Intracranial Rosai-Dorfman disease complicated by mucosa-associated lymphoid tissue: A case report

GENGHUAN WANG[1], YINGCONG LIN[2], HEPING SHEN[1], YIFEI WANG[1] and WEN LAI CHU[3]

[1]Department of Neurosurgery, The Second Affiliated Hospital of Jiaxing University, Jiaxing, Zhejiang 314000;
[2]Department of Neurosurgery, Zhejiang Chinese Medicine University, Hongzhou, Zhejiang 310053;
[3]Department of Neurosurgery, Jiaxing Maternal and Child Health Hospital, Jiaxing, Zhejiang 314000, P.R. China

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Abstract. Intracranial Rosai-Dorfman disease (RDD) is a rare, self-limiting histiocytic disease of unknown etiology. Extranodal marginal zone lymphoma of the mucosa-associated lymphoid tissue (MALT lymphoma) is also rare and intracranial RDD complicated by MALT lymphoma is even rarer. The present study reports a case of a 55-year-old female who was admitted to The Second Affiliated Hospital of Jiaxing University (Jiaxing, China) with headache for half a month and ptosis of the right eyelid for 4 days. Computerised tomography and magnetic resonance imaging revealed a right parasellar tumor and, subsequently, subtotal resection of the tumor was performed. Postoperative pathology revealed intracranial RDD complicated by MALT lymphoma. The patient received chemotherapy after surgery and achieved good therapeutic effects. After 12 months of follow-up, the residual tumor disappeared and the ptosis prominently improved. To the to the best of the authors' knowledge, the present case is the first reported case of an adult intracranial RDD complicated by MALT lymphoma.

Introduction

Sinus histiocytosis with massive lymphadenopathy (SHML), also known as Rosai-Dorfman disease (RDD), is a rare and benign self-limiting histiocytic disease of unknown etiology (1). Since the first report of RDD in 1969, >400 cases have been reported worldwide to date (2). Patients with RDD have differing disease durations and varying clinical manifestations. Although extranodal manifestations of RDD are common, intracranial RDD is rare, with the literature mostly reporting individual cases (3). In 1983, Isaacson and Wright were the first to describe extranodal marginal zone lymphoma of mucosa-associated lymphoid tissue (MALT lymphoma) in the gastrointestinal tract (4,5). Despite successive reports of MALT lymphomas developing in other locations, intracranial MALT lymphomas are rare, all of which are reported as individual cases (6). RDD coexisting with MALT lymphoma is even rarer. The present study reports a rare case of adult intracranial RDD complicated by MALT lymphoma. To the best of our knowledge, the case reported in the present study is the first case of adult intracranial RDD complicated by MALT lymphoma in the literature.

Correspondence to: Dr Heping Shen, Department of Neurosurgery, The Second Affiliated Hospital of Jiaxing University, 1518 North Part of the Ring Road, Jiaxing, Zhejiang 314000, P.R. China
E-mail: shenege1977@126.com

Dr Wen Lai Chu, Department of Neurosurgery, Jiaxing Maternal and Child Health Hospital, 2468 Jiaxing Central East Road, Jiaxing, Zhejiang 314000, P.R. China
E-mail: way20150903@126.com

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Case report

A 55-year-old female patient was admitted to The Second Affiliated Hospital of Jiaxing University (Jiaxing, China) due to headache for half a month and ptosis of the right eyelid for 4 days. The patient was in good health and had no other medical conditions. On physical examination, the bilateral pupillary light reflex was sensitive, the right eyelid was ptosed and eyeball movement was normal. Cranial computed tomography (CT) revealed high-density lesions at the right parasellar region (Fig. 1). MRI revealed a right parasellar lesion, ~30x25 mm, with equal signal on T1, low signal on T2 and fluid-attenuated inversion recovery (FLAIR) and uniform enhancement (Fig. 2). Subtotal resection of the tumor was performed and postoperative pathology revealed a MALT lymphoma complicated by RDD (Fig. 3). Immunohistochemistry (IHC) findings revealed the presence of the following proteins: i) CD20(+); ii) CD79a(+); iii) S-100(+); iv) CD68(+); v) κ (partially +); vi) CD3(-); vii) CD5(-); viii) CD10(-); ix) CD43(-); x) CD21(-); xi) CD23(-); xii) epithelial membrane antigen(-); xiii) Bcl-6(-); xiv) progesterone receptor(-); and xv) Ki-67(+, 15%) (Fig. 4). The rearrangements of the immunoglobulin heavy chain (IGH) gene were positive.

