Int J Clin Exp Pathol 2017;10(3):3551-3557
www.ijcep.com /ISSN:1936-2625/IJCEP0045730

Case Report

Primary malignant triton tumor of the heart: a case report and review of literature

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Received December 4, 2016; Accepted December 22, 2016; Epub March 1, 2017; Published March 15, 2017

Abstract: Background: malignant triton tumor is a very rare malignant peripheral nerve sheath tumor (MPNST) with rhabdomyosarcomatous differentiation. In the present paper, we report aprimary malignant triton tumor in the heart of a 34-year-old woman who underwent resection of the left atrial tumor. To the best of our knowledge, this is the second case of primary malignant triton tumor of the heart reported in English. Case presentation: A 34-year-old woman underwent resection of the left atrial tumor. The tumor was fleshy white-tan, texture partial crisp and partially translucent. Histologically, the mass was composed of interlacingfascicles of hyperchromatic serpentine spindle cells. The cells had elongated and comma shaped nuclei and sparse cytoplasm with indistinct borders. Hypercellular and hypocellular zones with areas of palisading necrosis and myxoid stroma were also present. In the more myxoid areas, the parallel orientation of the cells was lacking. Large pleomorphic cells with abundant eosinophilic cytoplasm and rounded eccentric nuclei were seen admixed with neoplastic spindle cells. The pleomorphic cells were striated, strap-like, or globoid rhabdomyoblasts. Immunohistochemically, the tumor cells were positive for vimentin, NSE, weak expression S-100, and focally positive formyogenin, desmin, and MyoD1, negative for cytokeratin (pan), EMA, Actin (SM) and HMB-45. Conclusion: According to the morphological and immunohistochemical findings, we diagnosed this primary cardiac tumor as a primary malignant triton tumor. Heretofore, the experience of treating primary intracardiac malignant triton tumor is still lacking and more experience in diagnosis and treatment needs to accumulate.

Keywords: Malignant triton tumor, rhabdomyosarcoma, malignant peripheral nerve sheath tumor, heart

Background

Malignant triton tumor is a very rare malignant peripheral nerve sheath tumor (MPNST) with rhabdomyosarcomatous differentiation [1, 2]. About 70% cases of malignant triton tumor are associated with Von Recklinghausen's disease, particularly in young men, and the remaining 30% are sporadic, mostly occurring in older women [2, 3]. The tumors are predominantly located across peripheral nerves in the head, neck, extremities and trunk [2, 4]. To date, there have been 202 reported cases [5-7]. As far as we know, this is the second intracardiac presentation and illustration of such anextremely rare tumor [8].

Clinical history

A 34-year-old woman caught a cold and developedshortness of breath, cough with white sputum, with no other cardiac symptoms of angina and arrhythmia. She visited her local city hospital and took the prescript anti-cold medicine then the symptom relieved slightly. Ten days later, she had a sudden headache, accompanied by nausea and vomiting. Herhead CT scan indicated cerebral hemorrhagein bilateral parietal lobe and occipital lobe, but digital subtraction angiography (DSA) did not find obviousblood vessel fracture (**Figure 1**). The heart color Doppler ultrasound indicated left atrial myxoma. A repeat transthoracic echocardiogram performed at our hospital demonstrated that a large mass within the left atrium (51 mm × 30 mm × 35 mm) arising from the posterior mitral annulus (**Figure 2A**, **2B**). The echo was irregular, loose and lobulated. Part of the tumor entered the left ventricle through the mitral valve during diastoleand returned to the left atrium during systolic period. The mitral valve

