Journal of Research in Clinical Medicine

J Res Clin Med, 2020, 8: 18
doi: 10.34172/jrcm.2020.018
https://jrcm.tbzmed.ac.ir

TUOMS PRESS

Case Report

Isolated intracranial Rosai-Dorfman disease in an adult man: Report of a rare case

Somaye Rezaei[1#], Fariba Zarzanalivan[1#], Pouya Pirouti[2], Mohammad Reza Amiri Nikpour[1], Abdolreza Javadi[3*], Shahram Torkamandi[4,5*]

[1]Department of Neurology, Imam Khomeini Hospital, Urmia University of Medical Sciences, Urmia, Iran
[2]Islamic Azad University of Urmia, Urmia, Iran
[3]Department of Pathology, Imam Hossein Hospital, Shahid Beheshti University of Medical Sciences, Tehran, Iran
[4]Neurophysiology Research Center, Urmia University of Medical Sciences, Urmia, Iran
[5]Department of Immunology and Medical Genetics, Faculty of Medicine, Urmia University of Medical Sciences, Urmia, Iran

Article info

Article History:
Received: 4 Apr. 2020
Accepted: 28 Apr. 2020
e-Published: 16 May 2020

Keywords:
- Rosai-Dorfman disease
- Intracranial
- Emperipolesis
- Meningioma
- Histo-proliferative

Abstract

Background: Isolated intracranial Rosai-Dorfman disease (RDD) is an extremely rare, idiopathic histo-proliferative disorder. RDD is associated with the proliferation of histiocytes and emperipolesis.

Case Presentation: we report a case with isolated intracranial RDD. A 47-year- old man presented with a dizziness, falling, and then secondary generalized seizure, hemiparesis and right hemisensory deficit. This case preoperatively was misdiagnosed with meningioma. Histopathological examination revealed pale histiocytes displaying emperipolesis which were positive for S-100 and CD68 proteins and negative for CD1a marker. *BRAF* ^{V600E} mutation was negative.

Conclusion: In this case, total resection was performed and clinical symptoms were regressed completely.

Background

Rosai-Dorfman disease (RDD), also known as sinus histiocytosis is a rare idiopathic disease that is characterized by bilateral massive and painless lymphadenopathy. It was first recognized by Rosai and Dorfman in 1969.[1] About 43% of patients were reported with extranodal involvement including skin, upper respiratory system, bones and orbits.[2] Central nervous system (CNS) involvement is extremely rare and due to rarity of RDD, it is not usually proposed in intracranial lesions diagnosis. RDD radiologically mimics meningioma and dural metastasis as dural-based lesions and histologically mimics plasma cell granuloma, Langerhans cell histiocytosis (LCH) and lymphoproliferative disease.[3] Here, we presented in details a 47-year-old man who had an extremely rare isolated intracranial involvement of RDD.

Case Presentation

A 47-year- old man presented with symptoms of dizziness, falling, and then secondary generalized seizure appearing by jerking of right upper limbs and loss of consciousness. After the attack, he developed hemiparesis and remained confused until 3 hours. Thereafter, the generalized tonic-clonic seizure occurred lasting for 20 seconds, followed by 2 hours of postictal confusion. Neurological examinations revealed hemiparesis (right upper extremity strength was 4/5 and right lower extremity strength was 3/5), and right hemisensory deficit. There was no evidence of papilledema, cranial nerve deficit, and cerebellar signs. Furthermore, there were not any systemic symptoms such as fever, weight loss, night sweet, and joints involvement. On systemic examination, there were no lymphadenopathy and hepatosplenomegaly. The hemiparesis partially improved in less than 24 hours. The family history of tumor was negative. Brain computed tomography (CT) revealed a hyperdense lesion in the left parietal lobe and consequently vasogenic edema was noted around the lesion. Magnetic resonance imaging (MRI) showed an iso-hypo signal extra-axial mass measuring 65 × 51 × 15 mm at left, with homogenously dense enhancement after

***Corresponding Authors:** Shahram Torkamandi, Email: torkamandi.shahram@yahoo.co.uk, Abdolreza Javadi, Email: reza.javadi@sbmu.ac.ir

# These authors contributed equally to this manuscript

contrast agent administration and there was an enhancing dural tail. T1-weighted image showed iso-hypointense lesion and predominant hypointense on T2-weighted images and fluid-attenuated inversion recovery (FLAIR) images (Figure 1). Meningioma and dural metastatic lesion were made as main differential diagnosis; also neurosarcoidosis and infectious disease such as fungal granuloma, tuberculosis and syphilis were suggested as differential diagnosis with less possibility.

