

Case Report

A histopathologic diagnosis of brain lymphangiomyoma, clinically misdiagnosed as simple angiomyxoma: case report

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Abstract: Introduction: Lymphangioliomyomatosis (LAM) is a rare disease which affects women of reproductive age almost exclusively as one of the most gender-specific diseases, and which can occur at any site in the body but most commonly in the lungs. Here we report a rare case of recurrent brain lymphangiomyoma which was misdiagnosed as angiomyxoma. Case presentation: A 28-year-old male complained of finding a recurrent mass at the right temporal lobe of his brain for the last 4 months. He had undergone a resection of a brain mass two years prior. One year after the operation, the mass recurred again and was resected another time. Both of the operations were performed in another hospital and he was postoperatively diagnosed with angiomyxoma. This time the patient underwent a third operation in our hospital to remove the lesion, which was confirmed as lymphangiomyoma. Unfortunately, the patient again discovered a re-emerging mass at the primary operation site on the 50th day post-surgically. Conclusion: There is currently no effective cure for LAM and treatment options and relevant literature remain limited. Hence other potential therapeutic targets need to be identified.

Keywords: Lymphangiomyoma, LAM, head, diagnosis

Introduction

Lymphangioliomyomatosis (LAM) is a rare disease which affects the lungs, lymph nodes, or any other organs with the feature of abnormal smooth muscle cells (LAM cells) proliferation [1]. LAM affects women of reproductive age almost exclusively as one of the most gender-specific diseases; therefore cases in males are extremely rare [2]. Here we report a remarkably uncommon case of recurrent brain lymphangiomyoma which was misdiagnosed as angiomyxoma.

Case report

A 28-year-old male was admitted into our department with the chief complaint of finding a recurrent mass progressively growing in the right temporal lobe of his brain for the last 4 months. He also mentioned that over the past 2 months, he has been experiencing a moder-

ate decrease of eyesight and hearing on the right side. On physical examination, we observed a firm subcutaneous mass measuring 15 × 15 cm in the temporal lobe. Two years prior, the patient found a 2 × 2 cm mass in the temporal lobe of his brain for the first time and had undergone resection of the mass. The mass re-emerged one year after the surgery and the patient had surgical treatment once again with a craniectomy. Both of the operations were performed in another hospital and he was postoperatively diagnosed with angiomyxoma. The patient denied other medical history. Chest radiography and all laboratory test results were normal. Magnetic resonance imaging of the head showed the presence of heterogeneous mixed signal intensity over the right frontal, parietal, and temporal domes as well as on the right ethmoid and sphenoid sinuses. Other lesions were noted on the right mastoid region and over the middle cranial fossa floor. There was significant ring-enhancement at the border

