Received: 14.02.2011 / **Accepted:** 27.10.2011
DOI: 10.5137/1019-5149.JTN.4275-11.2

Case Report

Isolated Intracranial Rosai-Dorfman Disease: Report of Two Cases and a Review of the Literature

İzole İntrakraniyal Rosai-Dorfman Hastalığı: İki Olgu Sunumu ve Literatür Derlemesi

Mamdouh ABDEL-RAZEK[1], Ghazi Ahmed MATTER[1], Waleed Abdelfattah AZAB[1], Kenneth Chukwuka KATCHY[2], Anupama Arora MALLIK[2]

[1]Ibn Sina Hospital, Department of Neurosurgery, Kuwait
[2]Al-Sabah Hospital, Department of Pathology, Kuwait

Corresponding Author: Waleed Abdelfattah AZAB / E-mail: waleedazab@hotmail.com

ABSTRACT

Rosai-Dorfman disease (RDD) is a rare but well-recognized idiopathic histioproliferative disease affecting the systemic lymph nodes. It is characterized by an unusual proliferation of histiocytic cells. Intracranial localization is a rare manifestation of RDD. The clinical and radiological differentiation from meningiomas is difficult, and can only be achieved after histological examination. This entity should be considered in the differential diagnosis of dural based lesions mimicking meningioma. We report 2 cases of isolated intracranial RDD. The first patient had a large frontal lesion in addition to smaller multiple intracranial lesions. The second patient had only one parasagittal lesion. The diagnosis was confirmed on histopathological examination after surgical excision. The pertinent literature is also reviewed.

KEYWORDS: Rosai-Dorfman disease, Meningioma, Sinus histiocytosis

ÖZ

Rosai-Dorfman hastalığı (RDH) sistemik lenf düğümlerini etkileyen nadir ama iyi bilinen bir idiopatik histiyoproliferatif hastalıktır. Olağandışı histiyositik hücre proliferasyonuyla karakterizedir. İntrakraniyal lokalizasyon RDH'nin nadir bir görünümüdür. Meninjiyomlardan klinik ve radyolojik ayırt etme zordur ve sadece histolojik inceleme ile yapılabilir. Bu hastalık, menenjiyoma benzeyen dural tabanlı lezyonların ayırıcı tanısında dikkate alınmalıdır. İki izole intrakraniyal RDH olgusunu bildiriyoruz. Birinci hastanın birçok küçük intrakraniyal lezyona ek olarak büyük bir frontal lezyonu vardı. İkinci hastanın sadece bir parasagittal lezyonu vardı. Tanı cerrahi eksizyon sonrasında histopatolojik incelemeyle doğrulandı. İlgili literatür de gözden geçirilmiştir.

ANAHTAR SÖZCÜKLER: Rosai-Dorfman hastalığı, Menenjiyom, Sinüs histiyositozu

INTRODUCTION

Rosai-Dorfman disease or sinus histiocytosis with massive lymphadenopathy was recognized as a unique histiolymphoproliferative disease of the lymph nodes by Rosai and Dorfman in 1969 (3,30). It is a rare condition characterized by massive cervical lymphadenopathy with fever, leukocytosis, mild anemia, elevated erythrocytosis rate and polyclonal hypergammaglobulinemia (34). Patients usually tend to be young at the onset of the disease and usually run a prolonged uncomplicated clinical course without treatment (21). Extranodal involvement either alone or in association with nodal disease is seen in approximately 43% of cases (12). The common extranodal sites are the skin, orbit, respiratory tract and bone (13,34). Isolated intracranial involvement is a very rare manifestation (46).

Case 1

A 43-year-old male patient with a few months history of headache and mild dizziness developed 2 episodes of generalized tonic-colonic convulsions. General examination was unremarkable and the patient had no clinical evidence of lymphadenopathy. He also had no neurological deficits apart from a right inferior visual field defect. Brain MRI showed multiple extra axial lesions that were isointense on T1-weighted and low signal intensity on T2-weighted MR images with vivid homogenous enhancement after IV contrast (Figure 1). The largest lesion was in the right frontal convexity causing marked edema and mass effect. Another small convexity lesion was seen in the left frontal region, 2 small lesions with falcine attachment, a lesion in the vicinty of the anterior clinoid process and one attached to the antero-superior border of the right petrous bone. The radiological diagnosis was that of multiple meningiomas. The patient underwent a right frontal craniotomy for resection of the large frontal lesion. The dura was vascular and the tumor was attached to it, circumferential incision around the tumor attachment was undertaken and a good arachnoid plane around the tumor was found except for the deeper parts. The lesion had a nodular grayish-pink appearance with firm consistency. It gave the