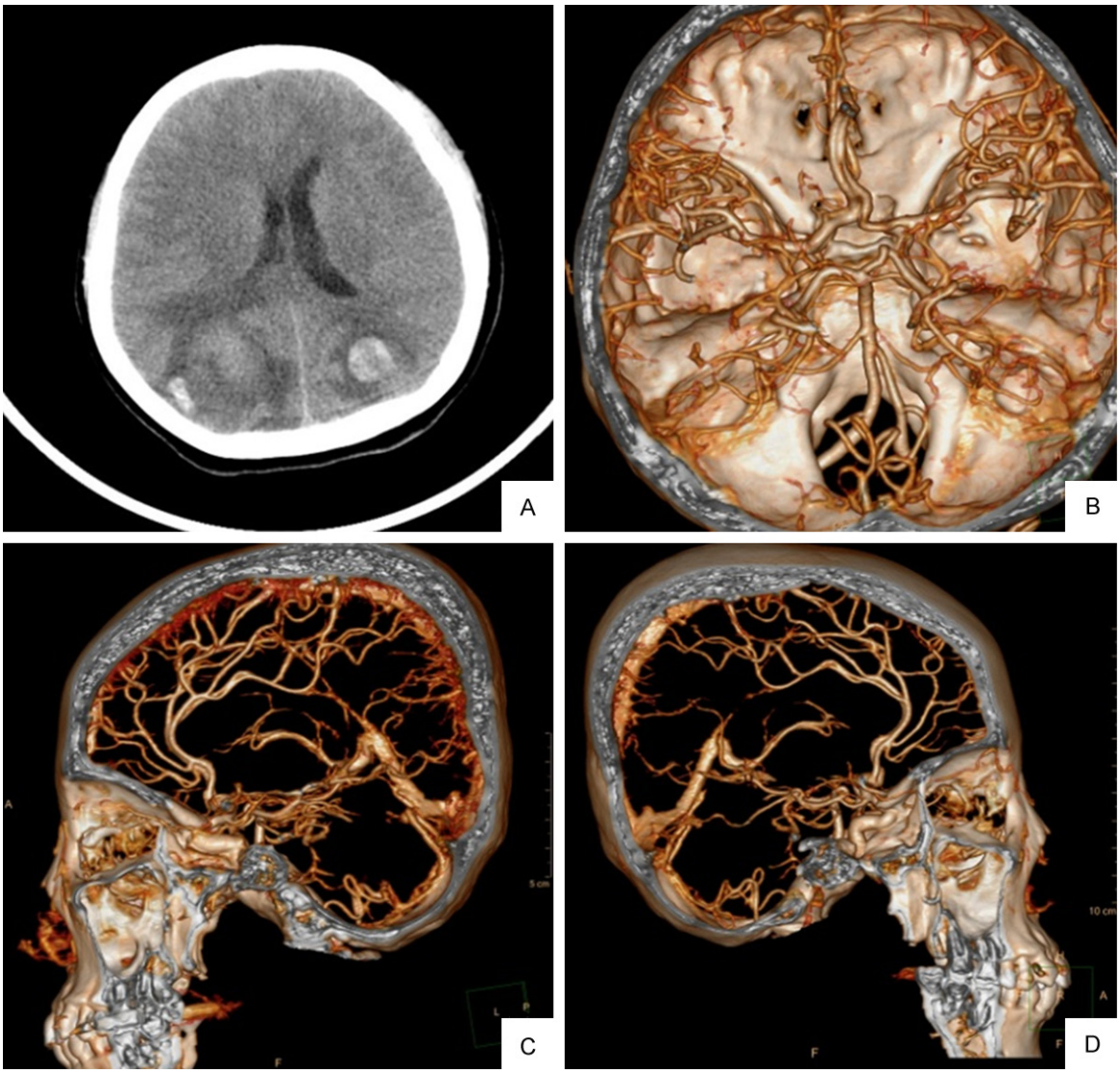

Figure 1. The head CT scan. Her head CT scan indicated cerebral hemorrhage in bilateral parietal lobe and occipital lobe (A). DSA did not find obvious blood vessel fracture (B-D).

orifice flow was blocked, and the left atrium enlarged. The patient underwent excision of the left atrial tumor and mitral valve plasty. Amedian sternotomy approach, atrio-aortic cardiopulmonary by pass and customary myocardial preservation techniques were used. The tumor was big and filled the left atrium. The pedicle of the tumor was located in the posterior wall of the left atrium and the P2 and P3 region of the posterior mitral valve. The tumor and its pedicle were resected completely and the defect was reconstructed using an autologous pericardium patch (**Figure 2C**, **2D**). There were no family history suggestive of or any clinical signs (e.g., Café-au-lait macules, iris hamartomas, or neurofibromas) consistent with von Recklinghausen's Disease. Unfortunately, the patient died of brain hernia on the 28th postoperative day.

Pathology

Gross

The tumor was a broken mass, about 5 cm in diameter. It was fleshy white-tan, texture partial crisp and had semitransparent gelatinous material within it (**Figure 3**).