To determine whether the patient had lymphomas in other locations, a bone marrow puncture was performed. Bone marrow biopsy revealed good hematopoiesis and no lymphocytosis. Rearrangements of the BCL-2, BCL-6 and IGH genes

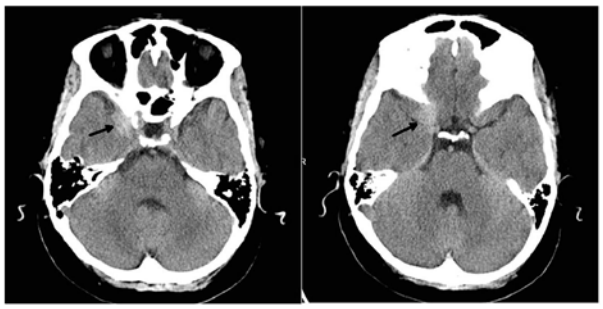

Figure 1. Cranial computerised tomography revealed high-density lesions at the right parasellar region.

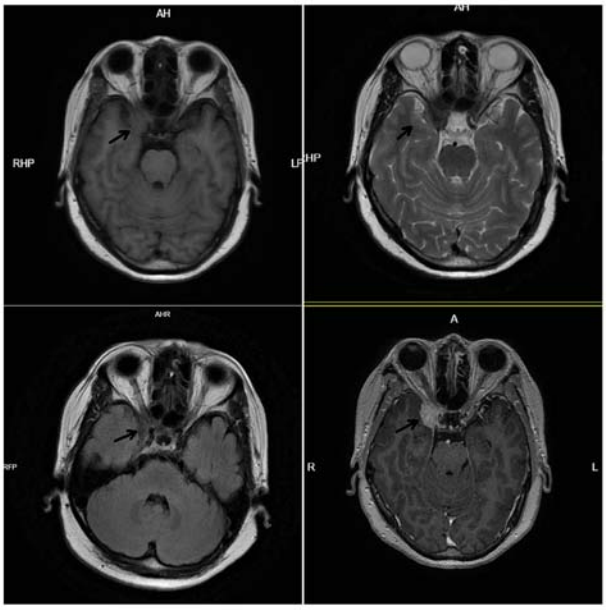

Figure 2. Magnetic resonance imaging showed the right parasellar lesion, ~30x25 mm, with equal signal on T1, low signal on T2 and fluid-attenuated inversion recovery and uniform enhancement.

were negative. PET-CT revealed that: i) The surgical site was slightly dense; and ii) that there were multiple lymph nodes in the right neck with increased ^{18}F-fluorodeoxyglucose uptake. Lymphoma infiltration was considered, which was treated using rituximab and lenalidomide. The patient recovered well and the ptosis of the right eyelid improved. Magnetic resonance imaging (MRI) examination 6 months after surgery demonstrated that the residual tumor had disappeared (Fig. 5). After >1 year of follow-up, the patient was generally in good condition and was going to work as normal.

