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Case Report

Intracranial Rosai-Dorfman disease mimicking melanoma: a case report and review of the literature

Zhibei Tang[1*], Fei Chen[2*], Yijie Shao[3], Chenguang Li[3], Jian Zhang[1]

[1]Department of Neurosurgery, Cangnan People's Hospital, Wenzhou 325800, Zhejiang, People's Republic of China; [2]Department of Neurosurgery, Zhuji People's Hospital of Zhejiang Province, Zhuji Affiliated Hospital of Wenzhou Medical University, Zhuji 311800, Zhejiang, People's Republic of China; [3]Department of Neurosurgery, Second Affiliated Hospital, School of Medicine, Zhejiang University, Hangzhou 310009, Zhejiang, People's Republic of China. [*]Equal contributors.

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Abstract: Intracranial Rosai-Dorfman disease is quite rare. Here, we report a 67-year-old man with a 90 day history of pain and numbness in his right limbs. The patient was suspected of suffering from melanoma. Then he received craniotomy and was finally diagnosed with intracranial Rosai-Dorfman disease. MEDLINE was used to search the related literature; and the diagnosis, mechanism, treatment and prognosis of this rare tumor are discussed.

Keywords: Rosai-Dorfman disease, melanoma, meningioma, central nervous system

Introduction

Rosai-Dorfman disease (RDD), also called sinus histiocytosis with massive lymphadenopathy, is a benign, non-neoplastic, self-limiting histiocytic disease characterized by generalized lymphadenopathy, weakness, anemia, and rarely extranodal involvement [1, 2]. The disease rarely affects the central nervous system (CNS), and the onset age is relatively large [3]. Isolated intracranial involvement is extremely rare. Here we report one case of intracranial Rosai-Dorfman in an old man mimicking melanoma. We also review the literature related to intracranial RDD found on the PubMed database.

Case report

A 67-year-old man presented with a history of right limb pain and numbness of 90 days' duration. No other symptoms such as headache, dizziness, and right limb weakness were present. There was no obvious abnormality in nervous system examination. Routine biochemical and hematologic measures were also normal. There were no systemic symptoms, such as fever or leukocytosis. After admission to our ward, the patient received a series of examinations. The MRI revealed a 15*17*15 mm mass in the left parietal region. The tumor was isointense on T1-weighed images (**Figure 1A**) and hypointense on T2-weighed images (**Figure 1B**), and showed inhomogeneous enhancement with obvious brain edema (**Figure 1C-F**). Other examinations such as pulmonary computed tomography, abdominal B-ultrasound, 2-[F-18]-fluoro-2-deoxy-D-glucose positron emission tomography and tumor biomarkers are normal. On the basis of the MRI findings, the patient was suspected of suffering from melanoma, and a craniotomy was performed.

During the operation, a solid mass of yellowish-brown appearance was found in the parietal lobe, with rich blood supply. The tumor boundary was not clear, and it adhered to dura mater closely. All the tumor tissues were resected under the microscope. The further course was uneventful and the postoperative MRI examination showed the preceding mass being totally removed. Histologic examination revealed fibrous tissue with an infiltrate of inflammatory cells composed of lymphocytes, neutrophils, plasma cells and histiocytes. Scattered histiocytes containing intracytoplasmic lymphocytes were present (emperipolesis) (**Figure 2A**). Imm-

