CARDIAC MYXOMA PRESENTING AS VERTIGO AND PARESTHESIA OF THE EXTREMITIES

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ABSTRACT

Cardiac myxomas are characterized by a triad of obstruction, embolization, and constitutional symptoms. Minority of the patients with a left atrial myxoma develops a neurologic event. Hereby we describe a case of left atrial myxoma whose onset was characterized by vertigo and paresthesia of the extremities. The patient was diagnosed with left atrial myxoma by echocardiography. Surgical resection of the tumor was performed successfully and the patient's symptoms disappeared after surgery. Histology revealed a diagnosis of myxoma. To distinguish a cardiac from a neurological etiology for such a patient is of great importance in making a definite diagnosis and further prompt management.

Key words: Cerebral infarction, cytokines, heart neoplasms, interleukin-6.

Introduction

Myxomas are the most common type of primary cardiac tumor, often found in the left or right atria. Although benign, its tendency of recurrence, multicentricity, metastases and inheritance may indicate the malignant potentiality of cardiac myxomas(1). At least 25% of the patients with left atrial myxoma may develop a neurologic event(2). Most cerebral emboli in children are of cardiac origin, with atrial myxoma being the most common underlying etiology(3). Cardiac myxoma may come to forensic attention because of sudden death. Neurologic involvement in left atrial myxomas occurs by various mechanisms. The most frequent one is ischemic stroke secondary to cardiac embolism. The source of embolus could be the tumor itself or thrombus on its surface(4,5). Cerebral ischemia caused by tumor embolization is the most common neurological manifestation. Other neurological disorders may include parenchymal brain metastasis, intracerebral hemorrhage, and oncotic aneurysmal formation(6). Patients with a cardiac myxoma do not often manifest multiple lacunar cerebral infarction and present with vertigo and paresthesia of the extremities like the present patient. Therefore, it is implicated in stroke differential diagnosis (cardiac or neurological etiology).

Case report

A 47-year-old female was referred to the Department of Neurology of this hospital due to repeated onset of vertigoes and visual rotation accompanied by nausea and vomiting for one year. She also complained of dysesthesia of her left fingers and muscular soreness of the lower limbs, which caused her fatigue and walking difficulty. On admission, her temperature was 36.5°C, pulse 78 beats/min and blood pressure 149/98 mmHg. There were no rales over both lungs. Cardiac auscultation revealed no heart murmurs. Laboratory examinations showed erythrocyte sedimentation rate was 32 mm/h (reference values: 0-20 mm/h), D-dimer was 0.53 mg/L (reference values: <0.5 mg/L), and lipoprotein (a) was 1.32 g/L (reference values: 0.6-1.10 g/L). Electrocardiogram disclosed sinus rhythm. Cranial magnetic resonance imaging displayed multiple lacunar infarctions in thalamus...
(bilateral), cerebral peduncles, basilar part of pons, cerebellar hemispheres and coronae radiatae, majority of which were malacias and part were ischemic, indicating multiple old infarctions with old hemorrhages in cerebellum (bilateral) (Fig. 1). She was diagnosed as posterior circulation ischemia and she received supportive treatment in order to improve her symptoms, but it failed. Echocardiography showed a well-defined highly mobile, heterogeneous, friable, sessile lesion measuring 3.5×2.5×1.5 cm attached to the intraatrial septum (Fig. 2). She was diagnosed as left atrial myxoma, and was transferred to Department of Cardiothoracic Surgery. Further chest computed tomography revealed a hypoattenuate mass measuring 33.51×24.71 mm in the left atrial cavity attaching to the interatrial septum. The diagnosis of left atrial myxoma was evidenced.

The operation was performed via the right atrium-interatrial septum approach. While entering into the right atrium, palpation with a finger on the interatrial septum disclosed that the mass was just attaching to the center of the fossa ovalis. A portion of the fossa ovalis, where the myxoma inserted, was excised. The tumor extended 3.5×2.5×1.5 cm. Two small bunches of the remnant myxomatous tissues measuring 1.5×0.5×0.3 cm each, which were left inside the left atrial cavity, were carefully taken out. Careful inspections of the atria did not reveal any remnant or multiple myxomas. The atria were rinsed thoroughly with saline solution. The defect of the fossa ovalis was closed by a Dacron patch. The myxoma was grossly sessile, brownish, semi-transparent, friable, attached broad-basely to the fossa ovalis (Fig. 3A). The patient became asymptomatic, and the atrial myxoma was no longer detectable on echocardiography. She had no postoperative complications and was discharged on the ninth postoperative day. Histology of the surgical sample proved the diagnosis of left atrial myxoma with complete resection of the broad base of the tumor (Fig. 3B-3D).

**Discussion**

Cardiac myxomas are characterized by a triad of obstruction, embolization, and constitutional symptoms, which may be present solely or in any combination. The most common clinical manifestation of cardiac myxoma is obstructive symptoms: heart failure, dyspnea, syncope, or sudden death, and are caused by obstruction of the mitral or tricuspid valves. Tumor fragments or thrombi from the surface of the tumor were responsible for the embolic events in cardiac myxoma patients, and result in metastases or destruction of arterial walls by myxoma-related pseudoaneurysms. Embolic complications like stroke or peripheral ischemia are often due to the left atrial myxoma fragments entering the arterial circulation. Embolism occurs in approximately one third of patients presenting with
myxomas. Because most myxomas occur in the left atrium, systemic embolism is much more common than pulmonary embolism. Central emboli occur more commonly than peripheral emboli, but both may possibly develop together\(^{(12)}\). Constitutional symptoms like fever, weight loss, arthralgias, and myalgias occur in 34-90% of patients with a cardiac myxoma\(^{(11)}\).