Discussion

Rosai and Dorfman first reported four cases of SHML in 1969, whose clinical manifestations are painless cervical lymphadenopathy with low-grade fever, leukocytosis, weight loss and elevated erythrocyte sedimentation rate (ESR) (1). Extranodal RDD is also common and may occur in ~40% of patients (7). It can be complicated by lymph node involvement, or be an independent lesion of extranodal origin without lymphadenopathy (8). Common extranodal sites of involvement include

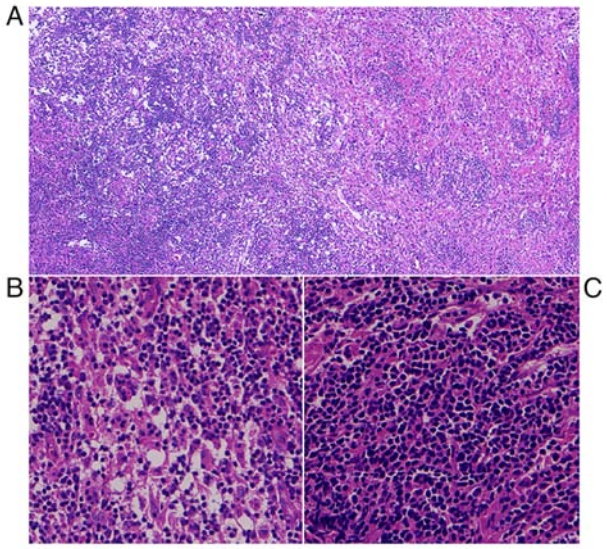

Figure 3. Pathological manifestations. (A) Postoperative pathology revealed mucosa-associated lymphoid tissue complicated with Rosai-Dorfman disease (x100 magnification). (B) Histopathology revealed characteristic inflammatory cell proliferation in the background of neoplastic small lymphocytes, with mature small lymphocytes predominating (x400 magnification). (C) Histopathology revealed diffuse distribution of small lymphocytes with single morphology (x400 magnification).

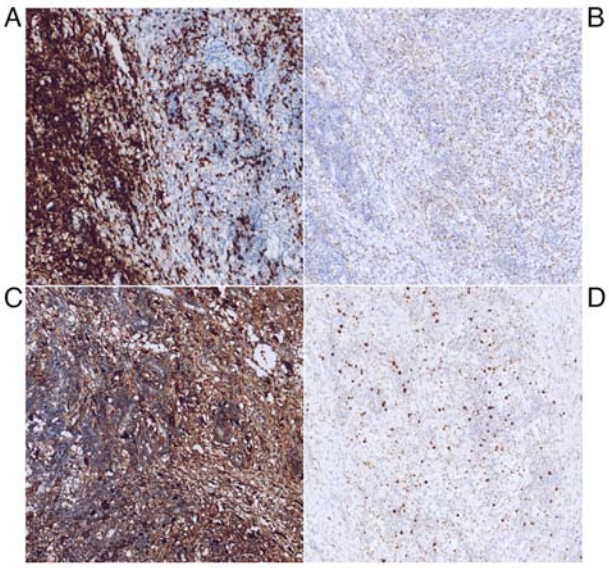

Figure 4. Immunohistochemical findings. Immunohistochemical results of (A) CD20(+), (B) CD68(+), (C) S100(+) and (D) Ki67(+) staining (x100 magnification).

the skin and soft tissues (17%); the nasal cavity and sinuses (16%); the eyes, orbits and ocular appendages (11%); the skeletal system (11%); and the salivary glands (7%) (7,9). RDD of the central nervous system (CNS) is rare and accounts for <5% of reported RDD (10-12). Overall, ~75% of CNS RDD occur intracranially, while 25% involve the spine (13). In addition, 70% are unassociated with lymphadenopathy and are only manifested as solitary lesions (13). Furthermore, >90% involve only the meninges (11).

In 1983, Isaacson and Wright (4) reported that the IHC of certain low-grade B-cell gastrointestinal lymphomas