Histology and immunohistochemistry

The tumor was fixed in 10% formalin and embedded in paraffin. Several 4-μm sections

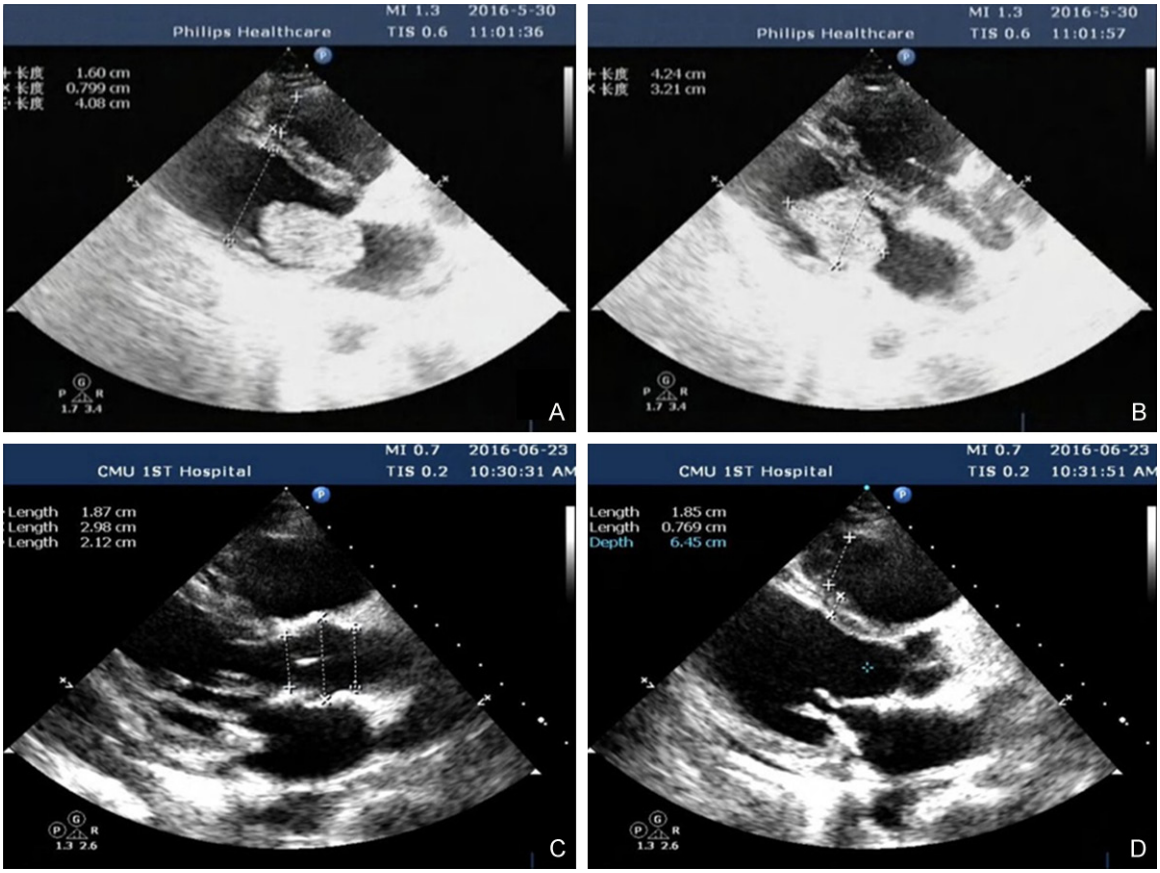

Figure 2. The transthoracic echocardiogram. Transthoracic echocardiogram demonstrated a large mass within the left atrium (51 mm × 30 mm × 35 mm) arising from the posterior mitral annulus (A). Part of the tumor entered the left ventricle through the mitral valve (B). Postoperative ultrasonography demonstrated the large mass was incised (C, D).

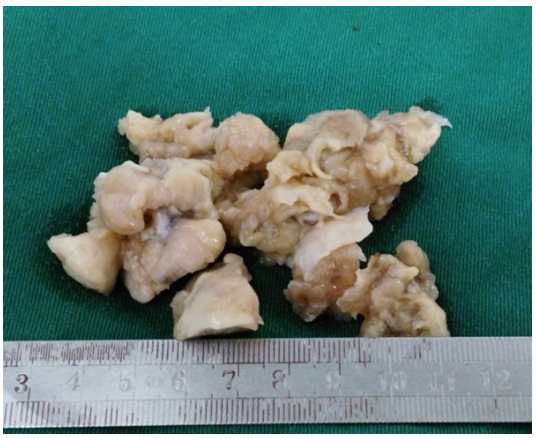

Figure 3. Gross pathology. The tumor was broken mass, 6 cm in diameter, fleshy white-tan, texture partial crisp and partially translucent.

were cut from each paraffin block, and one was stained with HE (hematoxylin and eosin), the others were stained with immunohistochemistry. Immunohistochemical staining was performed using the streptavidin-peroxidase system (Ultrasensitive; Mai Xin Inc., Fuzhou, China) according to the manufacturer's instruction. Commercially available prediluted monoclonal antibodies against the following antigens were employed: vimentin, cytokeratin, EMA, S100, NSE, synaptophysin, myogenin, MyoD1, desmin, actin (SM), CD34, HMB-45, CD68 and Ki-67 (Thermo Fisher Scientific Inc., Fremont, CA, USA).