impression of a meningioma (Figure 2). The tumor was totally removed and the patient had a smooth postoperative course. Histopathological examination of the specimen demonstrated meningeal infiltration by large pale cells mixed with lymphocytes and plasma cells. The lesion demonstrated dense fibrosis. The cell infiltration was conspicuous around blood vessels and extended into the brain parenchyma. The large pale cells were positive for CD68 and S100 protein, but negative for EMA and GFAP. Emperipolesis was identified and a diagnosis of Rosai-Dorfmans disease was made.

Case 2

A 38-year old female patient presented to the emergency room with a generalized seizure for the first time that lasted for a few minutes. General physical examination was unremarkable. No neurological deficits were detected. Her fundus examination revealed bilateral early papiledema. MRI brain showed an isointense right parietal parasagittal mass with perifocal edema. The lesion enhanced intensely after IV contrast injection. The superior sagittal sinus was patent and the lesion was diagnosed as a meningioma. The tumor was approached through a right high parietal craniotomy. It was brownish-gray in color with firm consistency and moderate vascularity. It was attached to the convexity dura with partial attachment to the superior sagittal sinus. It was easily dissected from the surrounding brain tissue through a good plane of cleavage and was completely excised along with the dural convexity attachment. Histological examination revealed sheets of histiocytes intermingled with many reactive plasma cells (Some with Russell Bodies), lymphocytes and neurtrophils. They were arranged in vague nodules in some areas and separated with hyalinised collagen. The cytoplasm of the histiocytes was pale to foamy with eosinophilic granular with lipofuschin pigment in some. The nuclei were round to oval in shape with vesicular chromatin and small nucleoli. There were some multinucleated giant cells (Figure 3). Immune stains were done for S-100 protein, CD 68, EMA and SMA. The pale large histiocytes were S-100 positive and displayed emperipolesis.

DISCUSSION

In 1969, Rosai and Dorfman described a newly recognized benign histioproliferative disorder characterized by massive cervical lymphadenopathy, fever, and leukocytosis (30). Pathologically the lymph nodes showed enlarged sinuses containing large histiocytes with phagocytosed lymphocytes and the entity was named sinus histiocytosis with massive lymphadenopathy (SHML) or Rosai-Dorfman disease (30). RDD is classified among idiopathic or reactive histiocytoses (5, 12, 44). Occasionally, patients present with only extranodal disease with no lymphadenopathy; accordingly, the originally proposed term "sinus histiocytosis with massive lymphadenopathy" may not be precise (11). Molecular studies have shown that RDD is a polyclonal and reactive process rather than a neoplastic one, however, the origin of RDD is not clear (26, 32, 38). It often occurs in the setting of nonspecific immune dysfunction and many cases occur after a viral illness (31). Epstein-Barr virus was demonstrated in about 50% of cases in serological studies (40). Nevertheless, the presence of Epstein-Barr virus was not documented in histiocytes and lymphocytes by in situ hybridization technique. The increased serological titers may be the result of a nonspecific host immune response and not the cause of RDD (11,39).

Isolated central nervous system (CNS) involvement is extremely rare (2,6,4,10,13,15,17-19,21-23,28,33,35,36,38,46). In a large series of RDD including 200 cases there were only 3 cases with intracranial manifestations (9).

Rosai-Dorfman disease involving the CNS occurs most commonly in patients between 22 and 63 years of age, with a clear male predominance (4, 10). The mean age at presentation is 41 and that is almost the same age like in our cases. Deodhare et al. noticed that the age of onset in patients with intracranial localization of RDD differ from those with nodal-based RDD (37.5 yr versus 20.6 yr) (11). The average age of patients at admission is in the second decade. Only one patient at the young age of 5-years was treated for clinical manifestations of RDD (35).