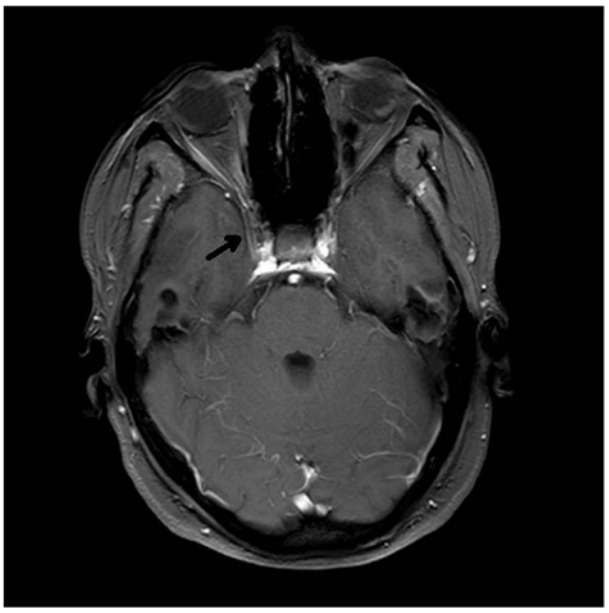

Figure 5. MRI examination 6 months after surgery. MRI revealed that the residual tumor had disappeared. MRI, magnetic resonance imaging.

indicated features of MALT. Subsequently, the authors extended these observations to include numerous other extranodal low-grade B-cell lymphomas (5). Paradoxically, the stomach is the most common site of MALT lymphoma, where the lymphoid tissues are often absent (14). In recent years, other sites of MALT lymphoma have been reported, including the lungs, ocular adnexa, breasts, skin, bladder, kidneys, prostate, liver, gallbladder and cervix (15). MALT lymphomas can also occur intracranially, although rarely (15,16). According to a literature review by Matmati *et al* (16), 57 cases of dural MALT lymphoma have been reported in total.

RDD is common among children and adolescents [median age, 13 (range, 5-65) years] and is characterized by long duration of the disease [median duration, 6 (range, 3-15) years], with a slight predominance in males (7,16). By contrast, intracranial MALT mainly occurs in adults and all patients reported so far have been between 39 and 62 years old (15). The majority occur in women, accounting for 85.7% of cases (17).

The etiology of RDD remains unclear and possible pathogeneses include infection [varicella-zoster virus, human herpesvirus 6, Epstein-Barr virus (EBV), cytomegalovirus, HIV, *Brucella* and *Klebsiella*] (18-20), genetics and immune and inflammatory processes (19-21). It is known that gastric MALT lymphomas are closely associated with *Helicobacter pylori*, while MALT lymphomas in other locations may not be associated with infectious stimuli (16). Its etiology remains to be elucidated.

Intracranial RDD and MALT lymphomas are mostly single intracranial lesions and extracranial lesions are rare (3,16). The patient in the present report was complicated by cervical lymph node infiltration in addition to the intracranial lesions, which is even rarer (16). Intracranial RDD shares similar onset locations and clinical symptoms with intracranial MALT lymphoma. Common clinical manifestations include headache, vomiting, epileptic seizures, limb weakness and cranial nerve deficit depending on the location and size of the lesions (16,18).

According to a literature report, ESR, C-reactive protein and D-dimer levels are elevated in numerous patients with RDD (16). These indicators were normal for the present patient and the present report did not find any potential pathogens (including EBV, cytomegalovirus, *Brucella, Salmonella*, hepatitis A, B and C viruses, HIV and tubercle bacillus).

The imaging findings of intracranial RDD are similar to those of intracranial MALT lymphoma. The majority of the reported cases are located extra-axially and are closely associated with the meninges (12,15,16). There may be varying degrees of cerebral edema and meningeal enhancement and only a few cases show invasion of the brain parenchyma (17). It is similar to meningioma in clinical and radiological aspects, so it is often misdiagnosed as a meningioma before surgery (12,16,22). Differential diagnosis includes meningiomas, eosinophilic granulomas, intracranial solitary fibrous tumors, plasma cell granulomas and dural metastases (12,23,24). For the patient in the present case, meningioma was also considered preoperatively. However, due to the short disease duration and rapid progression, lymphoma was considered as well. In intracranial RDD, free radicals generated by macrophage phagocytosis may appear as hypointense on T2-weighted or FLAIR images of MRI, which may be a manifestation of intracranial RDD (12,25). According to literature reports, DWI in MRI of intracranial RDD reveal restricted diffusion of lesions (11,12,16). Meningiomas typically show increased choline levels, and alanine is also present in some meningiomas (26). RDD has a higher choline peak (26). The low intensity of MRI T2 and limited diffusion of MRI DWI are also imaging features of intracranial MALT lymphoma that can help distinguish between MALT lymphoma and typical meningiomas (16,27).