To rule out the metastatic lesions, we performed abdominopelvic, prostate and testis ultrasonography, chest and abdominal CT scans with/without contrast and the whole body scan that were unremarkable. Routine biochemical and hematologic investigations and erythrocyte sedimentation rate, C-reactive protein and prostate specific antigen were within the reference range. Hepatitis B surface antigen, HIV antibody, venereal disease research laboratory and purified protein derivative were also negative. The patient was started on anti-epileptic drug (phenytoin). He was treated with steroid in order to decrease brain edema before the surgery and then the drug was discontinued. The tumor was dural-based, gray-white, and well circumscribed that was totally resected. One month after surgery, phenytoin was tapered down and stopped. The patient was followed up after almost three months; he was well without the recurrence of any clinical symptoms.

RDD was found on pathological examination. Hematoxylin and eosin stain showed small pieces of meningeal tissue with nodular structures composed of lymph aggregations with few germinal centers and proliferations of spindle cells that were embedded in collagenous tissue (Figure 2 A-B); there were scattered areas of hyalinization and fibrosis (Figure 2 C). The collections of histiocytes with vesicular nuclei and abundant eosinophilic cytoplasm exhibiting lymphocyte and neutrophil emperipolesis (lymphophagocytosis) were seen (Figure 2D). Immunohistochemical staining results showed diffuse strong positivity for cytoplasmic S100 and CD68 protein with negative expression of CD1a (Figure 2E-H).

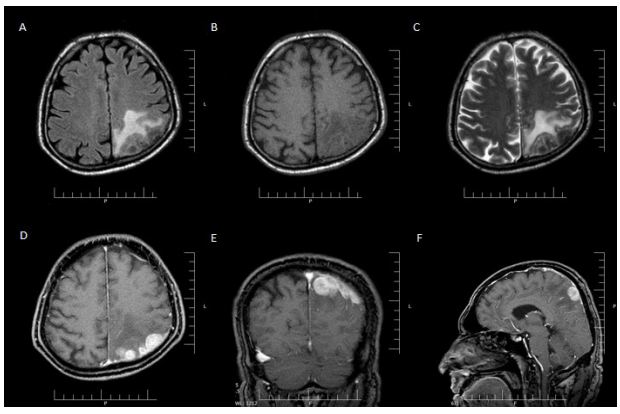

Figure 1. FLAIR, T1 and T2 weighted showed iso-hypointense parietal lobe lesion with surrounding edema (A-C). T1 weighted with enhancement showed extra axial and dural-based densely enhanced lesion (D-F).

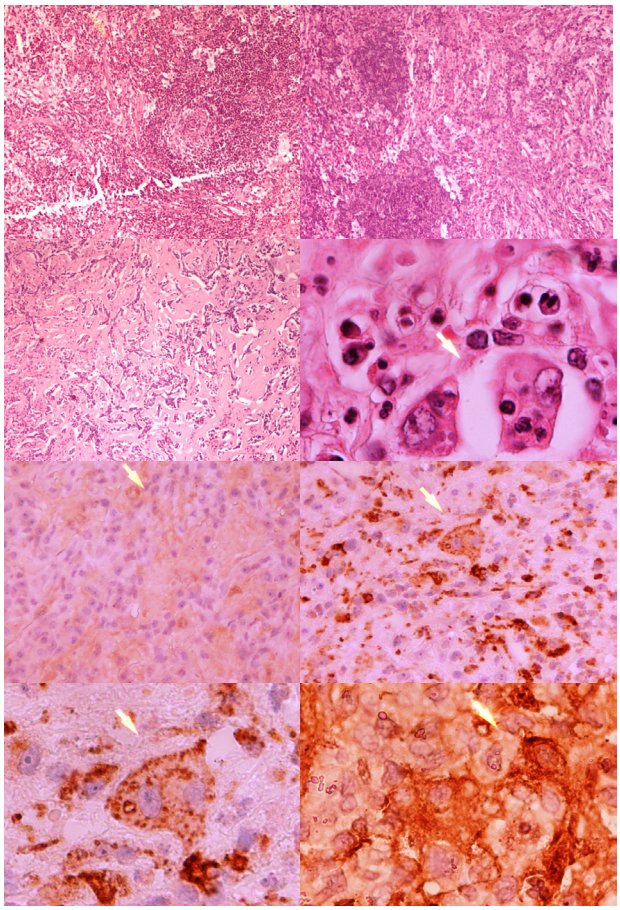

Figure 2. Photomicrograph of dural-based mass, exhibiting nodular structures composed of lymph aggregations with few germinal centers and proliferations of spindle cells (A). Nodular lymphocytic aggregation (dark areas) and histiocytic collections (Light areas) (B). Extensive areas of hyalinization and collagen depositions (C). Histiocytes shows characteristic feature of lymphocytes and neutrophils emperipolesis (D). Immunohistochemical staining demonstrates diffuse strong positivity for cytoplasmic S100 and CD68 protein with negative expression of CD1a (E-H). Scale bar: 10 μm.