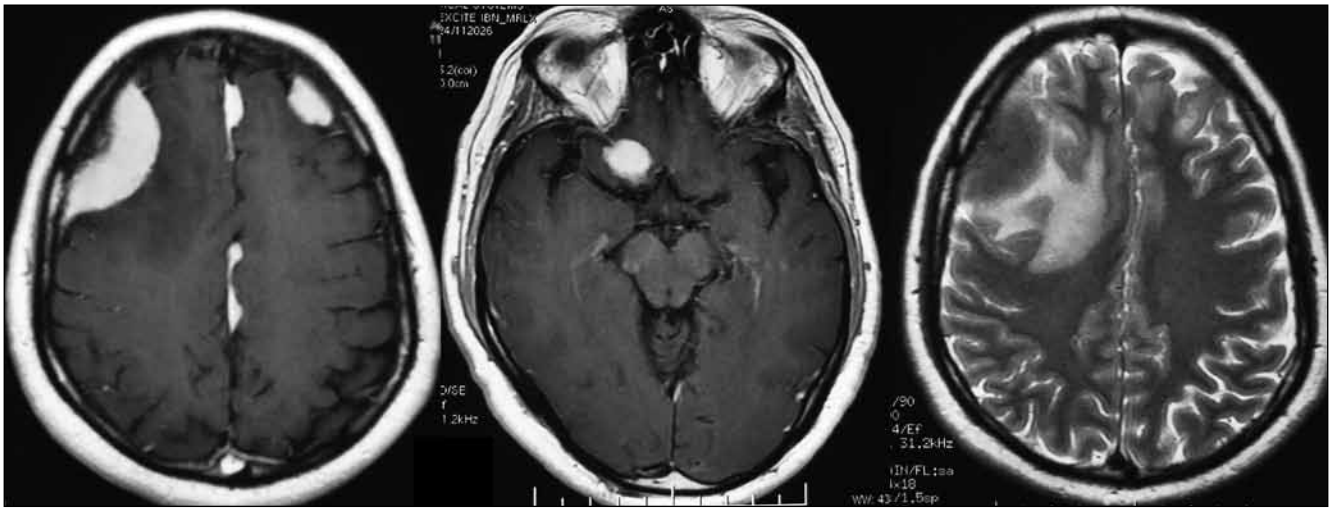

Figure 1: Axial T1-Weighted with contrast (left and right), T2-Weighted (middle) MRI images of case 1, showing the dural-based lesions.

Clinically, patients with intracranial RDD usually present with headaches, seizures, numbness, and paraplegia (4). In a meta-analysis of 32 cases by Petzold et al (28) there was 25% incidence of visual symptoms, which were the presenting feature in 19% of all cases. One of the main symptoms in our first case was impairment of vision. Seizures were among the symptoms in that case and were the only symptom at presentation for our second case. Massive and painless cervical lymphadenopathy was noticed in 90% of reported cases (35). None of our patients had lymphadenopathy. Other manifestations like anemia, leukocytosis, polyclonal hypergammaglobulinemia, and raised erythrocyte sedimentation rate are common but are not always present (12, 34). Extra nodal involvement, such as the eyes and its appendages, skin, upper respiratory tract, bone, salivary gland, testis, and meninges of the cranium and spine are seen in one third of the cases (34).

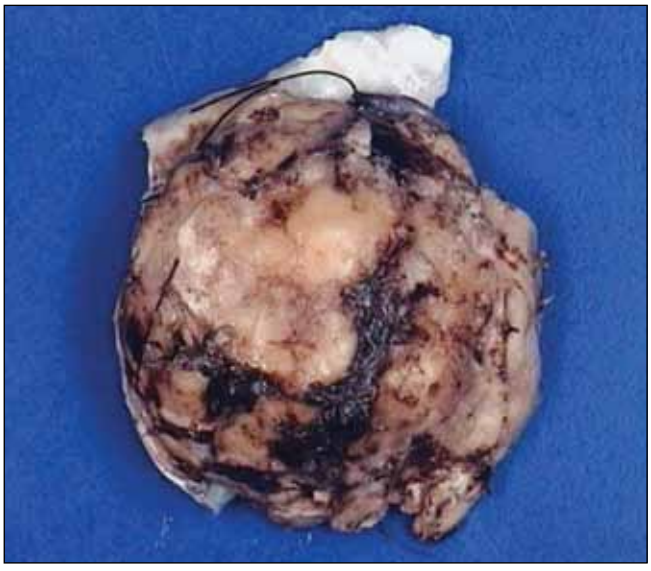

Figure 2: Gross appearance of the mass in case 1. Round lobulated mass attached to the dura.

