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CASE REPORT

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Multiple Metastatic Intracranial Lesions Associated with Left Atrial Myxoma

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Summary

Background: One of the most common cardiac tumors is myxoma. Despite its predominantly benign course, diverse cardiological, systemic as well as neurological complications have been reported.

Case Report: We are the first from Poland to present the case of a patient with multiple central nervous system metastases associated with the left atrial myxoma. Various diagnostic, neuroradiological and histopathological procedures were described. The patient underwent cardiac surgery.

Conclusions: Follow-up studies excluded the recurrence of the heart tumor and confirmed partial resolution of brain metastases. Nevertheless, subsequent neurological assessment was advised according to the literature data and possible late relapses mainly due to cerebral emboli.

Keywords: Atrial Myxoma • Hemorrhagic Brain Lesions • Cerebral Embolism • Brain Metastases

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Background

Cardiac myxoma belongs to mostly benign primary cardiac tumors. However, it may cause a wide variety of complications including cardiac obstructive symptoms, systemic embolism and cerebral infarcts [1]. Cardiac complications are mainly related to mitral valve obstruction by the tumor and include dyspnea, palpitations and heart failure. As for systemic symptoms, fatigue, fever, weight loss and muscle weakness should be mentioned. Cerebral infarcts result mainly from embolic events. However, myxomatous aneurysms as well as hemorrhagic lesions were also described [1,2]. It seems that early diagnosis and cardiosurgery allow to significantly reduce the morbidity and mortality [3]. Transthoracic and in some cases transesophageal echocardiography are one of the most helpful methods in the diagnostics of abnormal masses in the heart [1]. There is no widely-accepted treatment of myxoma metastases. However, in single cases, chemotherapy or chemoradiotherapy are suggested [1]. We reported a case of a patient with multiple central nervous system metastases associated with the left atrial myxoma. The disease course as well as various studies with sequential neuroradiological imaging were presented. Despite advanced morphological investigations of the surgically removed tissue, the presence of myxoma was neither confirmed nor excluded in a brain sample. Nevertheless, no other cause of brain metastases was found and further neurological and cardiological observation is recommended.

Case Report

A 41-year-old woman was admitted to the local hospital in November 2011 because of a sudden onset of the left limb weakness which lasted for a few minutes. Brain computed tomography (CT) showed seven heterogeneous haemorrhagic lesions surrounded by edema. The lesions were spread throught both hemispheres – one in the right frontal lobe, one in the right parietal lobe, four in the left parietal lobe and one in the left occipital lobe (Figure 1A). Magnetic resonance imaging (MRI) confirmed the presence of multiple lesions which were surrounded by edema and contained hemosiderin deposits (Figure 1B). They also demonstrated predominantly central contrast enhancement.