For *BRAF* ^{V600E} mutation analysis, DNA was extracted from unstained paraffin-embedded tissue with 30 percent tumor and was checked with PCR-Pyrosequencing method. No mutation had been identified in *BRAF* gene.

Discussion

RDD or sinus histiocytosis with massive lymphadenopathy is a rare, idiopathic and reactive disorder which is characterized by a benign lymph node lymphohistiocytic proliferative condition.[4] RDD is a systemic histoproliferative disease mostly characterized by massive painless cervical lymphadenopathy, but 30%-40% of patients present with extra nodal involvement; most commonly the skin, nasal cavity, paranasal sinus,

orbit, salivary gland, bone, testis and CNS. Less than 5% of patients are presented by only CNS involvement which 75% of them is in brain and the rest is in spinal cord.[5] The cause of RDD remains controversial. Some studies demonstrated that autoimmune process triggered by Epstein-Bars virus, human papilloma virus type 6, parvovirus B19 and immune system impairment might play a role in RDD pathogenesis.[6] RDD has mainly been reported in childhood and young adults in the second and third decade of life.[7] Constitutional symptoms are generally absent in the patients with CNS involvement. Neurological symptoms vary depending on the size, location and number of lesions; seizure and headache are the most common complaint in RDD patients.[8] Other symptoms include focal neurological deficits hemiparesis, visual disturbance, gait impairment, cranial nerve deficit, hearing loss and pituitary dysfunction.[9] The present patient came with the symptoms of seizure and acute hemiparesis.

Neuroimaging commonly shows extra-axial dural-based lesions that enhance homogeneously, making the disease to be usually misdiagnosed with meningioma. The MRI, usually T1-weighted shows hypo- or isointense lesions with well-defined border that after gadolinium administration have dense homogenous enhancement and dural-tail sign. On T2-weighted image, the lesions are isointense or slightly hyperintense.[10] In our report, the lesion was iso to hypointense on T1-weighted and predominantly hypointense on T2-weighted MRI images and was markedly enhanced. Dural-based tail was determined after contrast agent administration. Therefore, this case was preoperatively misdiagnosed with meningioma and less possibly dural metastasis, infectious disease, and neurosarcoidosis but more investigations for metastatic lesion and inflammatory disease ruled out these diagnoses.

Plasma cell rich granuloma, lymphoplasmacyte rich meningioma, LCH and RDD were made as histologic differential diagnosis on the surgery resected biopsy. Chronic inflammation with infiltrate of lymphocytes, plasma cells and histiocytes in the fibrous stroma can be seen microscopically. Some large histiocytes engulfing lymphocytes are noted as emperipolesis, the most representative feature of RDD. Meningioma is also positive for S-100 but can be readily differentiated from RDD; meningioma highlights with epithelial membrane antigen, whereas they are not present in RDD. Plasma cell granuloma presents with discrete and dural-based inflammatory lesions and needs to be ruled out with immunohistochemistry; plasma cells are negative for S-100 protein and emperipolesis. LCH also expresses S-100 protein in histiocytes and can be presented as a dural-based lesion. LCH has characteristic nuclear groove and large number of eosinophils that contain pathognomonic Birbeck granule, irregular cell membrane and chromatin in electron microscopy. However, unlike RDD, CD1a is strongly positive in LCH patients. In our case, the histiocytes positively stain for S-100 and CD68 and negatively for CD1a that were consistent with the diagnosis of RDD.[11]

Recent studies have identified recurrent mutation in MAPK/ERK pathway genes in LCH, Erdheim-Chester disease and rarely in some RDD cases. Distinct mutation of MAPK/ERK pathway genes such as BRAF causes ERK over-activation and unrestrained cell proliferation in tumor. Fatobene et al founded *BRAF* ^{V600E} mutation as a MAPK/ERK pathway gene in an 18–year-old RDD patient.[12] Richardson et al identified a single somatic deletion mutation in exon 12 of the *BRAF* gene.[13] However, we did not find *BRAF* ^{V600E} mutation in our case. The discordance between our results with the aforementioned studies may be a result of undetected mutations located in other exons and genes that we did not examine in this study and also different methodology.

