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Case Report

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Metastatic High-Grade Intimal Sarcoma of the Middle Cranial Fossa

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Abstract

Sarcomas are the most common malignant tumors of the heart. The intimal sarcomas of the heart and large vessels are extremely rare tumors with very poor prognosis, mostly due to delayed diagnosis as well as their aggressive metastatic behavior.

We present a case of a 63-year-old patient, who underwent total resection of cardiac sarcoma with biological valve implantation and subsequent chemotherapy. Two years following cardiac surgery she developed aphasia and right hemiparesis. Brain imaging confirmed the left middle fossa tumor. Left temporal craniotomy was performed and the tumor was removed. The pathology established the diagnosis as high-grade intimal sarcoma. Patient died 6 months post-operatively. We believe this is the first case of high-grade intimal sarcoma metastasising to the skull base and originating from left atrium.

Conclusion: The metastatic high-grade intimal sarcoma presents a therapeutic challenge, mostly to its aggressive behavior. This subtype of sarcomas should be considered as a part of the differential diagnosis for metastatic middle cranial fossa tumors.

Introduction

Intimal Sarcoma of the heart (IS) is a malignant tumor derived from the intima. It develops predominantly intraluminally within the large vessels and the heart. It is the least reported primary tumor of the heart [1]. The histological classification of the IS is still under debate [2]. The initial diagnosis can be delayed due to the its clinical and radiological resemblance to the acute or chronic pulmonary thromboembolism [3]. Depending on the location it can also mimic symptomatic pulmonary artery stenosis, mitral valve stenosis or aortic dissection [4,5]. The initial treatment usually comprises of the aggressive surgical resection followed by chemotherapy and radiotherapy [6]. The prognosis still remains poor [3,7]. The most common metastatic sites were described for IS and include liver, kidneys, adrenal glands lungs and bones [8,9]. Central nervous system metastatic sites included several supratentorial regions as well as cerebellum [10-16].

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Case description

63 year-old female patient with confirmed diagnosis of the left atrium IS was admitted with history of aphasia and right hemiparesis. Two years prior, she underwent left atrium sarcoma resection followed by implantation of the biological mitral valve. Subsequently, chemotherapy of doxorubicin and dacarbazine was initiated and carried out during 5 months following cardiac surgery.

Brain MRI (Figure 1) revealed large middle fossa tumor. Left temporal craniotomy was performed. As observed intraoperatively, the tumor was invading cortex of the temporal lobe. It presented with a distinct site of attachment to the floor of the middle cranial fossa. Gross total removal of the tumor in one piece was achieved and the skull base attachment site was extripated as well as coagulated.

Postoperative period presented no complications. The control brain CT was performed on 1st post-operative day (Figure 2). Patient was discharged on the 5th post-operative day in a stable neurological condition.

The pathologic diagnosis was established based on traditional pathological staining followed by immunochemistry. Mouse Double Minute 2 Homolog (MDM2) staining was positive, CD34 negative and ERG were slightly positive. Fluorescence In Situ Hybridization (FISH) confirmed the presence of MDM2 amplification which is very common in intimal sarcomas.

No gene fusion including NTRK1, NTRK2, NTRK3, ROS1, ALK was detected. Additional mutations in NRAS, p.Gln61Leu (p.Q61L) genes were detected. Based on the correlation with clinical data and the initial diagnosis of the primary tumor, metastatic tumor was confirmed to be high-grade intimal sarcoma.

The diagnosis was followed by radiotherapy planning. Follow-up MRI performed 3 moths post-operatively showed cerebral mass of 20 x 7 mm diameter within left temporal lobe. The additional pathological mass of 22 x 16 mm diameter was found on the chest MRI within the right inferior pulmonary artery (Figure 3). Additionally, ultrasound of the lower limb revealed 5cm large tumor of the left leg. The general clinical status of the patient worsened. She died 6 months following surgery do to cardiopulmonary insufficiency.

