a highly malignant cardiac spindle cell sarcoma, who developed a brain metastasis shortly after initial treatment for the heart tumour. Currently – after eight years – the patient remains free of local recurrence or a second brain metastasis. The limiting factor in the patient’s disease is his heart dysfunction that was worsened by severe mitral valve insufficiency and an atrioventricular blockade.

Cerebral metastases of a primary cardiac sarcoma – a spindle cell sarcoma in our case – are an extremely rare complication. With optimal treatment, the survival rate of affected patients can be much higher than described in the literature. Chemotherapeutic strategies should be included in a multidisciplinary approach to avoid metastatic spread to the brain.

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Disclosure

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References