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CASE REPORT

Soft Tissue Rosai-Dorfman Disease

Case report

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مرض روزاي-دورفمان المعزول في الأنسجة الرخوة

تقرير حالة

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ABSTRACT: Rosai-Dorfman disease (RDD) is a rare benign proliferative histiocytic disorder characterised by massive lymphadenopathy. While extranodal involvement can occur in generalised RDD, isolated soft tissue RDD (STRDD) is extremely rare. We report a 17-year-old male patient who presented to the maxillofacial outpatient department of the Sultan Qaboos Hospital, Salalah, Oman, in 2015 with a painless cheek mass which had been slowly growing over the previous two months. Routine histopathological examinations and immunohistochemistry confirmed a diagnosis of STRDD. Currently, surgical excision is considered to be the most effective curative treatment for STRDD, as the outcomes of other treatment modalities are still unknown. Despite its rarity, STRDD should be considered in the differential diagnosis of histiocytic soft tissue lesions.

Keywords: Histiocytosis; Rosai-Dorfman Disease; Emperipolesis; S100 Proteins; Case Report; Oman.

الملخص: مرض روزاي دورفمان هو مرض نادر حميد ناتج عن تكاثرو اضطراب خلايا الهيستيوسايت ويتميز بوجود عقد لمفاوية ضخمة. وبالرغم من امكانية حدوث مرض روزاي-دورفمان المعمم خارج الغقد الليمفية الا انه من النادر جدا حدوث مرض روزاي-دورفمان المعزول في الأنسجة الرخوة. هذا تقرير حالة عن مريض يبلغ من العمر 17 عاما قدم إلى قسم العيادات الخارجية للوجه والفكين في مستشفى السلطان قابوس، صلالة، عمان، في عام 2015 مع كتلة خديه غير مؤلمة كانت تنمو ببطء خلال الشهرين الماضيين. وأكدت فحوصات الأنسجة المرضية والمناعية الكيميائية تشخيص روزاي-دورفمان المعزول في الأنسجة الرخوة. حاليا، يعتبر الاستئصال الجراحي هو العلاج الأكثر فعالية لهذا المرض حيث أن نتائج اساليب العلاج الأخرى لا تزال غير معروفة. على الرغم من ندرته، ينبغي وضع مرض الروزاي-دورفمان المعزول في الأنسجة الرخوة في التشخيص التفريقي لأمراض الأنسجة الرخوة لخلايا الهيستيوسايت.

الكلمات المفتاحية: أمراض الهيستيوسيتوزيس؛ مرض روزاي-دورفمان؛ اختراق الخلية؛ البروتينات S100؛ تقرير الحالة؛ عمان.

Also known as sinus histiocytosis with massive lymphadenopathy, Rosai-Dorfman disease (RDD) was first described as a unique clinicopathological entity in 1969.[1] Clinically, it is characterised by massive bilateral painless lymphadenopathy of the head and neck region, with affected patients often presenting with fever, leukocytosis, an elevated erythrocyte sedimentation rate and polyclonal hypergammaglobulinaemia.[2] Isolated soft tissue RDD (STRDD) may occur as part of a generalised process involving the lymph nodes or may involve extranodal sites independent of lymph node status.[3,4] The clinical presentation is similar to that of nodal RDD.[5] Nodal-based RDD usually regresses spontaneously, whereas isolated STRDD is indolent in nature and may recur years or even decades later.[6] This report describes a case of isolated STRDD which presented initially as a painless nodular cheek mass. The importance of including this rare entity in the differential diagnosis of histiocytic soft tissue lesions is highlighted.

Case Report

A 17-year-old male patient presented to the maxillofacial outpatient department of the Sultan Qaboos Hospital, Salalah, Oman, in 2015 with a firm painless nodular mass in his right cheek which had been progressively increasing in size over the previous two months. In addition, he had mild *proptosis* of the right eye. There were no significant findings in the patient's medical history or laboratory investigations. On clinical examination, the cheek mass measured 4 cm in diameter and was not associated with any lymph node enlargement. The differential diagnosis was of either a neoplastic or inflammatory soft tissue lesion. An excisional biopsy was performed.

The excised mass was formed of two separate pieces of tissue with a firm whitish cut surface. The larger piece measured 1.7 x 0.8 x 0.3 cm and the smaller one measured 1.5 x 0.7 x 0.4 cm. A microscopic examination revealed fibrocollagenous and adipose

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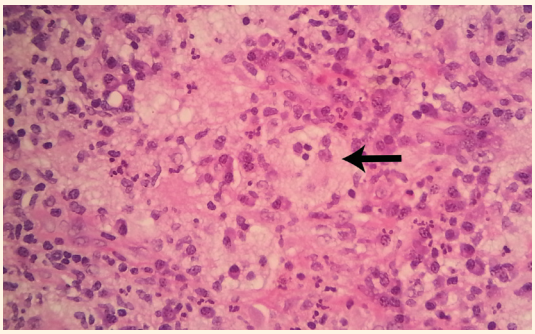

Figure 1: Haematoxylin and eosin stain at x400 magnification showing lymphoid aggregates of mixed inflammatory cells including mature lymphocytes, neutrophils and plasma cells. Note the evidence of emperipolesis as shown by the histiocytes engulfing the intact lymphocytes, neutrophils and plasma cells (arrow).

tissue with nodular infiltration of lymphocytes, plasma cells, eosinophils, neutrophils and foamy histiocytes. Many of the histiocytes showed ingested lymphocytes, plasma cells, eosinophils or neutrophils in the cytoplasm [Figure 1]. No necrosis or mitosis was noted and the histiocytes were immunoreactive to S100 proteins [Figure 2]. As a result, a diagnosis of RDD was made.