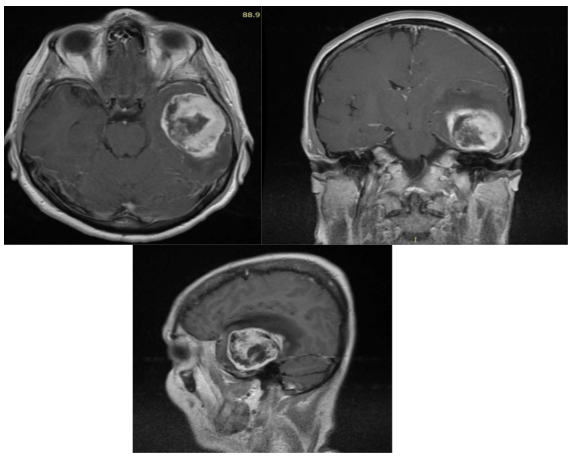

Figure 1: Initial head MRI.

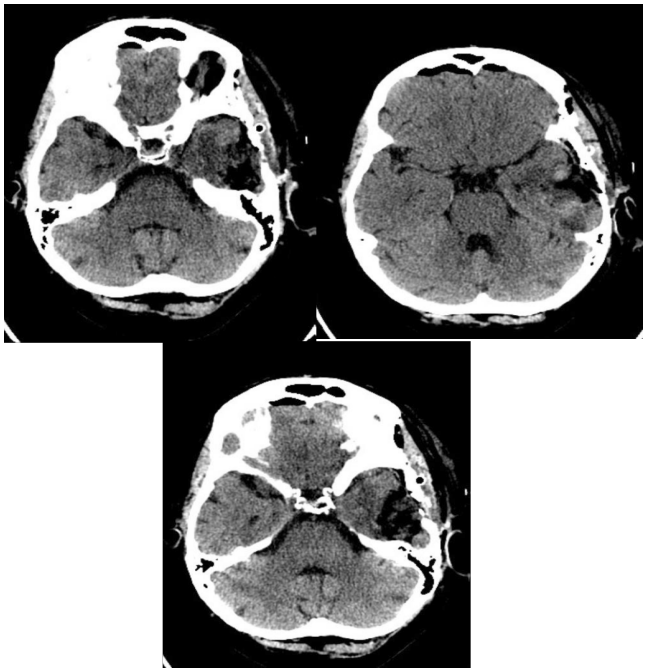

Figure 2: Post operative head CT.

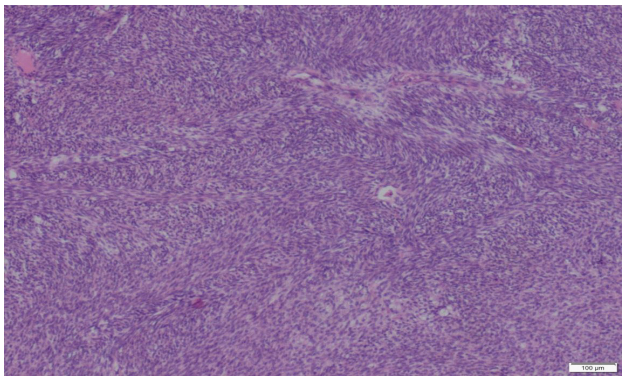

Figure 3a: The pattern typical for high grade spindle-cell sarcoma. (HE, 40x).

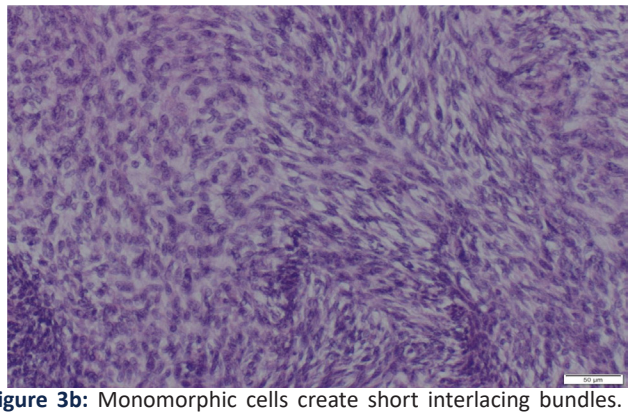

Figure 3b: Monomorphic cells create short interlacing bundles. In other areas neoplasmic necrosis was visible. (HE, 100x).