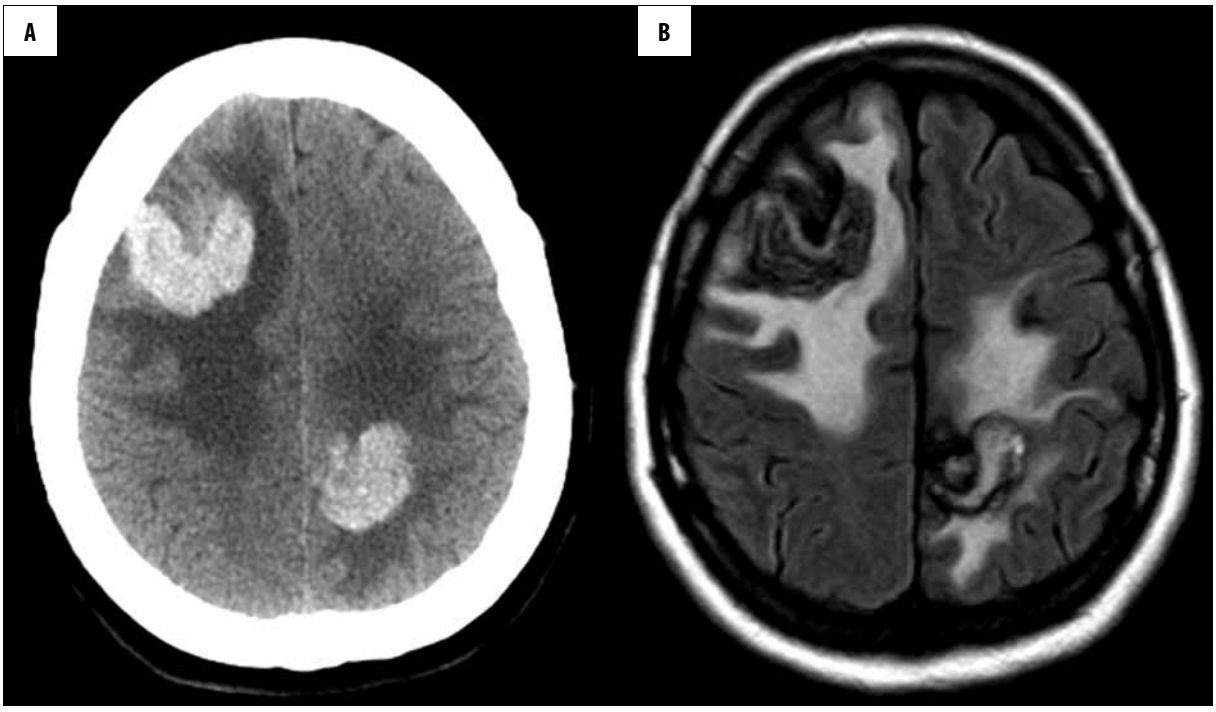

Figure 1. November 2011. Multiple hemorrhagic brain lesions surrounded by edema – (**A**) CT and (**B**) MRI (axial FLAIR image).

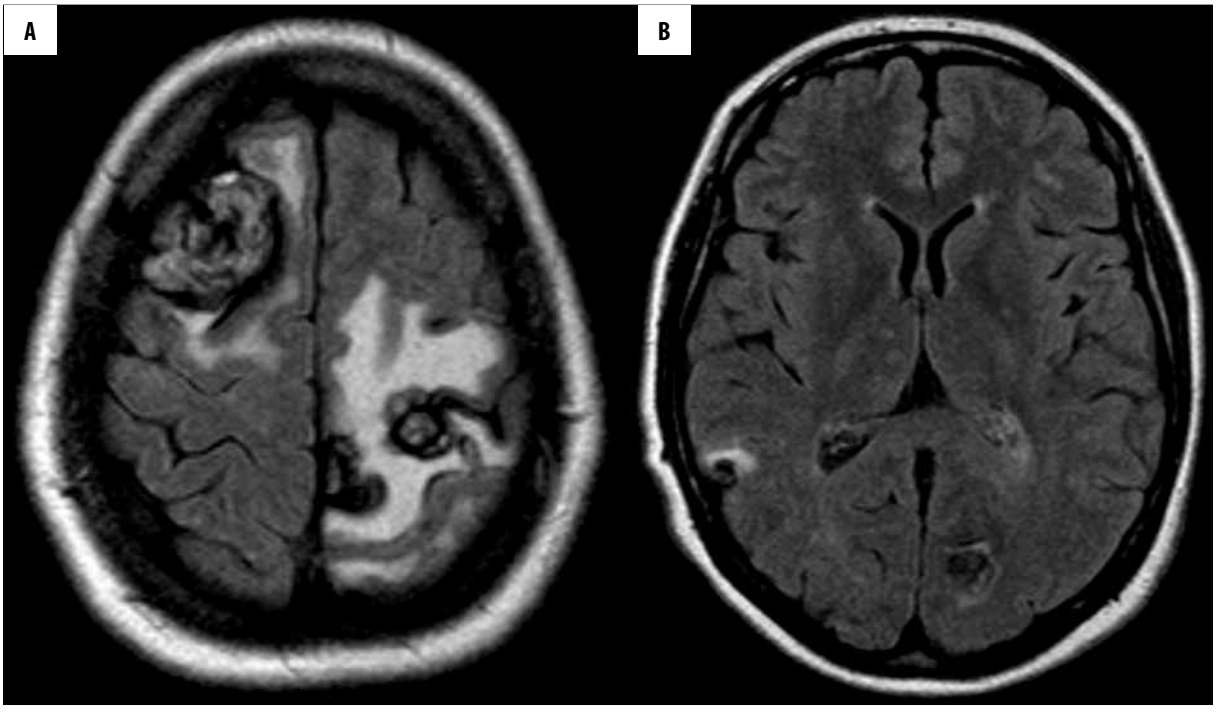

Figure 2. (**A, B**) The MRI **(**axial FLAIR images) one month follow-up.