Radiologically, intracranial lesions in cases of RDD appear to be attached to the dura and radiologically resemble meningioma. (1, 9) The surgical and neuroradiological features seen in our patient resembled those of a meningioma. Nonetheless, Sze and Zimmerman (37) suggested that the low signal intensity on T2-weighted MR imaging is a very unlikely a characteristic of meningioma and may reflect the presence of free radicals produced by macrophages during active phagocytosis. Focal necrosis, fibrosis, and erythrophagocytosis may also contribute to low signal intensity on T2-weighted MR imaging. This low intensity of the lesion on T2-wieghted images was similarly demonstrated in our cases. Moreover, N-isopropyl-P-[123I] iodoamphetamine ([123I] IMP) single-photon emission computerized tomography (SPECT) reveals a hot lesion on early and delayed images in RDD and is not a feature of meningiomas (41).

Typical nodal Rosai–Dorfman disease has a pathognomonic, histopathological cytoarchitecture consisting of massive expansion of the sinusoids by numerous large histiocytes with large vesicular nuclei and abundant pale eosinophilic cytoplasm with ill-defined borders. The histiocytes contain intact lymphocytes or erythrocytes in their cytoplasm, a phenomenon known as emperipolesis (X) lymphoplasmacytic inflammatory cell infiltrate is evident (4,25,45) and is immunoreactive for kappa and gamma light chains (4,11). The histopathological differential diagnosis of intracranial RDD includes Langerhans cell histiocytosis (LCH) or histiocytosis X, infectious processes, lymphoproliferative disorders, and plasma cell granulomas, which are well described in other papers (7,42,43). Langerhans cell histiocytosis may produce meningeal and dural lesions (20). However, the diagnosis of RDD is based on the morphological characteristics. There are

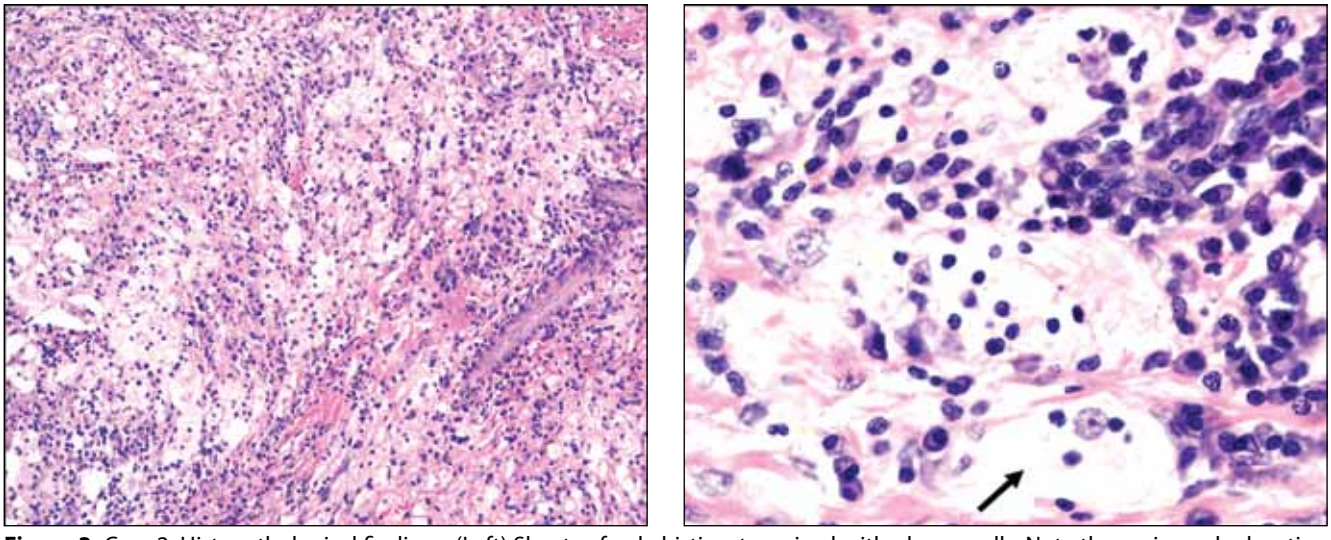

Figure 3: Case 2. Histopathological findings. (Left) Sheets of pale histiocytes mixed with plasma cells. Note the perivascular location of plasma cells. Emperipolesis is seen in some histiocytes (H&E x100). (Right) Higher magnification highlighting emperipolesis (H&E x 400).