Diagnosis of intracranial RDD and MALT lymphoma mainly depends on pathological examination (28,29). In addition to typical cytological findings, the positive expression of S-100 and CD68 on IHC staining are also the main basis for differentiating RDD from other diseases (15,21). Meanwhile, MALT lymphomas express B-cell-associated antigens (such as CD20), but do not express CD5, CD10 or CD23 (16,30). The patient in the present report was diagnosed as intracranial RDD complicated by MALT lymphoma based on typical pathological manifestations and IHC findings.

Occasionally, RDD can be complicated by other conditions, including malignant diseases (such as lymphoma and leukemia) and benign diseases (such as rheumatoid arthritis and Sjögren's syndrome). There have been reports of RDD complicated by lymphoma in the literature, which are extremely rare and are individual cases (21). Literature reviews have indicated that, as of 2018, <30 cases of RDD complicated with lymphomas have been revealed, mainly occurring with Hodgkin's lymphoma (31,32). Reports of RDD complicated by MALT lymphoma are even rarer, with only four cases identified through literature retrieval (21,32-34). RDD can appear before or after lymphoma diagnosis and these two pathological processes mostly involve different anatomical sites (33,34). However, in a minority of patients, RDD and lymphoma are found concurrently in the same specimens (2,35,36).

Regarding the treatment of RDD and MALT lymphoma, there is currently no standard therapeutic regimen due to the rarity of the disease. For the majority of patients with RDD, follow-up observation can be performed (37). As for patients with progressive, symptomatic or refractory RDD, such treatments as radiotherapy, chemotherapy and surgery are available (37,38). Some researchers consider MALT lymphomas to be biologically inert and thus can be followed closely after surgical resection, with or without chemotherapy, or with delayed radiotherapy (16). The management of intracranial RDD is similar to that of MALT lymphoma. Surgical resection is an effective therapy, while other treatments include chemotherapy and radiotherapy (12,15). The tumor in the present report was not completely resected and PET-CT revealed lymphoma infiltration in the neck. Considering that RDD and MALT lymphoma are sensitive to chemotherapy, postoperative chemotherapy was used, which achieved good efficacy.

Prognosis of RDD is associated with the number of involved lymph nodes and/or the number of extranodal sites (39). Overall, the prognosis is good (39). RDD with poor outcome is often accompanied by malignancy or immune disease (40). Intracranial MALT lymphoma is almost always localized, which rarely presents with systemic involvement and has a mean progression-free survival >29 months (16). The patient in the present report underwent subtotal surgical resection supplemented with chemotherapy. After >1 year of follow-up, the patient had no symptoms and was going to work as normal.

In conclusion, both intracranial RDD and intracranial MALT lymphoma are rare and occur primarily in the meninges, with imaging manifestations resembling meningiomas. The primary treatment is surgery, which can be supplemented by chemotherapy and radiotherapy and the outcome is good.

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Availability of data and materials

The datasets used and/or analyzed during the current are available from the corresponding author on reasonable request.

Authors' contributions

GW, HS and WC were responsible for designing and conceiving the study. YL and YW acquired the data. YL and YW analyzed and interpretated the data. GW, HS and WC drafted or revised the manuscript for intellectual content. GW and HS confirm the authenticity of all the raw data. All authors have read and approved the final manuscript.

Ethics approval and consent to participate

The Ethics Committee of the Second Affiliated Hospital of Jiaxing University approved the study protocol (approval no. jxey-20180021).

Patient consent for publication

The patient provided written informed consent for publication of the article (including imaging results).

Competing interests

The authors declare that they have no competing interests.

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