Those findings were suggestive of neoplasmatic metastases or vascular malformations. MRI angiography was performed. However, apart from hypoplasia of part A1 of the left anterior cerebral artery no other abnormalities were noted. Abdominal ultrasound as well as chest X-ray showed no significant changes. Erythrocyte sedimentation rate was slightly elevated (18 mm after one hour, normal range up to 15 mm). Adequate blood tests excluded the presence of antibodies against *Borrelia burgdorferi* in M and G classes. Moreover, the *Candida*, *Cryptococcus* and *Aspergillus* antigens were not detected in the serum. Only antibodies against *Toxoplasma gondii* in G class were positive. In December 2011 the patient was admitted to hospital again due to the right limb weakness. MRI revealed multiple lesions very similar to those reported in November 2011 (Figure 2A, 2B). Similarly to those in the previous study, they were surrounded with edema and showed central contrast enhancement. Chest X-ray was normal. Erythrocyte

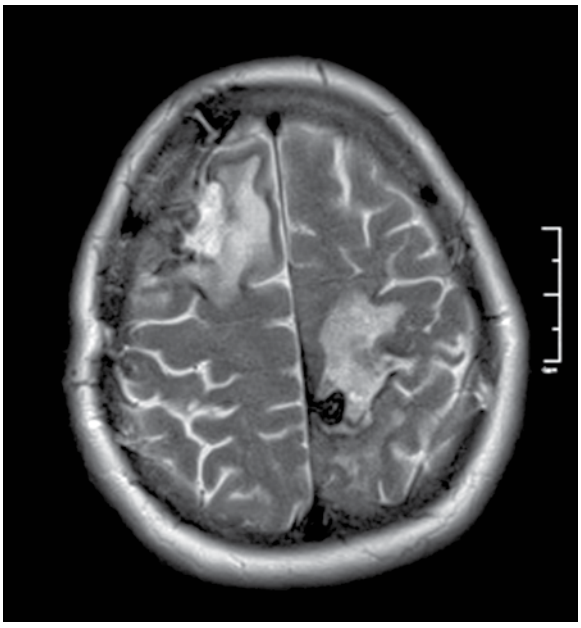

Figure 3. Brain MRI (axial T2-weighted image) from May 2012. The post-surgical changes in the right frontal lobe and partial resolution of lesion in the left parietal lobe.

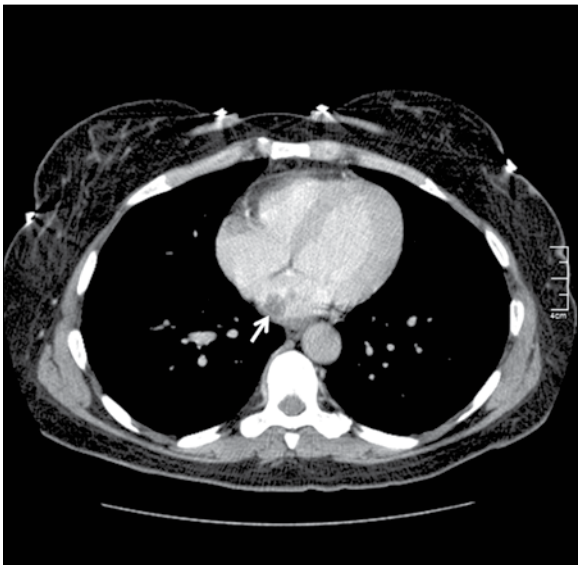

Figure 4. Chest CT. Abnormal mass in the left atrium (arrow).

sedimentation rate was elevated up to 37 mm after one hour. Finally, the patient was qualified to a neurosurgical operation and in January 2012 the tumor from the right frontal lobe was removed. The histopathological assessment revealed hemorrhagic areas with calcifications.

In May 2012 the patient, because of the diagnostic problems, was admitted to the Department of Neurology, Medical University of Warsaw, for the first time. Neurological examination revealed a slight weakness of the right limbs and subtle superficial sensation impairment in the right limbs and chest. Routine blood tests showed anemia (hemoglobin level of 11.1 g%, normal range 12–16 g%), decreased vitamin B_{12} level (162.3 pg/ml, normal range 191–663 pg/ml) and increased erythrocyte