The patient was subsequently referred to a tertiary hospital in Oman for further examination and management. Additional immunostaining of the mass revealed that the histiocytes were positive for S100 proteins and cluster of differentiation (CD)68, but negative for CD1a, CD30 and CD15. The plasma cells were polyclonal on both kappa and lambda light chain stains. Moreover, even though a few cells were stained by immunoglobulin G (IgG)4, the IgG4:IgG ratio did not increase. These findings confirmed the diagnosis of extranodal RDD, with a final diagnosis of isolated STRDD. The patient was followed up continuously without any active treatment. Five months later, a computed tomography scan of the right eye showed an enhancing lesion in the posteroinferior and lateral aspect of the right orbit measuring 3 x 2 cm. This lesion was continuous with another mass measuring 3.2 x 3.4 cm in the right infratemporal *fossa*, with obliteration of the fat planes. The optic nerve and extraocular muscles were in contact with the mass, but the globe was still intact. Clinically, this lesion was considered to be of the same disease as the cheek lesion and no specific treatment or biopsy was attempted. After two years of follow-up, there was no evidence of disease progression in either lesion.

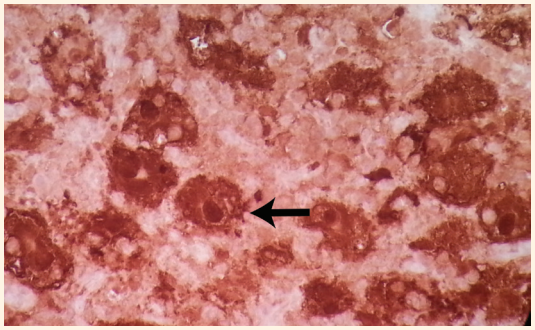

Figure 2: Immunohistochemistry stain at x400 magnification showing the S100 protein positivity of large histiocytes (arrow).

Discussion

While RDD has been reported worldwide, it is more common among patients of African descent.[7] Up to 80% of cases occur among individuals in the first two decades of life, although other age groups can also be affected; in addition, RDD tends to occur more frequently among males.[7,8] In the largest known study of RDD, 43% of 423 patients had associated extranodal disease along with lymphadenopathy; in comparison, only 3% of patients had no detectable lymphadenopathy.[2] The skin and the paranasal sinuses are the most common sites for extranodal involvement.[9]

In an extensive review of the literature, Komaragiri *et al*. identified only 36 STRDD cases reported between 1969 and 2012.[10] The current report adds an additional case to the existing literature concerning this rare entity. Two large case series of STRDD have been reported from the USA; the first described 17 cases of STRDD, of which four presented with lymphadenopathy, whereas the second found that only one of 18 patients with STRDD had associated lymph node involvement from a single node.[5,11] In both series, STRDD was more common in the trunk and proximal extremities and tended to grow rapidly, although the actual size of the lesion varied. The age of the affected patients also ranged widely and there was a slight female predominance.[5,11] Multifocal STRDD is extremely uncommon but recurs more frequently than a solitary lesion.[11,12] The rate of recurrence of STRDD after excision has been reported to range from 21.4–54%.[5,11]

Immunohistochemistry is key to differentiating soft tissue lesions in order to determine the correct diagnosis. Morphologically, STRDD is similar to nodal RDD in exhibiting the diffuse subcutaneous infiltration of large polygonal histiocytes, which in turn demonstrate emperipolesis predominantly of lymphocytes, although sometimes plasma cells, erythrocytes and neutrophils are also affected.[5] Infiltration of lymphocytes, plasma cells and neutrophils may also occur, along with the histiocytes. However, mitosis and necrosis are rare.[5] While some researchers have

reported frequent spindling of the histiocytes, others have claimed this is uncommon.[5,11] In cases with histiocyte spindling, STRDD may be confused with a sarcoma.[10] In terms of immunohistochemistry, RDD histiocytes are consistently positive for S100 proteins and CD68 and negative for CD1a.[13] The microscopic appearance of an inflammatory pseudotumour can resemble STRDD; however, the histiocytes of inflammatory pseudotumours are negative for S100. These lesions may reflect a histological continuum.[14] Another differential diagnosis of STRDD is Langerhans cell histiocytosis, in which the histiocytes are positive for both S100 proteins and CD1a.[15]

The histogenesis of RDD is still unclear, but may be the result of an aberrant immunoresponse.[7] The disease has also been associated with lymphoproliferative disorders.[2] In cases of Hodgkin's lymphoma, certain cytokines have been found to alter the morphology of histiocytes to that seen in RDD.[16] A relationship between polyomavirus infections and intra-abdominal STRDD has also been postulated.[11] Due to its rarity, there is as yet no definitive treatment strategy for patients with STRDD; however, surgical excision has been proven effective in preventing disease recurrence.[10] Further studies are required to establish evidence-based treatment strategies for this disease and to increase our understanding of its outcomes and natural history.

Conclusion

STRDD is a very rare benign proliferative histiocytic disorder. Morphologically, it may mimic an inflammatory pseudotumour, sarcoma or Langerhans cell histiocytosis. As such, it is important that STRDD be considered in the differential diagnosis of histiocytic soft tissue lesions.

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