

A case study on Rosai-Dorfman disease occurring within the pelvis

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Introduction

Rosai-Dorfman disease, also termed sinus histiocytosis with massive lymphadenopathy (SHML), represents a rare proliferative disorder of histiocytes, that commonly affects the cervical lymph nodes. It was first described as a unique clinicopathological entity by Rosai and Dorfman in 1969.¹ Extranodal disease is encountered in almost half of all cases, presenting within the skin, soft tissue, salivary glands, bone or central nervous system. We describe a case of a young female who presented with an iliac fossa mass. Radiological imaging failed to demonstrate abnormalities within the uterus or the adnexae. A biopsy of the mass revealed sinus histiocytosis with emperipolesis, consistent with a diagnosis of Rosai-Dorfman disease. The patient was treated with conventional chemotherapy, followed by surgical intervention in the form of complete pelvic lymph node clearance. The patient has remained disease free to date.

Case report

A 33-year-old woman presented to our gynaecological outpatient department in October 2012 with an abdominal mass in the left iliac fossa, as well as pain radiating into the medial aspect of the left thigh, unassociated with a history of fever, menstrual irregularities or trauma. Past medical history was unremarkable. No pertinent family history was available.

Upon computed tomography (CT) scan, a solitary, large left iliac mass was discovered, with a maximum diameter of 46 mm, abutting the ipsilateral iliac vessels, considered to be suspicious for a lymph node. A biopsy thereof showed sinus histio-

cytosis with emperipolesis, and the patient was subsequently treated with Wysolone® (prednisolone), 40 mg daily. At one month follow-up, ultrasonography revealed persistence of the mass, with increased dimensions (maximum diameter of 70 mm). She was then placed on Endoxan® (cyclophosphamide) 100 mg daily. Follow-up ultrasound investigation at three months showed no diminution in the size of the pelvic mass.

A repeat biopsy of the mass confirmed the earlier diagnosis of sinus histiocytosis with characteristic emperipolesis (Figures 1a and b). Re-evaluation with magnetic resonance imaging (Figures 2 a and b) revealed close proximity of the mass to the left iliac vessels, yet the CT angiography showed no direct vascular involvement. A positron emission tomography-CT scan demonstrated no evidence of metastatic disease. Owing to the persistence of clinical symptoms, surgical exploration was undertaken, entailing resection of the mass with the attendance of a vascular surgeon. Complete dissection of the left pelvic lymph node basin was performed. The postoperative course was uneventful and the patient has remained well and disease free to date.

Discussion

Rosai-Dorfman disease, also termed SHML, represents a rare, predominantly nodal-based proliferative disorder of histiocytes, originally described by Azouary and Reed, and then later, by Rosai and Dorfman in 1969.¹

Rosai-Dorfman disease primarily involves the lymph nodes, and yet extranodal involvement is encountered in as many

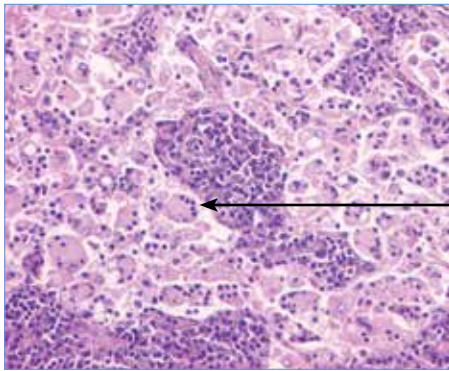
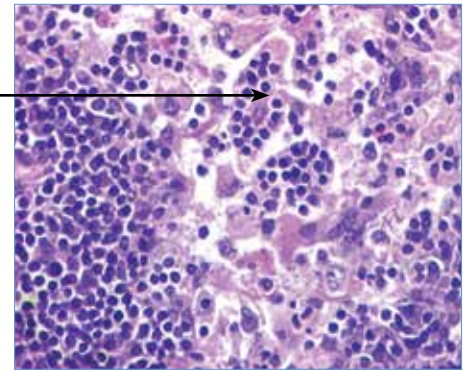


Figure 1 a: Emperipolesis: a cut section of the lymph node mass

The cell seen here has abundant cytoplasm and multiple nuclei. On 4 x view, the cell was a histiocyte that had engulfed multiple lymphocytes. The phenomenon of "emperipolesis" helped to confirm the diagnosis



Another Histiocyte showing emperipolesis on 40x view

Figure 1 b: Another histiocyte, showing emperipolesis on 40 x view

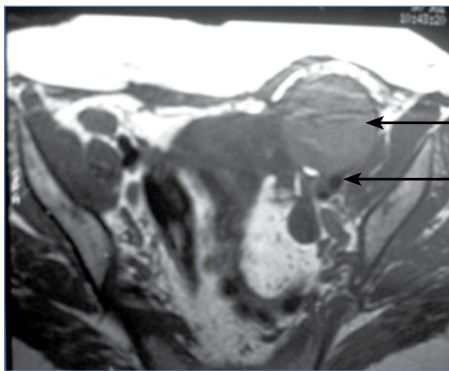


Figure 2 a: Magnetic resonance imaging of the pelvis [T1 image (sagittal view)]