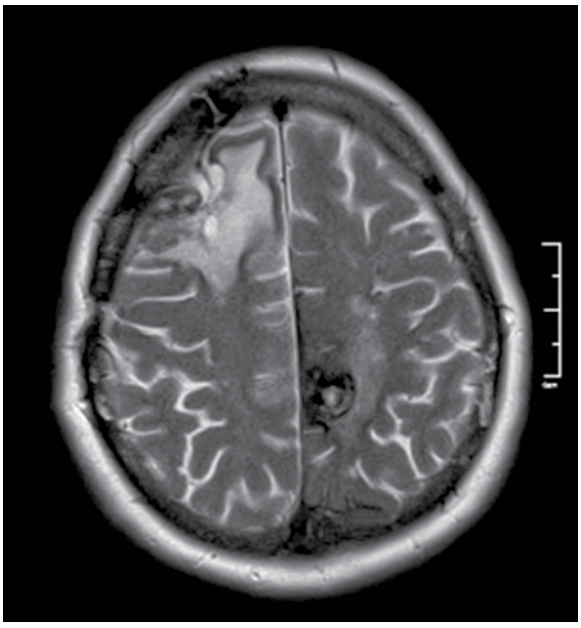

Figure 5. Brain MRI (axial T2-weighted image) from January 2013 with no signs of regression.

sedimentation rate (33 mm after one hour, normal range up to 12 mm). MRI presented a slight reduction in the size of the lesion in the left parietal lobe. As previously, central contrast enhancement and edema were noted (Figure 3). Based on these findings, vascular abnormality was suspected and therefore digital subtraction angiography (DSA) was performed. However, it showed no abnormalities. Disseminated pathological discharges were detected on electroencephalography. The ophthalmological examination showed irregular deficits in the visual field. There were no symptoms or signs of endometriosis, which may rarely cause intracystic hemorrhages in the central nervous system. The lumbar puncture was performed, and apart from a slightly elevated protein level (62 mg/dl, normal range 15–45 mg/dl), the analysis of the cerebrospinal fluid (CSF) was normal. An additional CSF examination excluded tuberculosis, neuroboreliosis and *Cryptococcus* infection. The level of thyroid hormones, rheumatoid factor, antibodies against Borrelia spp. in the serum were within normal ranges. Furthermore, the presence of antineutrophil cytoplasmic antibodies, antinuclear and anticardiolipin antibodies, lupus anticoagulant, trombophilia, syphilis and HIV infection were excluded by appropriate tests. The antithrombin III level was within normal ranges. The computed tomography of the chest aroused a suspicion of an abnormal mass in the left atrium (Figure 4). Transthoracic echocardiography confirmed the presence of a floating and fragmented mass in the left atrium and based on that the atrial myxoma was recognized. The patient was transferred to the Department of Cardiosurgery and Transplantology, Institute of Cardiology, where at the end of May 2012, heart surgery was performed. Histopathological assessment confirmed the presence of atrial myxoma.

The patient was admitted for the second time to the Department of Neurology in July 2012. Neurological examination showed a slight weakness of the right lower

