Intracranial Rosai-Dorfman Disease in Pregnancy: A Case Report

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Received 15 May 2014; Published online 16 August 2014

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Abstract

Rosai-Dorfman disease (RDD) is a well-described entity that rarely presents as a solitary intracranial mass. In this case report, we describe progesterone receptor (PR) positivity on immunostain in a recently pregnant patient. The possibility of meningioma was raised. However, the presence of emperipolesis and positive S100 staining in combination with negative EMA stain excluded meningioma from the differential. Additional cases of RDD underwent immunostain for PR and were found to be negative. We also present a review of the literature regarding dural based masses and discuss the limited literature regarding the treatment of solitary intracranial RDD.

Keywords: Rosai-Dorfman disease; Meningioma; Dural based mass; Progesterone receptor; Pregnancy

1. Introduction

Rosai-Dorfman Disease (RDD) was first described as a benign proliferative process of histiocytes in lymph nodes, most prominently in the neck, under the name “sinus histiocytosis with massive lymphadenopathy”. While usually a widespread systemic disorder involving many lymph nodes, extranodal mass lesions of RDD have been recognized, including cases with isolated involvement of the central nervous system. The rarity of isolated CNS cases is highlighted by the paucity of case reports in the neurosurgical literature. While systemic RDD typically has onset at age 20, with a slight male predominance of 1.4 to 1, patients with solitary intracranial disease are typically found in the fourth or fifth decade of life, and there is a stronger male predominance. Nonspecific findings indicative of a generalized inflammatory process such as fever, elevated sedimentation rate, elevated C-reactive protein, leukocytosis, and polyclonal hypergammaglobulinemia may be found in patients with RDD. Typically, CNS lesions are dural based lesions, multiple or single in nature, which mimic the neuroradiological findings and the gross surgical impressions of meningiomas.

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Most such lesions are not highly vascular but they usually enhance homogenously following administration of gadolinium for magnetic resonance imaging (MRI). We report a case of isolated intracranial RDD in a young woman who was pregnant.

2. Case History

This 29 year old G2 P1 woman with medical history of Crohn’s disease, tobacco abuse, and chronic narcotic use for abdominal pain was followed in obstetrical clinic for prenatal care. She was counseled to stop tobacco use and to reduce her dependence on narcotic medication during multiple prenatal visits. The patient had an otherwise unremarkable prenatal course. She had a previous child via Caesarian section and did not experience any perinatal complications. Following the birth of her second child, she experienced progressively worsening headaches which began the day after her second Caesarian section. These were managed conservatively with pain medication but continued to occur. After several weeks of progressively worsening headache, she presented to the emergency room. A CT scan revealed a large parafalcine mass which was also seen subsequently by MRI as a homogeneously enhancing parafalcine mass (Figures 1 and 2). The CT and MRI findings were suggestive of meningioma. She elected to proceed with surgical intervention.

Fig. 1. Large parafalcine mass detected on non-contrast CT head obtained during headache workup.
Fig. 2. Noncontrast and contrast axial T1 images demonstrating homogeneously enhancing parafalcine mass.

The patient underwent preoperative embolization prior to surgery given the large size of the parafalcine mass and the desire to minimize hemorrhage at the time of surgery. Angiographically the tumor was supplied by several branches that emanated from the middle meningeal artery which was further suggestive of meningioma (Figure 3). The feeding supply to the tumor was successfully embolized using NBCA via Prowler microcatheter. She was taken to the operative room the following day for definitive surgical resection. There appeared to be good tissue planes and the mass was successfully dissected off the sagittal sinus and falx. Post-operative MRI confirmed gross total resection of the dural-based mass (Figure 4). Her postoperative recovery in the hospital was unremarkable, and her headache was improved.

Fig. 3. Angiographic images demonstrating supply of the tumor off the middle meningeal artery prior to embolization and subsequent occlusion after NBCA embolization.
Histopathological examination, beginning with frozen sections during an intraoperative consultation, showed no evidence of meningioma. Instead, the lesion consisted of numerous histiocytes with pale cytoplasm and irregular small nuclei in a fibrous matrix with scattered lymphocytes (Figures 5 and 6). In the paraffin sections of fixed tissues small lymphocytes were seen within multiple histiocytes, a feature characteristic of RDD and known as emperipolesis (Figure 7). The histiocytes were immunopositive for S100 protein but not for CD1a. These features are characteristic of Rosai-Dorfman Disease.

Fig. 4. Contrast enhanced axial T1 images post-operative MRI demonstrating gross total resection of the mass.

Fig. 5. Sheets of histiocytes, H&E stain, original objective 4X.
In view of the history that the headache began immediately after delivery, and the size of the lesion suggested it had grown during the pregnancy, immunohistochemical stains for estrogen receptors and for progesterone receptors were done; these showed no immunopositivity for ER, but strong and widespread PR immunopositivity in the nuclei of the histiocytes (Figure 8). A literature search has disclosed no reports of PR immunopositivity in any cases of RDD. Since a large majority of meningiomas are PR immunopositive, this result raised a question as to whether this was a peculiar
variant of meningioma after all. An immunostain for Epithelial Membrane Antigen (EMA) was entirely negative; this epithelial marker is almost always expressed by meningioma cells. The patient was referred to the hematology-oncology service. A PET CT scan showed no evidence of systemic disease. MRI scan performed 3 months post-resection showed no recurrence.

![Image](image_url)

**Fig. 8.** Widespread positive nuclear immunostaining for progesterone receptor (PR), original objective 10X

We were unable to obtain access to tissue blocks from any other cases of solitary intracranial RDD masses. With IRB approval we obtained paraffin blocks from our files of 5 cases of non-CNS RDD and examined new sections of each with immunostains for ER and PR; all cases were wholly negative for each receptor type.