Pelvic Mass
Flow void representing Iliac vessels

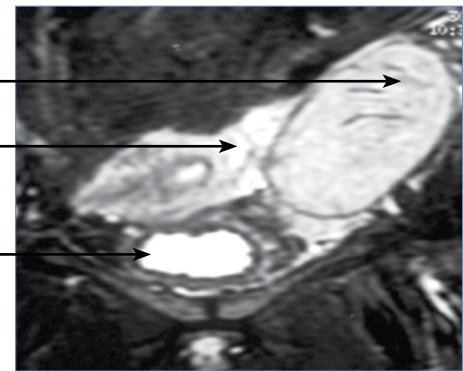


Figure 2 b: Magnetic resonance imaging of pelvis [T2 image (coronal view)]

Pelvic Mass
Uterus
Bladder

as 43% of cases. Common sites of extranodal disease include the skin, soft tissue, orbit, bone and pancreas,^{2,3} as well as the head and neck, the nasal cavity and major salivary glands.⁴ Rosai-Dorfman disease is presently considered a benign disorder, but it may be aggressive in certain cases, leading to significant morbidity and mortality.⁵

Any age group may be affected, yet Rosai-Dorfman disease usually peaks in the second decade of life. The aetiology of the disease remains uncertain (and controversial). Two theories describe the presumed pathogenesis of this disorder. The first proposes an infectious aetiology, based upon clinical onset, low-grade fever and localised adenopathy, citing agents such as herpes viruses, Epstein-Barr virus, cytomegalovirus, *Brucella* and *Klebsiella* spp.^{6,7} The second hypothesis postulates immune dysregulation, which is supported by the study by Middel et al⁸ that showed that stimulation of monocytes or macrophages via macrophage colony-stimulating factor led to immunosuppressive macrophages, representing a main mechanism for the pathogenesis of Rosai-Dorfman disease. The presence of massive, yet painless, bilateral cervical lymphadenopathy is the characteristic clinical feature of the disease, with possible involvement of other sites, including axillary, inguinal, para-aortic and mediastinal lymph nodes.

Laboratory alterations are frequent, and include anaemia in 66% of the cases, leukocytosis in 59%, neutrophilia in 68%, increased erythrocyte sedimentation rate in 88% and hypergammaglobulinaemia in 90%. The histopathology of Rosai-Dorfman disease is most characteristic. The affected lymph nodes show massively distended sinuses, the presence of numerous large histiocytes with abundant pale cytoplasm, vesicular nuclei with distinct nucleoli, and emperipolesis. Emperipolesis, a biological phenomenon, was defined by Humble, Jaynee and Pulvertaft in 1956 as "the active penetration of one cell by another which remains intact".⁹ This differs from phagocytosis since the engulfed cell exists within another cell, remains viable, and may exit with no physiological and morphological consequence for either cell.⁹

The histiocytes of Rosai-Dorfman disease are immunoreactive to S100 protein,¹ "pan-macrophage" antigens such as EBM,¹¹ HAM 56 and Leu-M3,² antigens functionally associated with phagocytosis (Fc receptor for immunoglobulin G and complement receptor 3),³ and lysosomal activity (lysozyme, alpha 1-antichymotrypsin and alpha 1-antitrypsin), antigens associated with early inflammation (Mac387 and 27E10),⁴ antigens commonly found on monocytes, but not tissue macrophages (OKM5 and Leu M1),⁵ and "activation" antigens (Ki-1 and receptors for transferrin and interleukin 2).⁶ These

data suggest that Rosai-Dorfman disease cells are true functionally activated macrophages, which may recently derive from circulating monocytes.¹⁰

Certain histological similarities may exist between Langerhans cell histiocytosis and Rosai-Dorfman disease, but distinguishing features include a lack of emperipolesis in the former, and the presence of pathognomonic Birbeck granules within Langerhans cells upon electron microscopy.¹⁰ The differential diagnosis may rarely also include lymphoma, since certain large B-cell lymphomas have been described to show extensive emperipolesis,¹¹ although immunohistochemistry for CD68 and S100 protein generally aids in this distinction. No ideal treatment exists for this disorder, yet options include medical therapy, i.e. steroids and chemotherapy, radiotherapy or surgery.¹²

Typically, the disease pursues an indolent clinical course. It resolves without any sequelae in approximately 50% of patients. One third of patients show residual, asymptomatic adenopathy, whereas 17% may have persistent symptomatology after 5-10 years.¹²

In our case, the patient was unresponsive to steroids and chemotherapy, and since the patient remained symptomatic, recourse to surgery was undertaken.

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