Histologically, the tumor was composed of spindle and oval cells arranged in a fasciculated pattern and whorls. The cells had irregular contours with oval, wavy configuration in some areas and a narrow, tapering outline in others, showing wavy, hyperchromatic nuclei with indistinct light staining cytoplasm (**Figure 4A**, **4B**). Hypercellular and hypocellular zones with areas

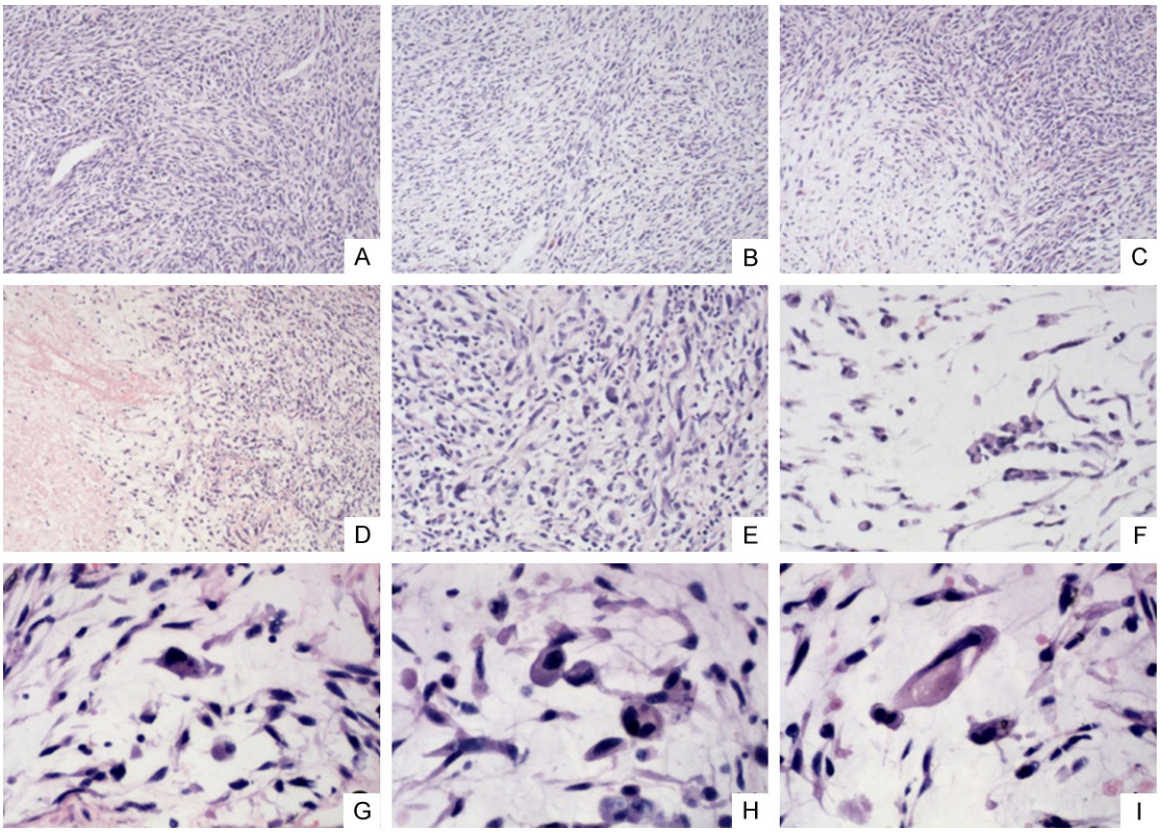

Figure 4. Histopathology (HE stain). The tumor was composed of spindle and oval cells arranged in a fasciculated pattern and whorls (A, 100 ×). The cells had irregular contours with oval, wavy configuration in some areas and a narrow, tapering outline in others (B, 100 ×). Hypercellular (right) and hypocellular (left) zones were present (C, 100 ×). Necrosis (left) and myxoid stroma were present (D, 100 ×). Scattered large round cells with eosinophilic cytoplasm and hyperchromatic nuclei were seen admixed with neoplastic cells (embryonal rhabdomyoblasts) (E, F, 200 ×, G-I, 400 ×).