other disease conditions with predominance of histiocytes, like some cases of leukemia, lipid storage disease, and histiocytosis X. Nevertheless, the classical findings of dilated nodal sinuses filled with foamy histiocytes, phagocytosed lymph nodes, and plasma cells make the diagnosis of this disease apparent (12). The histological differentiation between Langerhans cell histiocytosis and RDD is based on the presence of the following features in the former; Langerhans cells with nuclear indentation and grooves, positive CD1a is only positive in LCH, and a confirmatory presence Birbeck's granules (41). Abscess formation and fibrosis can be seen in some cases of RDD. However, prominent emperipolesis and S-100 protein–positive histiocytes are rarely seen in the infectious process. In RDD the lymphocytic infiltrate is usually mild and consists of a mixture of T and B lymphocytes (11). Cases of plasma cell granulomas demonstrate a polymorphic cellular infiltrate, composed of lymphocytes, plasma cells, histiocytes, and foamy macrophages and are associated with fibrosis (8). In RDD the plasma cells are polyclonal (immunoreactive for k and c light chains) (4,11). Necrotic areas may also be found (11, 45). In contrast to RDD cells characterized by S-100 positivity (4,11,29), plasma cell granulomas do not show S-100 protein–positive histiocytes or lymphophagocytosis (27). Immunophenotypical studies show that the cells in RDD share the features of both mononuclear phagocytic cells and dendritic cells (interdigitating reticulum or Langerhans cells) (24,26,35). Mononuclear and dendritic cells commonly show positive expression for CD68, alpha-1-antitrypsin, and alpha-1-antichymotrypsin. But S-100 protein expression is only positive in dendritic cells. However, dendritic cells typically showing CD1a expression are not observed in any cells of RDD (24).

Most of the patients with intracranial lesions were treated surgically. At surgery, Rosai–Dorfman disease lesions in the central nervous system are firm, lobular, whitish gray or yellowish tan in color and adherent to the dura. The diagnosis can only be confirmed by histopathological/immunohistochemical examination of affected tissues. Intraoperative pathological diagnosis can be misleading (3).

Some patients received corticosteroid treatment (35), chemotherapy (16), and radiotherapy was used in some cases (12). Involvement of the central nervous system in RDD especially in the absence of nodal disease seems to have a benign prognosis. Surgery is essential for diagnosis (3,46), and when total removal is achieved, the outcome is generally good without risk of recurrence (14).

CONCLUSION

Rosai-Dorfman disease is an uncommon condition that rarely involves the brain. In spite of the absence of massive lymphadenopathy in some cases, it should be considered in the differential diagnosis of any dural-based lesions on imaging studies including meningiomas. Low signal intensity on T2-weighted MR imaging is a very unlikely characteristic of meningioma and [123I] IMP uptake are characteristics of RDD. Even with the absence of enough follow-up information, surgical excision seems to be the most appropriate treatment of these lesions when they start causing symptoms.