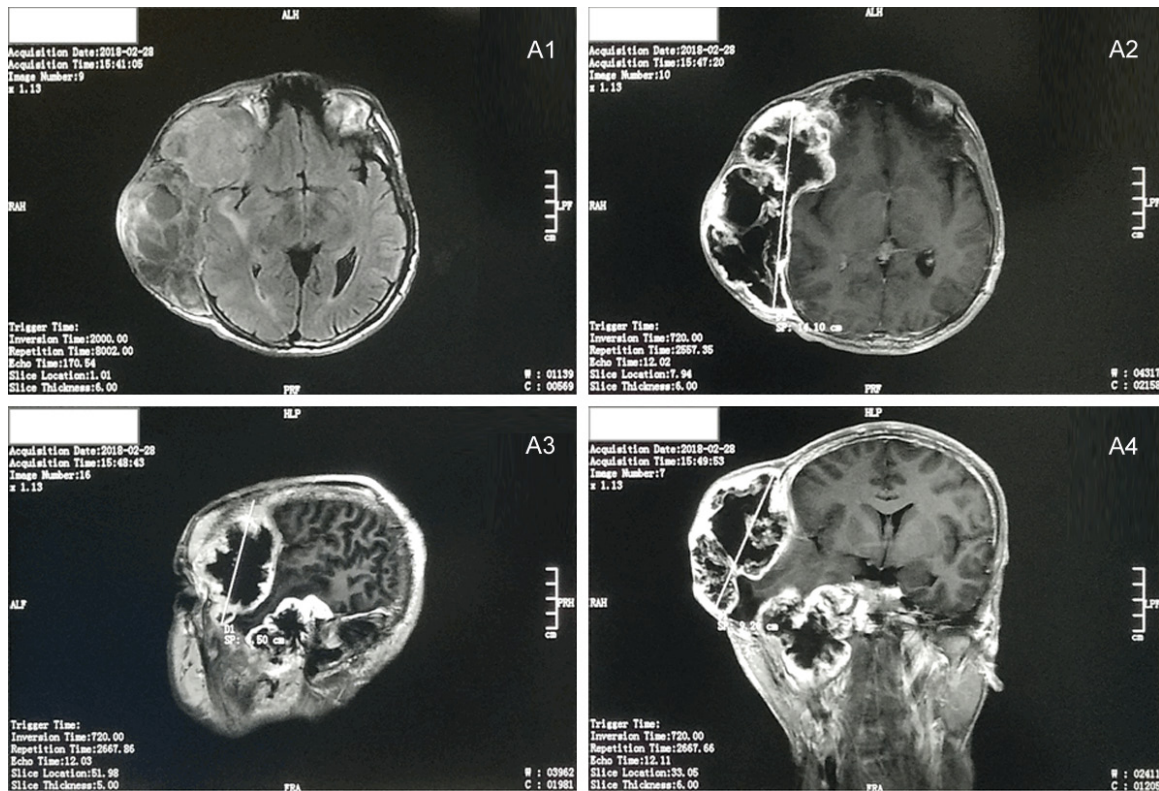


Figure 1. Magnetic resonance imaging of the head showed multiple and large masses (A1-A4).

of the lesion and the right hemisphere was compressed slightly with an anomalous signal-halo shape (**Figure 1**).

The patient was taken to the operating room and we performed a right hemispheric exploration. Intra-operative findings were: one pink-grey firm mass growing exteriorly at the previous craniotomy area. We exposed and resected the bulging portion of the mass along the bone surface and found a mass with a versatile blood supply; the mass was filled with necrotic and cystic fluid. Furthermore, the mass eroded the dura mater and grew interiorly. Under the microscope, we performed a complete resection of the mass, measuring $10 \times 8 \times 8$ cm in the right frontal, parietal and temporal lobe. A second yellowish-white, solid mass with a poor blood supply was discovered in the mid-cranial fossa. It was challenging to totally remove this mass because the mass had already grown deep into the ethmoid and cavernous sinuses. Unfortunately, the patient developed hemorrhagic shock so we had to terminate the operation just with a partial resection of this mass. The patient was monitored in the Intensive Care Unit, and then transferred to the general

ward in good condition on the third day. The patient's diagnosis was confirmed as lymphangiomyoma by histopathologic and immunohistochemical examinations of the resected specimen (**Figure 2**). Immunohistochemical findings showed positive cells for anti α -SMA, D2-40, CD34 and vimentin, and the expression of Ki-67 was 7%. After the operation, neither his eyesight nor hearing impairment had improved. Unfortunately, the patient again discovered a re-emerging mass measuring 4×4 cm at the primary operation site on the 50th day post-surgically (**Figure 3**). In the end, the patient had quit medical treatment and was lost to follow-up.

Discussion

Lymphangiomyomas are rare malformations of the lymphatic system. They can occur at any site in the body but most commonly in the lungs. Lymphangiomyoma of the brain appears extremely uncommon. The diagnosis of brain lymphangiomyoma is a challenge for neurosurgeons due to its rare presence in nature and its similarity to other cerebral diseases such as angiomyolipoma, leiomyoma, sarcoma, and