of palisading necrosis and myxoid stroma were also present. In the more myxoid areas, the parallel orientation of the cells was lacking (**Figure 4C**, **4D**). Large pleomorphic cells with abundant eosinophilic cytoplasm and rounded eccentric nuclei were seen admixed with neoplastic spindle cells. The pleomorphic cells were strap-like, or globoid rhabdo myoblasts. The presence of the alternating hypercellular and hypocellular arrears is suggestive of nerve sheath origin, and scattered large round cells with eosinophilic cytoplasm and hyperchromatic nuclei were seen indicating the presence of rhabdomyoblasts (**Figure 4E-I**). The histological grade of the tumor is grade-3 according to the French National Federation of Cancer Centers (FNCLCC) grading system [9].

Immunohistochemically, the tumor cells were positive for vimentin, NSE, weak expression S-100, and focally positive for myogenin, desmin, and MyoD1, negative for cytokeratin (pan), EMA, actin (SM) and HMB-45. The large, round or oval eosinophilic pleomorphic cells were immunoreactive for muscle-specific myogenin, MyoD1 and desmin (**Figure 5**). Immunohistochemical staining with S-100 and MyoD1 indicated that the tumor cells originated from Schwann cells and showed rhabdomyosarcomatous differentiation. Ki-67 was expressed in a lot of cells (about 40%).

Discussion

Primary cardiac tumors are rare neoplasms with an incidence from 0.017‰ to 0.19‰, of which about 1/4 are malignant [10, 11]. In the most cases, triton tumors are located usually close to the spine, in the head and neck region, or in the upper and lower extremities [4]. The male-to-female ratio was 1.5 to 1, and the median age at diagnosis was 29 years old. Guo