Acute focal deficits resulting from tumor embolization can sometimes be the onset of cardiac myxoma. Emboli may originate from fragmentation of the tumor or the release of thrombosis covering the tumor surface\(^{(13)}\). The branching morphology of the myxoma, generally with a friable or gelatinous texture, enables fragmentation, erosion and embolization, and increases the risk of embolization\(^{(14)}\). Irregular, friable or villous myxomas are more likely to be associated with embolic events than a tumor with a smooth surface\(^{(12,15)}\). The tumors may have no significant hemodynamic compromise but with embolic events, Emboli from solid myxomas may result from cracking of the surface subjected to turbulent flow. Swartz et al.\(^{(13)}\) reported 60% of patients with solid myxoma presented with congestive heart failure and 44% of patients with a papillary myxoma presented with neurologic symptoms.

Symptomatic emboli occur in 20-45% of patients with a cardiac myxoma, and about half of all myxomatous emboli from the left heart to the brain\(^{(3)}\). Shimono et al.\(^{(16)}\) reported two distinct anatomic types, a solid, ovoid type and a friable, papillary type. They also noted an increased incidence of preoperative brain infarction in patients with papillary tumors (75%) compared to those with solid tumors (12.5%). The pedunculated tumors are irregular and more likely to embolize because of their mobile state\(^{(17)}\). These emboli consist of either myxomatous tissue or thrombus adherent to the myxoma mass. Embolic myxoma has been described as invading, displacing, and disrupting arterial walls, increasing the risk of aneurysm formation\(^{(18)}\). Nearly 50% of the patients present with neurologic signs and symptoms usually resulting from cerebral ischemia, which may be hemorrhagic\(^{(18)}\). Atrial myxomas have been estimated to cause up to 0.5% of ischemic strokes\(^{(19)}\). The median delay between onset of symptoms and diagnosis in myxoma patients with neurologic manifestation was 36 months\(^{(20)}\).

Patients with a cardiac myxoma presenting with a peripheral demyelinating neuropathy are not common. Santangeli et al.\(^{(21)}\) reported their patient had burning dysesthesias over the soles, paresthesia over both feet associated with weakness of toes dorsiflexion, a significant reduction of nerve conduction velocity (21.4 m/s) associated with significantly high values of C-reactive protein and erythrocyte sedimentation rate. Mariano et al.\(^{(22)}\) demonstrated a pediatric patient with left atrial myxoma manifested paresthesia of the lip and fingers of the right hand following a transient ischemic accident. Cardoso et al.\(^{(23)}\) reported a case of left atrial myxoma in a 12-year-old girl who presented with sudden dizziness and right-sided paresthesia of the lips and fingers of the right hand. Yamamoto et al.\(^{(24)}\) reported a case of left atrial myxoma causing cerebral embolism. Serial magnetic resonance imaging showed frequent episodes of cerebral infarction. Surgical resection of the myxoma was performed on the 10\(^{th}\) day after the onset of the neurological symptoms and the patient was uneventful after the operation. Similar to the above reported cases, the present patient onset was characterized by vertigo and paresthesia of the extremities and was diagnosed with multiple lacunar infarctions. Links between lipoprotein (a) and neurologic events have been elaborated\(^{(25)}\). Her normal blood lipoprotein (a) level may exclude an atherogenic origin of the neurologic events. In addition, a cardiogenic cause was evidenced by echocardiography.

Interleukin-6 (IL-6) secretion by the cardiac myxomas has been hypothesized as a possible explanation for the inflammatory and immune reactions developed in these patients\(^{(12)}\). A direct relation was noted between plasma IL-6 levels and the tumor size\(^{(11)}\), however, this relation did not exist in the condition of tumor recurrence\(^{(26)}\). Systemic manifestations of cardiac myxoma seem to be caused by pro-inflammatory cytokines release, in particular IL-6 and tumor necrosis factor-α\(^{(27)}\). Secretion of cytokines is indispensable to tumor development and proliferation\(^{(28)}\). Studies have shown that myxomas were positive for vascular endothelial growth factor (VEGF) mRNA, whereas atrial septum and atrium tissues were negative\(^{(29)}\).

Similar to the expression of IL-6, it has been found that there was a direct relation between the size of myxomas and the level of VEGF expression. Nevertheless, there was an inverse correlation between the tumor size and PCNA (proliferating cell nuclear antigen)-labeling index. In addition, co-expression of basic fibroblast growth factor (bFGF) and fibroblast growth factor receptor-1 (FGFR-1)
was frequently observed in the myxoma cells (30). Immunohistochemistry for Nkx2.5/Csx, GATA-4, and eHAND was slightly-to-intensely positive in all myxoma cases (31). These data suggested that the cytokines may probably participate in myogenic differentiation of cardiac myxomas.

In conclusion, patient with a cardiac myxoma may manifest a triad of obstructive, embolic or constitutional symptoms. The embolic phenomena of the cardiac myxoma patients may result from the tumor debris and the impact of cytokine secretion. Physicians should always bear in mind that an embolic event has to be distinguished a cardiac tumor from a neurological etiology. Due to the high embolic and obstructive risk of myxoma, a prompt surgical resection is mandatory in the event a definite diagnosis of cardiac myxoma is established.

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