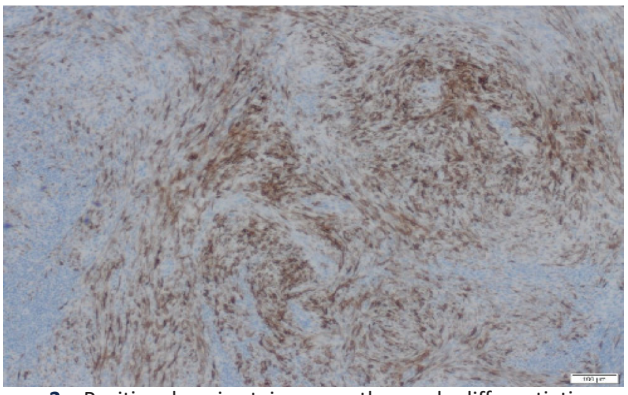

Figure 3c: Positive desmin stain - smooth muscle differentiation (typical for sarcoma) (HE, 40x).

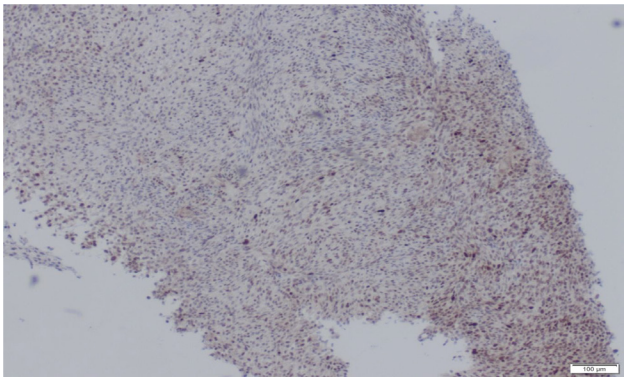

Figure 3d: Focally positive nuclear reaction IHC MDM2 (FISH confirmed the presence of MDM2 amplification) (HE, 40x).

Discussion

There are only a few reported cases handful of cases of cerebral metastases of intimal sarcoma [10-16]. Metastases can cause the embolisation of large brain vessels causing wide infarction regions [14]. Multiple metastases were present supratentorially [11,15] as well infratentorially [11]. Single IS metastasis at the time of presentation was observed within frontal lobe at parafalcine location [12] or white matter of right periventricular area [16]. There were, in literature, additional two cases of single metastasis at the time of diagnosis with no specific cerebral location provided [13].

These lesions might be responsible for the onset of symptoms [16] or might be found only during the autopsy [10,15]. The location of a single tumor with parallel MRI appearance including gadolinum enhancement might initially suggest meningioma [12], as in our case.

Here, the metastasis was located at floor of the middle cranial fossa. Such location might be related to the metastatic invasion of the carotid canal at the skull base. This could explain the site of tumor attachment at the floor of the fossa, observed during resection.

The approaches to the treatment of the brain metastases included total removal of a tumor [12,16] or radiation and/or palliative treatment [11,13].

Prognosis of these tumors still remains poor. The most optimal therapeutic approach includes aggressive surgical treatment, followed by chemotherapy and radiotherapy. Radiotherapy might include radiosurgery which is already used in treatment of some types of brain metastases [17]. The diagnosis of IS is extremely challenging because there is no specific pattern of diagnostic markers [18]. Most common marker seems to be MM2 - but lacks specificity. Some attention has recently been drawn to more detailed pathological profiling of these tumors, which might be helpful while establishing new therapeutic targets. Especially mutations in platelet-derived growth factor receptor alpha (PDGF-Ralpha) gene, platelet-derived growth factor receptor beta (PDGF-Rbeta) gene as well as epidermal growth factor receptor (EGF-R) [18,19].

Conclusion

We believe the SI, although rare, should be included in the differential diagnosis of the brain metastatic disease. The onset of neurological symptoms in patients with diagnosed SI should raise a suspicion of the brain involvement and provoke the broadening of the diagnostics in order to continue treatment.

Conflict of interest disclosures: The authors have no financial conflicts of interest to declare.

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