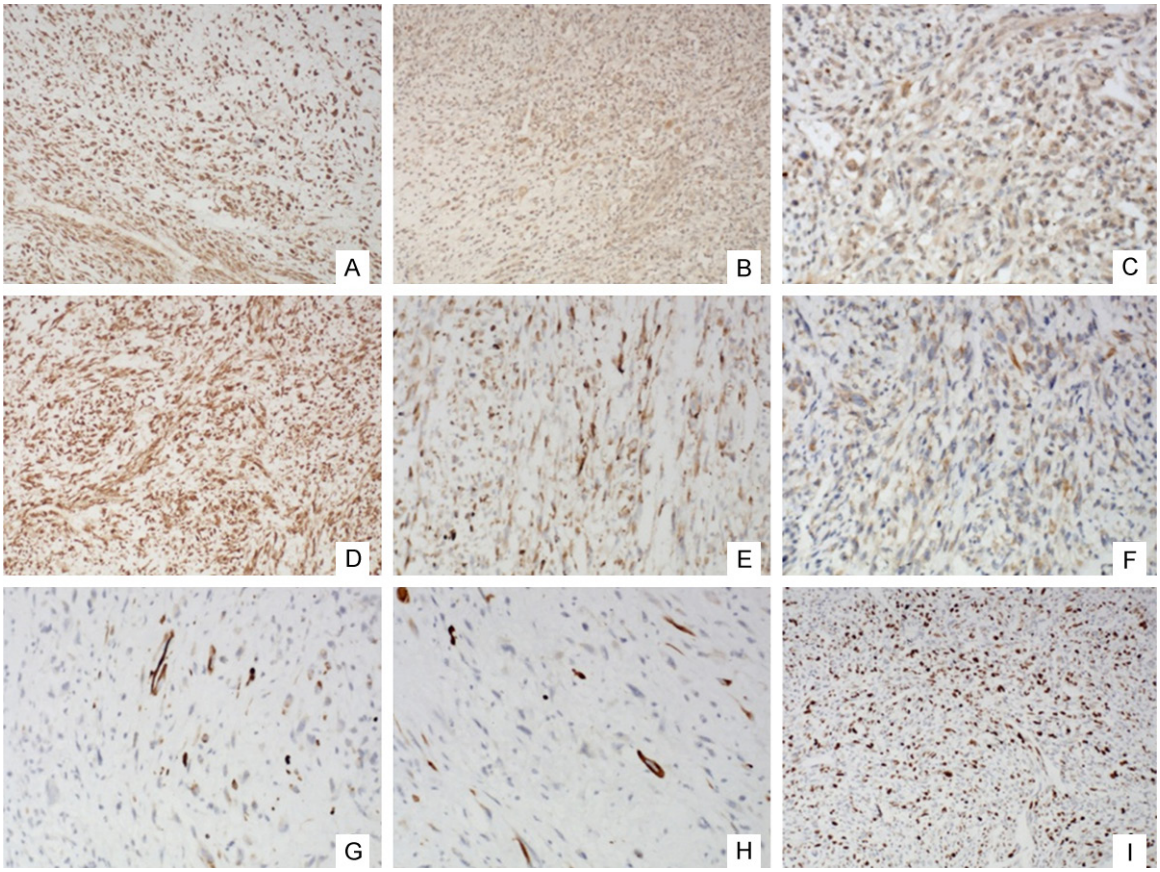

Figure 5. Immunohistochemistry. The tumor cells were positive for Vimentin (A, 100 ×), S-100 (B, 100 × C, 200 ×), NSE (D, 100 ×), focally positive for MyoD1 (E, 200 ×), Myogenin (F, 200 ×), Desmin (G, H, 200 ×). Ki-67 was expressed in a lot of cells, 40% positive (I, 100 ×).

L et al. reviewed 200 malignant triton tumorsand analyzed 133 cases with follow-up. Their Kaplan-Meier survival analysis demonstrated that age, presence of NF-1, complete resection, radiotherapy and presence of metastasis had a statistically significant effect on the prognosis. The factors of gender, onset site, chemotherapy and relapse had no significant effect on the survival curves [5]. Malignant triton tumor ismore aggressive than sporadic MPNST with a natural history as a high-grade sarcoma (Grade-3). Local recurrence is common after excision and the 5-year survival rate is about 12% [3].

Large pleomorphic cells with abundant eosinophilic cytoplasm and rounded eccentric nuclei were seen admixed with the neoplastic spindle cells. These large pleomorphic cells (myogenin, desmin and MyoD1 positive) were strap-like or globoid rhabdomyoblasts with no obvious striate, for they were not mature striated muscle cells. As we know, S-100 is normally present in cells which derived from the neural crest (Schwann cells, and melanocytes), chondrocytes, adipocytes, myoepithelial cells, macrophages, Langerhans cells, and dendritic cells, etc. Myogeninis a myogenic transcriptional regulatory protein which is expressed in the early phase of skeletal muscle differentiation (rhabdomyogenic differentiation). This protein has been usually accepted as a sensitive and specific immunohistochemical marker for rhabdomyosarcoma or tumors with rhabdomyoblastic differentiation [12]. A few tumor cells showed positive reactivity for MyoD1, which function is to commit mesoderm cells to a skeletal myoblast lineage, and to regulate the continued state in development. MyoD mRNA levels are elevated in aging skeletal muscle [13]. Desmin is an earliest protein marker for muscle tissue in embryogenesis. Although Desmin is present early in the development of muscle cells, it is only expressed at low levels, and increases with the cell terminal differentiation [14]. Based

on the above morphological and immunohistochemical findings, we diagnosed this primary cardiac tumor as a primary malignant triton tumor.

We think the cause of nausea and vomiting of the patient was intracranial hemorrhage, and the cause of intracranial hemorrhage was the brain metastasis of the malignant tumor, although there wereno clear vascular abnormalities reported by the cerebrovascular DSA. At present, there is still lack of experience in treating primary intracardiac malignant triton tumor. Unfortunately, the patient died of brain hernia on the 28th postoperative day.

Conclusion

Based on the morphological and immunohistochemical findings, we diagnosed the primary cardiac tumor as a primary malignant triton tumor, although it is extremely rare. At present, there is still lack of experience in treating this malignanttumor and we need to accumulate more cases and experience for treatment.

Acknowledgements

We wish to thank the patient, who requested anonymity, her husband and her younger sister for agreeing our report and provided a detailed history. This work was supported by grants from the National Natural Science Foundation of China (No. 81000995) and Natural Science Foundation of Liaoning (No. 2015020491) to Dr. Yang Han.

Written informed consent for publication of their clinical details and/or clinical images was obtained from the patient/relative of the patient. A copy of the written consent is available for review by the Editor-in-Chief of this journal.

Disclosure of conflict of interest

None.

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