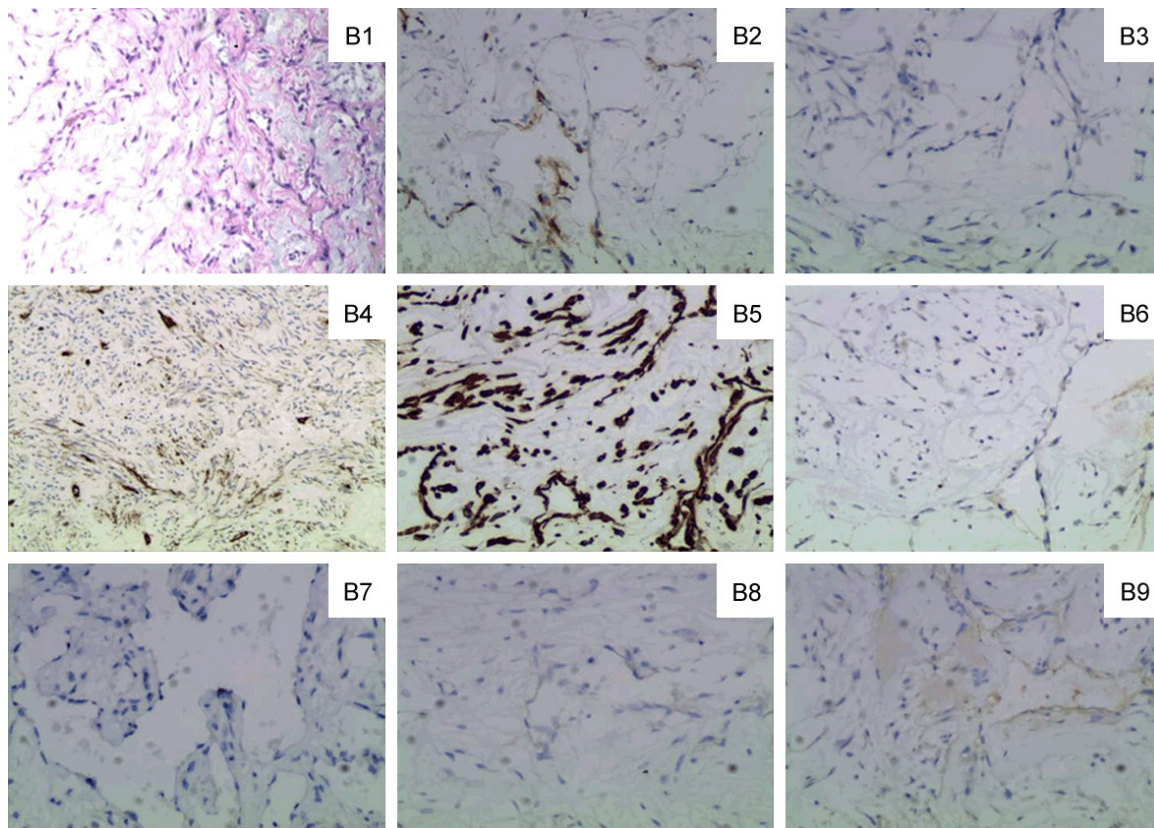


Figure 2. The histopathologic findings showed the papillary proliferative spindle-shaped LAM cells and sinusoid cavities which contain a small number of erythrocytes (B1). Immunohistochemical findings showed cells positive for α -SMA, D2-40, CD34 and vimentin (B2-B5). The expression of Ki-67 was 7% (B6), while the expressions of desmin, HMB-45, and progesterone receptors (PR) were negative (B7-B9).

perivascular epithelioid cell tumors. Our patient was misdiagnosed postoperatively in another hospital with brain angiomyxoma but the final diagnosis was based on pathologic examination in our hospital which was confirmed as brain lymphangiomyoma. Pathological hallmark features of lymphangiomyoma include the infiltration and proliferation of LAM cells causing the formation of LAM nodules and cystic destruction of the tissue with excessive formation of lymphatic vessels. LAM lesions consist of two kinds of LAM cells: those at the center are spindle-shaped and those at the periphery are epithelioid in shape. The spindle-shaped cells stain positive for smooth muscle markers, for example, smooth muscle α -actin (α -SMA), vimentin, desmin, and proliferating cell nuclear antigen (PCNA), while the epithelioid cells stain positive for the HMB-45 antibody which recognizes as premelanosomal protein-gp100. In addition, estrogen and progesterone receptors, as well as the cell surface receptor CD44v6 are

other markers of LAM cells [3]. In our case, immunohistologic findings of the resected specimen showed cells positive for α -SMA, D2-40, CD34 and vimentin, confirming the final diagnosis of lymphangiomyoma. LAM was originally regarded as benign but recently it has been categorized as a “low grade, destructive, metastasizing neoplasm” due to recurrence of recipient LAM cells in transplanted lungs. The appearance of LAM cells in the blood and other body fluids demonstrates that LAM cells express metastatic behavior [4, 5]. As the Ki-67 expression was 7% in the above described case, the mass recurred with a low tendency toward metastasizing.