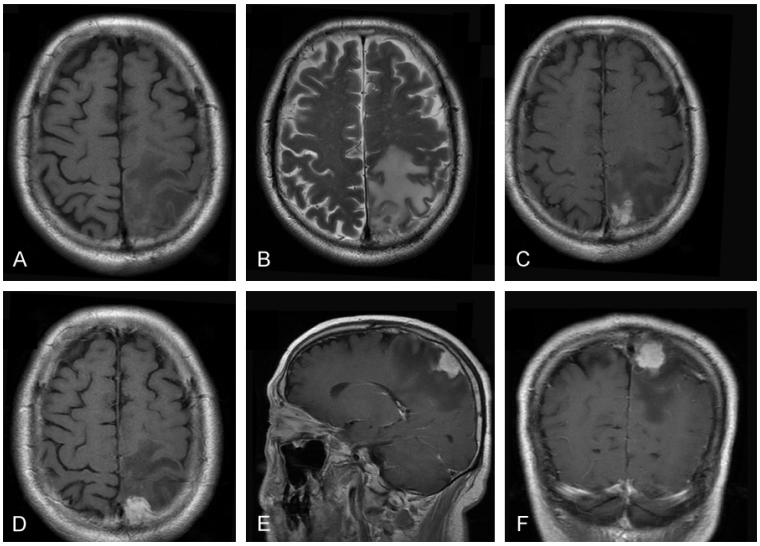

Figure 1. (A, B) Axial T1-weighted MRI reveals a 15*17*15 mm isointense mass on T1-weighed images and hypointense on T2-weighed images in the left parietal region. (C, D) Axial, (E) Sagittal and (F) Coronal enhanced T1-weighted MRI shows an inhomogeneous enhancing mass with obvious brain edema.

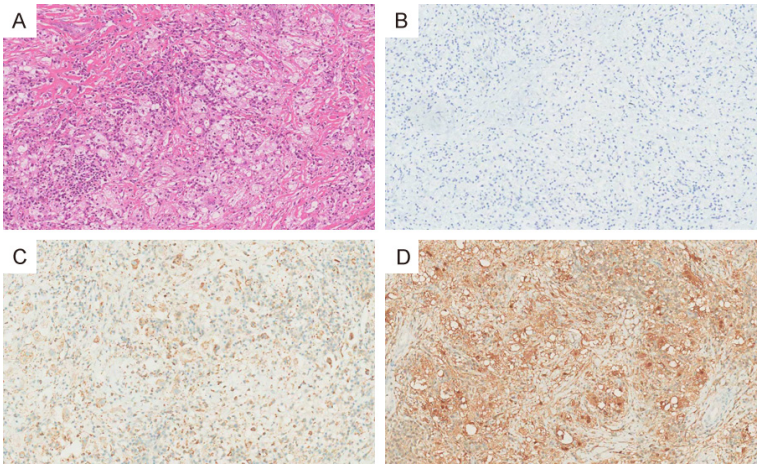

Figure 2. (A) Histologic examination showed fibrous tissue with an infiltrate of inflammatory cells composed of lymphocytes, neutrophils, plasma cells, and histiocytes. Emperipolesis with histiocytic engulfment of intracytoplasmic lymphocytes was conspicuous (Hematoxylin and eosin, 200×). Immunohistochemically, the tumor cells were nonimmunoreactive for CD1A (B) and positive for CD68 (C), and S-100 protein (D).

unohistochemically, the tumor cells were positive for S-100, CD68, and EMA and not immunoreactive for CD1A, P53, and ALK-1 (**Figure 2B-D**). The tumor tissues also showed focal positively for SSTR2, and the Ki-67 index was 10% (+). These results were confirmed by department of pathology of University of California, Los Angeles. Thus, the diagnosis of intracranial Rosai-Dorfman disease was established. The patient's symptoms improved after the operation. Although there was slight fine motor disturbance in the left upper limb, there were no other neurologic symptoms or signs after the operation. During the 24-month follow-up, the patient was still in good condition and had no clinical or neuroimaging evidence of recurrence.

Discussion

Rosai-Dorfman disease (RDD) is an idiopathic histiocytic proliferative disorder first described in 1965 [4]. Then in 1969, two pathologists Juan Rosai and Ronald Dorfman described the same entity characterized by a proliferation of histiocytes exhibiting emperipolesis of both lymphocytes and plasma cells [5]. It usually presents with bilateral cervical lymphadenopathy, leukocytosis, fever, weakness, anemia, increased erythrocyte sedimentation rate, and hypergammaglobulinemia.