REFERENCES

1. Abraham J, Chandy J: Meningiomas of posterior fossa without dural attachment: Case report. J Neurosurg 20:177-179, 1963
2. Ambekar S, Somanna S, Bhat DI, Ranjan M: Isolated craniospinal involvement of Rosai-Dorfman disease: Case report. Br J Neurosurg 25: 297-299, 2011
3. Adeleye A, Amir G, Fraifeld S, Shoshan Y, Umansky F, Spektor S: Diagnosis and management of Rosai–Dorfman disease involving the central nervous system. Neurol Res 32: 572-578, 2010
4. 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 14:172-178, 2001
5. Woda BA, Sullivan JL: Reactive histocytic disorder. Am J Clin Pathol 99:459-463, 1993
6. Beros V, Houra K, Rotim K, Zivkovic DJ, Cupic H, Kosec A: Isolated cerebellar intraparenchymal Rosai-Dorfman disease--case report and review of literature. Br J Neurosurg 25: 292-296, 2011
7. Bhattacharjee MB, Wroe SJ, Harding BN, et al: Sinus histiocytosis with massive lymphadenopathy-isolated suprasellar involvement. J Neurol Neurosurg Psychiatry 55:156–158, 1992
8. Cannella DM, Prezyna AP, Kapp JP: Primary intracranial plasma-cell granuloma. Case report. J Neurosurg 69:785–788, 1988
9. Cantore G, Ciappetta P, Delfini R, Raco A: Meningiomas of the posterior fossa without dural attachment. Surg Neurol 25:127-130, 1986
10. Castellano-Sanchez AA, Brat DJ: 57-year-old-woman with acute loss of strength in her right upper extremity and slurred speech. Brain Pathol 13:641-645, 2003
11. Deodhare SS, Ang LC, Bilbao JM: Isolated intracranial involvement in Rosai-Dorfman disease: A report of two cases and review of the literature. Arch Pathol Lab Med 122: 161-165, 1998
12. Foucar E, Rosai J, Dorfman RF: Sinus histiocytosis with massive lymphadenopathy: Current status and future directions. Arch Dermatol 124:1211-1214, 1988
13. Fukushima T, Yachi K, Ogino A, Ohta T, Watanabe T, Yoshino A, Katayama Y: Isolated intracranial Rosai-Dorfman disease without dural attachment—case report. Neurol Med Chir (Tokyo) 51: 136-140, 2011
14. Gaetani P, Tancioni F, Di Rocco M, Baena RR: Isolated cerebellar involvement in Rosai-Dorfman Disease: Case Report. Neurosurgery 46:479, 2000
15. Gupta K, Bagdi N, Sunitha P, Ghosal N: Isolated intracranial Rosai-Dorfman disease mimicking meningioma in a child: A case report and review of the literature. Br J Radiol 84:1003, 2011
16. Haas RJ, Helmig MSE, Pretchel K: Sinus histiocytosis with massive lymphadenopathy and paraparesis: Remission with chemotherapy-A case report. Cancer 42:77-80, 1978