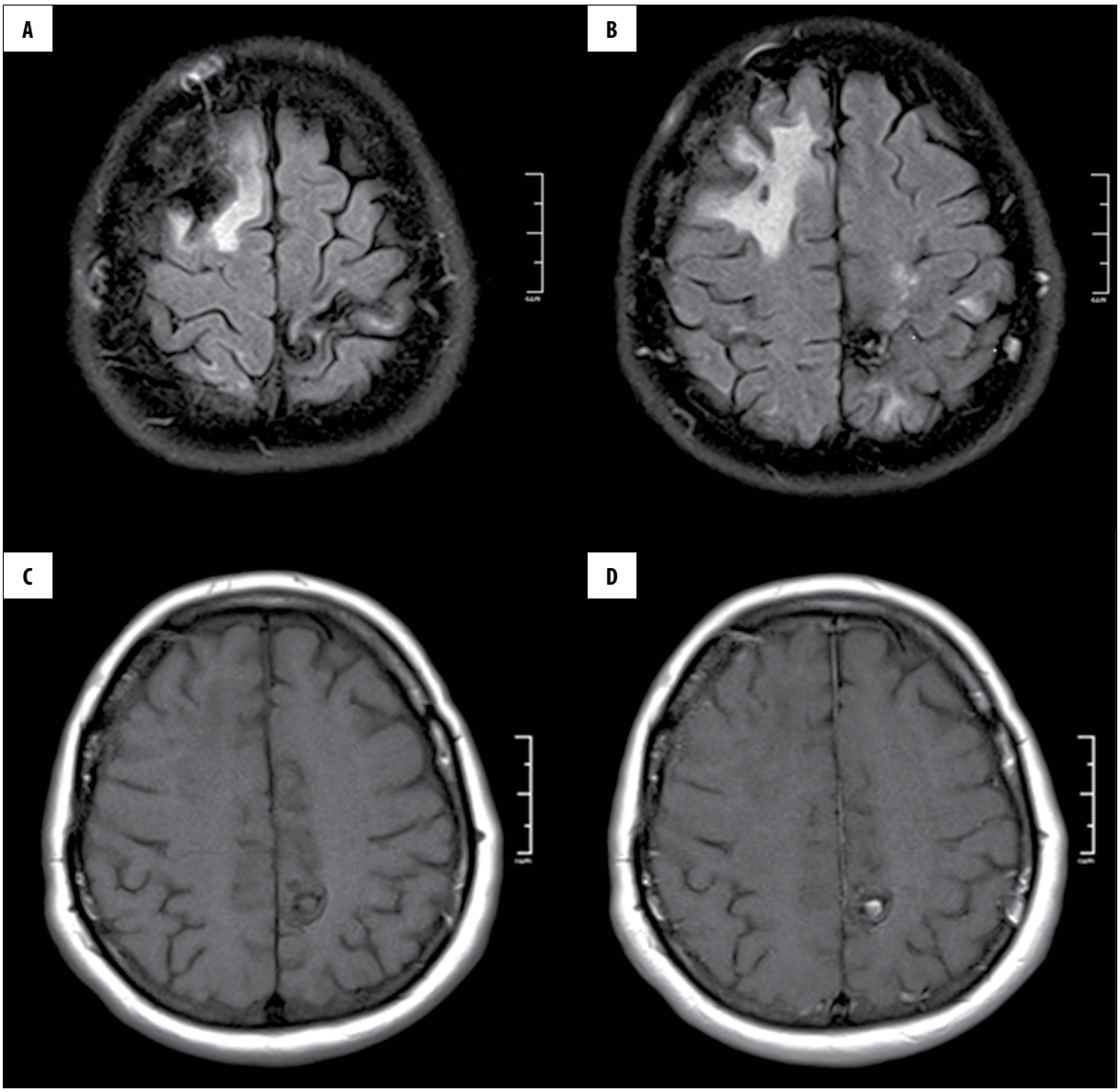

Figure 6. MRI from July 2013 showed partial resolution of edema (**A, B**, axial FLAIR images) and preserved central contrast enhancement (pre (**C**) and post contrast (**D**) axial T1 weighted images).

limb and a discrete superficial sensory deficit in the right lower limb and on the left side of the chest. Laboratory tests revealed anemia with iron deficiency and appropriate treatment was introduced. MRI showed reduction in size of the lesion and decreased edema in the left frontal lobe. Other lesions had similar appearance to those previously described. Meanwhile, the histopathological brain sections were examined once again, and chronic inflammation and hemorrhagic process with hemosiderin-laden macrophages, and glial and mesodermal severe reaction with vessel and collagen fiber calcifications were found. There were no signs of fungal infection, neoplastic lesion or cerebral endometriosis.

The third hospitalization in the Department of Neurology took place in January 2013. The neurological examination was comparable with the previous one. The echocardiography showed no signs of myxoma recurrence. Abdominal ultrasound demonstrated no significant abnormalities. The ultrasound of thyroid gland disclosed nodular goiter. Antithyroid antibodies were not detected. MRI of the brain revealed lesions comparable to those already described (Figure 5). Partial resolution of edema surrounding brain lesions was seen on follow-up MRI in July 2013 (Figure 6A, 6B). However, central contrast enhancement was still present (Figure 6C, 6D). There were no new metastases. The neurological examination was similar to the one carried out six months ago. However, further observation and control investigations were recommended.

Discussion

Cardiac myxoma represents mostly benign, slowly proliferating tumor which originates from subendocardial mesenchymal cells [4]. The incidence of surgically treated cases in some reports was estimated to be about 0.5–0.7 myxomas

Table 1. Classification of atrial myxoma metastases (adapted from DeSousa et al., 1978).

Type of metastases	Characteristic signs
Only intraluminal	• Symptomatic (infarct) • Asymptomatic
With vessel wall invasion	• Occlusion of vessel, gradual • Aneurysm formation
With vessel wall transgression	• Asymptomatic • Mass lesion effect
Local cardiac recurrence	• At original site • At different site