The etiology of RDD remains poorly understood [2, 6] though there are several theories which may explain the pathogenesis at least to some extent. Jiang et al. [7] postulated etiology including infectious causes, immunodeficiency, autoimmune disease, and a neoplastic process. Immunologic studies show that immune system dysfunction may be the causative factor. Epstein-Barr virus and human herpesvirus type 6 have also been detected using in situ hybridization in some RDD specimens, suggesting that these viruses could be involved in the pathogenesis of RDD [7, 8]. Other researchers proposed an underlying dysimmune state as the main mechanism for the pathogenesis of RDD [2, 9]. Some germline mutations such as SLC29A3, KRAS, and MAP2K1 have been reported in patients with familial RDD [10, 11].

RDD has also been reported in patients with immunoglobulin G4 related disease. It is apparent that these disorders may have a common pathogenesis [12, 13]. All these results contribute to the understanding of the RDD pathogenesis. However, the occurrence of RDD may be caused by multiple factors, rather than a single factor. Its specific pathogenesis needs further study [7].

On CT, intracranial RDD is homogeneous hyperdense or isodense [14]. MRI is currently the optimal diagnostic modality for evaluating lesions of intracranial RDD [1]. It usually reveals multiple well-defined, dural-based or intraventricular, extra-axial masses with possible perilesional cerebral edema that are hypointense or isointense on T1-weighted images and isointense or slightly hyperintense on T2-weighted images [7]. On contrast-enhanced T1-weighted images with gadolinium, the lesion shows homogeneously or inhomogeneously intense enhancement, and the dural tail sign can commonly be found [15]. These above radiologic findings are difficult to preoperatively distinguish RDD from meningioma. However, the absence of hyperostosis, bony erosion, or calcification should suggest RDD as the differential diagnosis of meningioma [15]. In addition, newer MRI sequences, such as diffusion tensor imaging, susceptibility-weighted imaging, and perfusion-weighted imaging, are suggested to diagnose RDD [16]. Also, Deshayes et al. described the use of fluorodeoxyglucose positron emission tomography/computed tomography to diagnose relapsed intracranial RDD of the hypothalamus in a patient [17].

Final diagnosis of RDD can only be confirmed by pathologic examinations, including histologic and immunohistochemical examinations [6]. Typically, the histiocytes contain abundant cytoplasm within intact lymphocytes which is called emperipolesis and histiocytes stain positive for S-100 and CD68, but negative for CD1a [1]. Emperipolesis is characteristic of RDD, but is present in only 70% of cases [5].

Treatment choices for intracranial RDD have been used with varying success, including surgery, radiation therapy, steroids, and chemotherapy [8]. Although treatment approaches for RDD remain controversial, surgical resection is essential for diagnosis. It is the most effective method of treatment and may be curative for RDD in the CNS [1, 6]. Surgery can relieve compression of vital structures, relieve symptoms, and preserve function. Recurrence after surgical therapy is rare and limited to uncompleted debulking, multiorgan involvement, and large masses [8]. However, complete resection cannot always be accomplished, because the lesions can have multiple foci, adhere to surrounding critical structures, or invade critical neurovascular structures [2, 7, 18]. In these cases, biopsy may be the first option to get the correct diagnosis, and then the further course may be followed.

Radiotherapy is generally considered to be an effective adjuvant treatment for residual, nonresectable or recurrent RDD [19, 20]. Some researchers consider the lesion to be extremely radiosensitive [19, 21] while others report little or no response [22]. It is unclear why radiotherapy has varying effects on patients with RDD. Thereafter, long term follow-up and further clinical studies are strongly recommended [18].