Research over the past decade has significantly increased our understanding of the pathogenesis of LAM, which contains mutational inactivation of the tuberous sclerosis complex genes (TSC1 and TSC2) and activation of the mammalian target of rapamycin (mTOR) path-

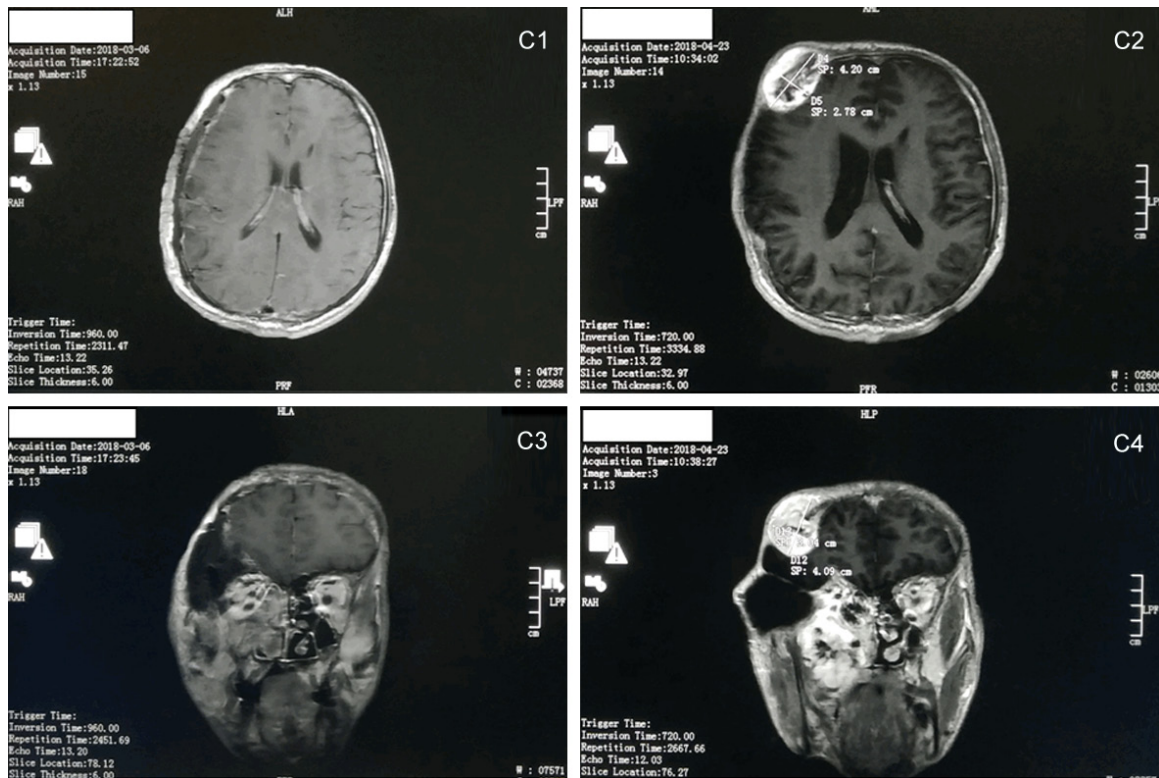


Figure 3. Magnetic resonance imaging on the 4th day after operation (C1 and C3); Magnetic resonance imaging showed a recurrent mass on the 50th day after operation (C2 and C4).

way, resulting in cell proliferation and migration, lymphangiogenesis, and metastatic spread by the blood and lymphatic circulations [6]. Despite this enhanced knowledge; there is currently no effective cure for LAM and treatment options remain limited. Hence other potential therapeutic targets are needed.

Conclusion

In the past few decades, remarkable breakthroughs have been made in understanding the pathogenesis of LAM, leading to a new therapeutic approach. However, the patient above may have been the first ever reported case of brain lymphangiomyoma and there is no such relevant guidance to effective treatments. Indeed, it is necessary to summarize recent advances regarding pathogenic mechanisms and clinical manifestations to highlight the most promising therapy.

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The manuscript has had ethics approval and consent to participate by medical ethics committee of First Affiliated Hospital of Xinjiang Medical University. Written informed consent regarding the publication of this case report and its accompanying images was obtained from the patient.

Disclosure of conflict of interest

None.

Abbreviations

LAM, Lymphangiomyomatosis; α -SMA, smooth muscle α -actin; PCNA, proliferating cell nuclear antigen; HMB-45, human melanoma black-45; TSC, tuberous sclerosis complex; mTOR, mammalian target of rapamycin.

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