Intracranial RDD is considered as a benign disease with good prognosis. Complete surgical resection is the best therapy, but subtotal resection is recommended as a safe approach for symptoms remission and diagnosis when the lesion is located near the critical structure.[9] After surgery, patients usually improves and recurrence and development of neurological deficits have rarely been reported. Adjutant therapy such as radiotherapy, chemotherapy and steroid can be utilized in the patients whose clinical symptoms are not improved, in some cases with recurrence and when resection of mass is not possible.[14] In our case, the total resection was performed and clinical symptoms were completely regressed. However, a wait-and-watch is recommended as follow-up treatment.

Conflict of Interest

The authors declare that they have no financial or other conflicts of interest in relation to this research and its publication.

Ethical Approval

This study was approved by the Ethics Committee of the Urmia University of Medical Sciences, Urmia, Iran. Additionally, informed consent was obtained from the patient.

Author's Contributions

S.R, F.Z and M.AN performed clinical examination and follow-up of the case; P.P obtained the specimen; A.J performed the pathological examination; S.T designed and performed sequencing and wrote the manuscript. All authors read and approved the final manuscript.

Acknowledgement

The authors sincerely thank the patient for participation in the study. The authors received no specific funding for this work.

Funding/Support

None.

References

1. Rosai J, Dorfman RF. Sinus histiocytosis with massive

lymphadenopathy. A newly recognized benign clinicopathological entity. Arch Pathol. 1969;87(1):63-70.
2. Foucar E, Rosai J, Dorfman R. Sinus histiocytosis with massive lymphadenopathy (Rosai-Dorfman disease): review of the entity. Semin Diagn Pathol. 1990;7(1):19-73.
3. Sandoval-Sus JD, Sandoval-Leon AC, Chapman JR, Velazquez-Vega J, Borja MJ, Rosenberg S, et al. Rosai-Dorfman disease of the central nervous system: report of 6 cases and review of the literature. Medicine (Baltimore). 2014;93(3):165-75. doi: 10.1097/md.0000000000000030.
4. Khan R, Moriarty P, Kennedy S. Rosai-Dorfman disease or sinus histiocytosis with massive lymphadenopathy of the orbit. Br J Ophthalmol. 2003;87(8):1054. doi: 10.1136/bjo.87.8.1054.
5. Andriko JA, Morrison A, Colegial CH, Davis BJ, Jones RV. Rosai-Dorfman disease isolated to the central nervous system: a report of 11 cases. Mod Pathol. 2001;14(3):172-8. doi: 10.1038/modpathol.3880278.
6. Taufiq M, Khair A, Begum F, Akhter S, Shamim Farooq M, Kamal M. Isolated intracranial Rosai-Dorfman disease. Case Rep Neurol Med. 2016;2016:1972594. doi: 10.1155/2016/1972594.
7. Leal PA, Adriano AL, Breckenfeld MP, Costa IS, de Sousa AR, Gonçalves Hde S. Rosai-Dorfman disease presenting with extensive cutaneous manifestation - case report. An Bras Dermatol. 2013;88(2):256-9. doi: 10.1590/s0365-05962013000200014.
8. Symss NP, Cugati G, Vasudevan MC, Ramamurthi R, Pande A. Intracranial Rosai-Dorfman disease: report of three cases and literature review. Asian J Neurosurg. 2010;5(2):19-30.
9. Yang X, Liu J, Ren Y, Richard SA, Zhang Y. Isolated intracranial Rosai-Dorfman disease mimicking petroclival meningioma in a child: case report and review of the literature. Medicine (Baltimore). 2017;96(47):e8754. doi: 10.1097/md.0000000000008754.
10. Wu M, Anderson AE, Kahn LB. A report of intracranial Rosai-Dorfman disease with literature review. Ann Diagn Pathol. 2001;5(2):96-102. doi: 10.1053/adpa.2001.23027.
11. Huang BY, Zong M, Zong WJ, Sun YH, Zhang H, Zhang HB. Intracranial Rosai-Dorfman disease. J Clin Neurosci. 2016;32:133-6. doi: 10.1016/j.jocn.2015.12.046.
12. Fatobene G, Haroche J, Hélias-Rodzwicz Z, Charlotte F, Taly V, Ferreira AM, et al. BRAF V600E mutation detected in a case of Rosai-Dorfman disease. Haematologica. 2018;103(8):e377-e9. doi: 10.3324/haematol.2018.190934.
13. Richardson TE, Wachsmann M, Oliver D, Abedin Z, Ye D, Burns DK, et al. BRAF mutation leading to central nervous system Rosai-Dorfman disease. Ann Neurol. 2018;84(1):147-52. doi: 10.1002/ana.25281.
14. Cohen Aubart F, Haroche J, Emile JF, Charlotte F, Barete S, Schleinitz N, et al. [Rosai-Dorfman disease: diagnosis and therapeutic challenges]. Rev Med Interne. 2018;39(8):635-40. doi: 10.1016/j.revmed.2018.02.011.