3. Discussion

Rosai-Dorfman Disease is uncommon and an isolated intracranial presentation is rare. This necessitates careful consideration of several differential diagnoses for this patient's intracranial dural-based mass, including meningioma, solitary fibrous tumor, Langerhans cell histiocytosis, Castleman's disease, granulomatous diseases (infectious or due to sarcoidosis) or an unusual case of central nervous system Hodgkin's disease.

Dural-based RDD can look radiographically similar to meningioma and the histopathologic distinction, while often straightforward, can be difficult in considering the lymphoplasmacyte-rich subtype of meningioma. This meningioma subtype is characterized by abundant infiltrates of lymphocytes and plasma cells that mostly conceal the meningothelial tumor cells. RDD also has a lymphoplasmacytic component but is dominated by sheets of histiocytes, some of which are
multinucleated. The S-100 immunoreactivity of RDD histiocytes helps eliminate the possible diagnosis of meningioma as most meningiomas are S100-negative. In addition, emperipolesis of lymphocytes is virtually pathognomonic for RDD and is not a feature of meningiomas, so when found it is definitive for this differential diagnosis. It is reported that only 70% of cases of RDD have emperipolesis, and it is claimed that it may be more difficult to observe with intracranial or other extranodal tumors. In our case, as with many, the S100 immunostain allows visualization of the intracellular lymphocytes and helped solidify the diagnosis. Lymphoplasmacyte-rich meningioma, like the classical subtypes, will have membranous immunopositivity for EMA, whereas RDD will not; of course, our case was EMA-immunonegative.

Solitary fibrous tumors (SFTs) may be included in the initial radiographic differential of dural-based lesions, but are clearly distinguished from RDD histologically. SFTs can have areas of spindled cells in fascicles with intervening broad bands of collagenous tissue, or a branching (“staghorn”) capillary pattern. The stromal spindled cells and endothelial cells are typically immunopositive for CD34, but are negative for EMA and S-100. SFT is now a preferred nosology for tumors previously regarded as meningeal hemangiopericytomas, although there remains some controversy about this among some neuropathologists. This controversy is not relevant to the differential diagnosis with RDD.

Although Castleman’s disease presents more commonly as systemic lymph node hyperplasia, intracranial Castleman’s disease can present as extra-axial dural-based lesions like those seen in lymphoplasmacyte-rich meningioma or RDD, and histologically is a benign lymphoproliferative process. Castleman’s disease is characterized histologically by hyperplastic lymphoid follicles with germinal centers that contain predominantly mature B-lymphocytes and occasional follicular dendritic cells, which are S-100 immunopositive. The interfollicular areas are comprised of T-lymphocytes, eosinophils and plasma cells with a background of hyalinized blood vessels. There is obvious overlap of several cell types with RDD and lymphoplasmacyte-rich meningioma. Specific histologic features, like layering of lymphocytes around follicles or “onion skinning” help to distinguish this benign disease from RDD, which lacks lymphoid follicular architecture.

Like RDD, Langerhans cell histiocytosis (LCH) histologically presents with the combination of massive histiocytosis, chronic inflammatory cells, multinucleated giant cells, and eosinophils. Because LCH can be locally destructive and cause destructive brain lesions, it is critical to distinguish the morphology and staining patterns of the histiocytes in LCH. Unlike RDD, LCH histiocytes characteristically are kidney shaped, their nuclei have grooves, they are immunopositive for CD1a, and do not exhibit emperipolesis.

Foamy histiocytes with eosinophils and polytypic lymphocytes should also raise the concern for Hodgkin disease (HD). Although intracranial presentations of HD most commonly represent metastatic disease in patients already known to have HD elsewhere, primary central nervous system disease has been reported. Hodgkin disease lacks the emperipolesis in RDD and the EMA staining characteristic of meningiomas. A Hodgkin disease diagnosis requires careful inspection for and identification of Reed-Sternberg cells with CD15 and CD30 immunopositivity.

Sarcoidosis, and granulomatous masses from tuberculosis or certain fungal infections (notably histoplasmosis and cryptococcosis) can also present as isolated dural-based mass lesions.
resembling meningiomas. Usually these diseases are more widespread and intracranial involvement is secondary, but isolated dural-based lesions are reported for each such disorder. Histologically, these are each characterized by well-formed granulomas, in distinction to the sheet-like proliferation of histiocytes in RDD. The infectious agents may be identifiable with appropriate special stains for acid-fast bacilli or for fungi.

4. Conclusions

The radiologic differential diagnosis for this case presentation was quite extensive, but meningioma was clearly the most common element of that differential diagnosis list. Therefore, the correct identification of Rosai-Dorfman disease relies heavily upon histopathologic examination, careful consideration of unusual diagnoses, and recognition of subtle key differences. Though this case was thought to be a straightforward meningioma prior to surgery, the negative EMA immunostaining of this tumor and the positive S-100 immunostain that highlighted emperipolesis were necessary to definitively diagnose Rosai-Dorfman disease.

Experience with the treatment of solitary intracranial RDD is limited. The literature suggests that recurrence of RDD disease is rare in the setting of total surgical resection, even in the setting of multifocal disease. If total resection cannot be achieved with acceptable morbidity, stereotactic radiosurgery and corticosteroid therapy may be a reasonable treatment modality although long term data on this are lacking. Sellar location of RDD may have a higher recurrence rate at other locations although the exact mechanism of this has yet to established. The late recurrence of RDD after initial surgical resection suggests that long term follow-up with serial imaging studies may be important.

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