A 55-year-old Malay woman presented with widespread, asymptomatic skin lesions of 4 years duration. She reported recurrent nasal blockage since 2005 requiring surgical excisions for nasal masses. There was associated lethargy without other constitutional symptoms. Physical examination revealed pallor, multiple indurated violaceous plaques and nodules over the bilateral upper and lower limbs, trunk, and back [Figure 1a-c]. There was no lymphadenopathy or hepatosplenomegaly.

Laboratory indices confirmed anemia with reticulocytosis (5.69%) and a positive indirect Coombs test. Computed tomography scan revealed right paratracheal lymphadenopathy measuring 4.9 cm × 4.5 cm × 6.5 cm. A punch biopsy was taken from one of the skin lesions.

Histopathological examination revealed dense, diffuse dermal infiltrates of foamy histiocytes, some multinucleated, admixed with abundant lymphocytes, plasma cells, and some neutrophils [Figure 2]. Russell bodies were occasionally sighted in the plasma cells. Emperipolesis was also noted [Figure 3]. Foamy cells were positive for CD68 and S-100 while negative for CD1a [Figure 4].

Question

What is your diagnosis?
Diagnosis – Rosai–Dorfman disease (RDD) with cutaneous and nasal involvement, in the context of warm autoimmune hemolytic anemia.

Discussion

RDD, also known as sinus histiocytosis with massive lymphadenopathy, is a rare pseudolymphomatous disorder, classified under non-Langerhans cell histiocytosis. First described by Rosai and Dorfman in 1969, this condition typically affects children and young adults although it can occur in older patients.\(^1,2\)

Painless lymphadenopathy is the main clinical manifestation of RDD.\(^2,3\) The cervical region is the most commonly affected nodal site, followed by axillary, inguinal, para-aortic, and mediastinal lymph nodes.\(^1\) Extranodal manifestation is observed in 43% of cases, with skin being the most common site.\(^3\) Clinical morphology of cutaneous lesions is nonspecific, ranging from papules, patches, plaques, nodules to pustules, depending on the duration and depth of lesions.\(^4\) These lesions are commonly erythematous although it could be hyperpigmented (dark red) or yellowish.\(^4\) Patients may also have systemic symptoms (fever, malaise, weight loss), hematological abnormalities (normochromic anemia, raised erythrocyte sedimentation rate, leukocytosis), and immunological abnormalities (hyperglobulinemia).\(^1,3\)

Histopathological tissue examination is useful in procuring a diagnosis of RDD. Findings include proliferation of histiocytes with abundant pale cytoplasm, lymphoplasmacytic infiltration, and absence of cellular atypia.\(^2,4,5\) Emperipolesis is the phenomenon in which hematological cells (commonly lymphocytes) exist within the cytoplasm of histiocytes.\(^2\) Although this phenomenon is an important feature of RDD, it is nonspecific and may be observed in other hematological conditions such as myeloproliferative disorders. RDD lesions are also characteristically S-100 and CD68 positive while CD1a negative.\(^2\)

RDD runs a benign and self-resolving course. Multi-organ involvement and associated immune dysfunction are poor prognostic factors and indicate the need for treatment.\(^5\) There is currently no standard effective treatment due to the lack of clinical trials. Various treatment modalities with variable results have been reported in the literature, including corticosteroids, thalidomide, interferon, radiotherapy, chemotherapy, and surgery.\(^3,4\)

Learning points

- RDD is a rare pseudolymphomatous disorder clinically characterized by bilateral painless cervical lymphadenopathy and fever
- Although the skin is the most common site of extranodal involvement, clinical morphology of cutaneous RDD is generally nonspecific
- Histopathology is important in procuring a diagnosis of RDD, especially in the absence of overt lymphadenopathy
• Although emperipolesis is an important feature of RDD, it is nonspecific and may be observed in other hematological conditions such as myeloproliferative disorders
• This condition may be associated with other immunological conditions such as autoimmune hemolytic anemia (as in our patient), rheumatoid arthritis, and glomerulonephritis.

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Conflicts of interest
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