Corticosteroids have produced a partial or complete resolution of post-operative residual, or even nonsurgically treated lesions in cases of CNS RDD [20]. Camp et al. reported successful treatment of a case in which masses resolved with steroid treatment [23]. Additionally, McPherson et al. reported a case in which residual masses resolved with steroids [21]. However, only a small percentage of RDD cases have proven to be responsive to steroids [8, 21]. Menon et al. found that an IgG4 positive subset of RDD represents a more steroid-responsive group just like IgG4-related disease, so they suggest that steroid drugs could be useful when surgery or radiosurgery has failed, especially for the IgG4 positive subset [25]. Chemotherapy has also been used as adjuvant therapy for patients with residual mass, nonresectable or recurrent RDD. The standard chemotherapy plan consists of 8 cycles of cyclophosphamide (1 g), vincristine (2 mg), doxorubicin (50 mg), and prednisone (50 mg) for 5 days every 3 weeks [19]. Bhat et al. reported two complicated cases treated by chemotherapy, and they recommend additional chemotherapy if there are signs of tumor persistence or recurrence [26].

Also, there are some potential treatment methods such as using 2-chlorodeoxyadenosine (2CDA), monoclonal antibody targeting with

indium labelled antiCD1a, or combination of corticosteroid (prednisolone) and vinca alkaloids (vincristine and vinblastine) with an alkylating agent (cyclophosphamide) [8]. However, the clinical effects of these drugs need to be further studied.

In conclusion, intracranial RDD is a rare benign disease, but we should pay attention to the differential diagnosis between intracranial RDD and meningioma, melanoma or lymphoma. The definitive diagnosis is made by immunohistochemistry, and surgical resection of all masses remains the most effective treatment to date. Adjuvant treatment such as chemotherapy, radiotherapy, and steroids are acceptable options in cases of incomplete resection, recurrence, or multiple masses. Future efforts should be directed at investigating the pathogenesis and postoperative management of RDD.

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Disclosure of conflict of interest

None.

Address correspondence to: Dr. Jian Zhang, Department of Neurosurgery, Cangnan People's Hospital, Wenzhou 325800, Zhejiang, People's Republic of China. Tel: +86-577-64810582; E-mail: 17557516@qq.com

References

[1] Wang C, Zou Y, Zeng Q, Hong H and Zheng C. Isolated Rosai-Dorfman disease with craniocervical junction involvement in the foramen magnum: a case report. Medicine (Baltimore) 2019; 98: e17433.

[2] Li Z, Zhou C, Chen G and Bao Y. Intracranial Rosai-Dorfman disease involving the cavernous sinus: a case report and review of the literature. World Neurosurg 2018; 119: 249-255.

[3] Patwardhan PP and Goel NA. Isolated intraventricular Rosai-Dorfman disease. Asian J Neurosurg 2018; 13: 1285-1287.

[4] Destombes P. Adenitis with lipid excess, in children or young adults, seen in the Antilles and in Mali (4 cases). Bull Soc Pathol Exot Filiales 1965; 58: 1169-1175.

[5] Rosai J and Dorfman RF. Sinus histiocytosis with massive lymphadenopathy. A newly recognized benign clinicopathological entity. Arch Pathol 1969; 87: 63-70.

[6] Tian Y, Wang J, Ge Jz, Ma Z and Ge M. Intracranial Rosai-Dorfman disease mimicking multiple meningiomas in a child: a case report and review of the literature. Childs Nerv Syst 2015; 31: 317-323.

[7] Jiang Y and Jiang S. Intracranial meningeal Rosai-Dorfman disease mimicking multiple meningiomas: 3 case reports and a literature review. World Neurosurg 2018; 120: 382-390.

[8] Huang BY, Zong M, Zong WJ, Sun YH, Zhang H and Zhang HB. Intracranial rosai-dorfman disease. J Clin Neurosci 2016; 32: 133-6.

[9] Breiner A, Dubinski W, Gray B and Munoz DG. A 63 year old woman with white matter lesions and pachymeningeal inflammation. Brain Pathol 2013; 23: 225-228.

[10] Melki I, Lambot K, Jonard L, Couloigner V, Quartier P, Neven B and Bader-Meunier B. Mutation in the SLC29A3 gene: a new cause of a monogenic, autoinflammatory condition. Pediatrics 2013; 131: e1308-13.