per one million people per year [5]. In about 75% of cases it is located in the left atrium [6]. Although atrial myxoma causes mostly obstructive cardiac symptoms, it is worth to remember its neurological complications which occur in approx. 20–30% of patients [1,3]. In the majority of cases such complications appear in rather young patients and are usually caused by cerebral embolism and subsequent cerebral infarcts [3,7]. Neuroimaging studies often reveal numerous lesions, many of which may be asymptomatic or cause non-characteristic symptoms such as headache, seizures or psychiatric disorders [3]. The review of the literature data of 113 patients with neurological manifestation of cardiac myxoma estimated that hemorrhagic lesions accounted for 12% of cases, and subarachnoid hemorrhages appeared in about 5% [3]. Both of them resulted probably from ruptured aneurysms. However, multiple hemorrhagic lesions in the brain always have to be differentiated with metastases in the course of other neoplasms such as choriocarcinoma, melanoma or renal and thyroid carcinoma [2]. It is speculated that myxomatous emboli can infiltrate the wall of a vessel, cause its weakening and result in aneurysmal development or initiate the growth of a metastatic lesion [7]. Sometimes atrial myxoma may be infected by bacteria or fungi and cause endocarditis or septic emboli [4]. There are also data connecting a tendency to metastasize with overproduction of CXC chemokines, interleukin-8 and growth-related oncogene by myxoma cells [4]. In 1978, a classification of atrial myxoma metastases was proposed (Table 1) [8]. Interestingly, the intracranial aneurysms were reported even several years after artial myxoma diagnosis and cardiosurgical removal [9]. However, there are no controlled studies which would establish a long-term prognosis. According to an analysis of 34 cases, the mean age of an onset of cardiac myxoma symptoms was 35 years (range of 6–68 years). About a quarter of patients presented cardiac symptoms, and about 74% had signs of an isolated cerebral embolism [10]. Aneurysms were found in 56% of patients when heart myxoma was diagnosed. However, in 44% they were detected later. The time from cardiac surgery to the recognition of aneurysms varies between 2 and 300 months [10]. The majority of aneurysms were located in the area of the middle cerebral artery (74%) and most of them were of fusiform type (91%) [10]. A review published in 1988 described a 12-year retrospective experience with patients with atrial myxoma [11]. It showed that recurrent cerebral emboli are frequent before myxoma surgery. However, delayed neurological complications are very rare. Another report of 74 patients with cardiac myxoma delineated that the initial manifestation may be often neurological symptoms [7]. Such symptoms were connected to ischemic cerebral infarction probably due to embolism. However, in one case metastatic myxoma was recognized.

Cardiac surgery is the method of choice in treating myxoma. Nevertheless, the recurrence frequency is estimated at 3% in sporadic cases and up to 20% in Carney complex, a heritable disorder including spotty pigmentation of the skin and endocrinopathy [6]. The decision on cardiac surgery has to be taken carefully in case of neurological manifestation, as the systemic heparin administration is indispensable during open heart surgery [12]. A cardiopulmonary bypass may trigger further deterioration of patient's condition due to bleeding from multiple aneurysms, metastatic or ischemic brain lesions and in some cases it has to be postponed for a few weeks [13]. Regarding possible treatment procedures of neurological complications, there are no precise guidelines. The use of anticoagulants or antiplatelet agents should be considered in order to prevent further emboli [3]. In a single aneurysm or brain lesion, surgeries are carried out. Moreover, some patients undergo chemotherapy with doxorubicin or ifosfamide with or without radiotherapy of the whole brain [2]. Radiotherapy is particularly recommended in multiple brain metastases [4].

Our case represents a particularly rare clinical condition of multiple brain metastases in a patient with left atrial myxoma. The brain is the most common site of myxoma metastases and till now only single and similar descriptions have been reported in the literature [4]. In our patient we did not find the evidence of any other neoplastic process such as melanoma, renal or thyroid cancer. A guided fine-needle biopsy of the thyroid gland was performed. However, it showed colloid nodular goiter. We considered also cerebral endometriosis, a rare complication of a rather frequent disease. Extrapelvic manifestations, such as gastrointestinal and genitourinary tracts, are widely known but single cases with brain lesions were also described [14,15]. In our case, no gynecological disorders were found. During a follow-up, the patient's condition remained stable and no other cause of metastases was recognized. Based on the cases described in the literature, we suspected multiple myxoma metastases in our patient [2]. However, no precise histopathological evidence of myxoma cells in brain tumor was found.

Conclusions

In summary, it is worth remembering that patients with atrial myxoma require careful and prolonged cardiological as well as neurological monitoring. In some cases, distant embolic events may occur even many years after cardiac surgery. Up to now, there have been no specific treatment guidelines. However, each patient should be discussed carefully in order to establish the most appropriate management.

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Disclosure

Authors report no conflict of interest.

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