17. Hadjipanayis CG, Bejjani G, Wiley C, Hasegawa T, Maddock M, Kondziolka D: Intracranial Rosai-Dorfman disease treated with microsurgical resection and stereotactic radiosurgery. Case report. J Neurosurg 98:165-168, 2003
18. Horneff G, Jurgens H, Hort W, Karitzky D, Gobel U: Sinus histiocytosis with massive lymphadenopathy (Rosai-Dorfman disease): Response to methotrexate and mercaptopurine. Med Pediatr Oncol 27:187-192,1996
19. Juric G, Jakic-Razumovic J, Rotim K, Zarkovic K: Extranodal sinus histiocytosis (Rosai-Dorfman disease) of the brain parenchyma. Acta Neurochir (Wien)145:145-149, 2003
20. Kepes JJ, Kepes M: Predominantly cerebral forms of histiocytosis-X. A reappraisal of "Gagel's hypothalamic granuloma", "granuloma infiltrans of the hypothalamus" and "Ayala's disease" with a report of four cases. Acta Neuropathol 14: 77-98,1969
21. Kim M, Provias J, Bernstein M: Rosai-Dorfman disease mimicking multiple meningioma: Case report. Neurosurgery 36:1185–1187, 1995
22. Konishi E, Ibayashi N, Yamamoto S, Scheithauer BW: Isolated intracranial Rosai-Dorfman disease (sinus histiocytosis with massive lymphadenopathy). AJNR AmJ Neuroradiol 24: 515-518, 2003
23. Krishnamoorthy V, Parmar CF, Panikar D: Isolated intracranial Rosai Dorfman disease. Neurol India 59:443-446, 2011
24. Lopez P, Estes M: Immunohistochemical characterization of the histiocytes in sinus histiocytosis with massive lymphadenopathy: Analysis of an extranodal case. Hum Pathol 20: 711–715, 1989
25. Natarajan S, Post K, Strauchen J, et al: Primary intracerebral Rosai–Dorfman disease: A case report. J Neurooncol 47: 73–77, 2000
26. Paulli M, Bergamaschi G, Tonon L: Evidence for a polyclonal nature of the cell infiltrate in sinus histiocytosis with massive lymphadenopathy (Rosai-Dorfman disease). Br J Haematol 91:415-418, 1995
27. Pettinato G, Manivel JC, De Rosa N, et al: Inflammatory myofibroblastic tumor (plasma cell granuloma). Clinicopathologic study of 20 cases with immunohistochemical and ultrastructural observations. Am J Clin Pathol 94:538–546, 1990
28. Petzold A, Thom M, Powell M, Plant GT: Relapsing intracranial Rosai-Dorfman disease. J Neurol Neurosurg Psychiatry 71:538-541, 2001
29. Purav P, Ganapathy K, Mallikarjuna V, et al: Rosai–Dorfman disease of the central nervous system. J Clin Neurosci 12: 656–659, 2005
30. Rosai J, Dorfman RF: Sinus histiocytosis with massive lymphadenopathy: A newly recognized benign clinicopathological entity. Arch Path 87:63-70, 1969
31. Rosai J, Dorfman RF: Sinus histiocytosis with massive lymphadenopathy: A pseudolymphomatous benign disorder: Analysis of 34 cases. Cancer 30:1174-1188, 1972
32. Sacchi S, Artusi T, Torelli U, et al: Sinus histiocytosis with massive lymphadenopathy. Leuk Lymphoma 7:189–194, 1992
33. Said R, Abi-Fadel F, Talwar J, Attallah JP, Dilawari A: Intracranial rosai-dorfman: A clinical challenge. Neurologist 17:117-119, 2011
34. Sanchez R, Rosai J, Dorfman RF: Sinus histiocytosis with massive lymphadenopathy: An analysis of 113 cases with special emphasis on its extranodal manifestations. Lab Invest 36:349-350, 1977
35. Shaver EG, Rebsamen SL, Yachnis AT, Sutton LN: Isolated extranodal intracranial sinus histiocytosis in a 5-year-old boy: A case report. J Neurosurg 79:769-773, 1993
36. Siadati A, Powell SZ, Shahab I, et al: Pathologic quiz case: A 48 year-old woman with a dural-based intracranial tumor. Arch Pathol Lab Med 125:1115–1116, 2001
37. Sze G, Zimmerman RD: The magnetic resonance imaging of infections and inflammatory diseases. Radiol Clin North Am 26:839–859, 1988
38. Triana-Pérez AB, Sánchez-Medina Y, Pérez-Del Rosario PA, Millán-Corada AM, Gómez-Perals LF, Domínguez-Báez JJ. Isolated intracranial Rosai-Dorfman disease: A case report and literature review. Neurocirugia (Astur) 22: 255-260, 2011 (Article in Spanish)
39. Trudel M: Dural involvement in sinus histiocytosis with massive lymphadenopathy: Case report. J Neurosurg 60: 850-852, 1984
40. Tsang WYW, Yip TTC, Chan JKC. The Rosai-Dorfman disease histiocytes are not infected by Epstein-Barr virus. Histopathology 25:88-90, 1994
41. Udono H, FukuyamaK, Okamoto H, Tabuchi K: Rosai-Dorfman disease presenting with multiple intracranial lesions with unique findings on magnetic resonance imaging: Case report. J Neurosurg 91:335–339, 1999
42. Warnke RA, Kim H, Dorfman RF: Malignant histiocytosis (histiocytic medullary reticulosis). Clinicopathologic study of 29 cases. Cancer 35:215–230, 1975
43. Wenig BM, Abbondanzo SL, Childers EL, et al: Extranodal sinus histiocytosis with massive lymphadenopathy (Rosai-Dorfman disease) of the head and neck. Hum Pathol 24: 483–492, 1993
44. Woda BA, Sullivan JL: Reactive histiocytic disorders. Am J Clin Pathol 99:459–463, 1993
45. Wu M, Anderson AE, Kahn LB: A report of intracranial Rosai-Dorfman disease with literature review. Ann Diagn Pathol 5: 96–102, 2001
46. Zhang JT, Tian HJ, Lang SY, Wang XQ: Primary intracerebral Rosai-Dorfman disease. J Clin Neurosci 17:1286-1288, 2010