[11] Garces S, Medeiros LJ, Patel KP, Li S, Pina-Oviedo S, Li J, Garces JC, Khoury JD and Yin CC. Mutually exclusive recurrent KRAS and MAP2K1 mutations in Rosai-Dorfman disease. Mod Pathol 2017; 30: 1367-1377.

[12] Zhang X, Hyjek E and Vardiman J. A subset of Rosai-Dorfman disease exhibits features of IgG4-related disease. Am J Clin Pathol 2013; 139: 622-632.

[13] Chen TD and Lee LY. Rosai-Dorfman disease presenting in the parotid gland with features of IgG4-related sclerosing disease. Arch Otolaryngol Head Neck Surg 2011; 137: 705-708.

[14] Wang C, Kuang P, Xu F and Hu L. Intracranial Rosai-Dorfman disease with the petroclival and parasellar involvement mimicking multiple meningiomas: a case report and review of literature. Medicine (Baltimore) 2019; 98: e15548.

[15] Raslan OA, Schellingerhout D, Fuller GN and Ketonen LM. Rosai-Dorfman disease in neuroradiology: imaging findings in a series of 10 patients. AJR Am J Roentgenol 2011; 196: W187-93.

[16] Idir I, Cuvinciuc V, Uro-Coste E, Penna M, Boetto S, Cognard C and Bonneville F. MR perfusion of intracranial Rosai-Dorfman disease mimicking meningioma. J Neuroradiol 2011; 38: 133-134.

[17] Deshayes E, Le Berre JP, Jouanneau E, Vasiljevic A, Raverot G and Seve P. 8F-FDG PET/CT findings in a patient with isolated intracranial Rosai-Dorfman disease. Clin Nucl Med 2013; 38: e50-2.

[18] Rivera D, Pérez-Castillo M, Fernández B and Stoeter P. Long-term follow-up in two cases of intracranial Rosai-Dorfman disease complicat-

ed by incomplete resection and recurrence. Surg Neurol Int 2014; 5: 30.
[19] Aljohani HT and Robin S. A rare case of isolated intracranial rosai-dorfman disease mimicking optic nerve meningioma: a case report and literature review. Asian J Neurosurg 2018; 13: 845-847.
[20] Qin G, Ye J, Lan S, Liang Y, Xu P, Tang X and Guo W. Rosai-Dorfman disease with spinal and multiple intracranial involvement: a case report and literature review. Br J Neurosurg 2019; 18: 1-5.
[21] McPherson CM, Brown J, Kim AW and DeMonte F. Regression of intracranial rosai-dorfman disease following corticosteroid therapy. Case report. J Neurosurg 2006; 104: 840-844.
[22] Sandoval-Sus JD, Sandoval-Leon AC, Chapman JR, Velazquez-Vega J, Borja MJ, Rosenberg S, Lossos A and Lossos IS. Rosai-Dorfman disease of the central nervous system: report of 6 cases and review of the literature. Medicine (Baltimore) 2014; 93: 165-175.
[23] Camp SJ, Roncaroli F, Apostolopoulos V, Weatherall M, Lim S and Nandi D. Intracerebral multifocal Rosai-Dorfman disease. J Clin Neurosci 2012; 19: 1308-1310.
[24] Yang X, Liu J, Ren Y, Richard SA and Zhang Y. Isolated intracranial Rosai-Dorfman disease mimicking petroclival meningioma in a child: case report and review of the literature. Medicine (Baltimore) 2017; 96: e8754.
[25] Menon MP, Evbuomwan MO, Rosai J, Jaffe ES and Pittaluga S. A subset of Rosai-Dorfman disease cases show increased IgG4-positive plasma cells: another red herring or a true association with IgG4-related disease? Histopathology 2014; 64: 455-459.
[26] Bhat A, Kupanur SS and Geethamani V. Isolated intracranial rosai-dorfman disease involving the meninges: report of a rare case. Turk Neurosurg 2015; 25: 186-189.