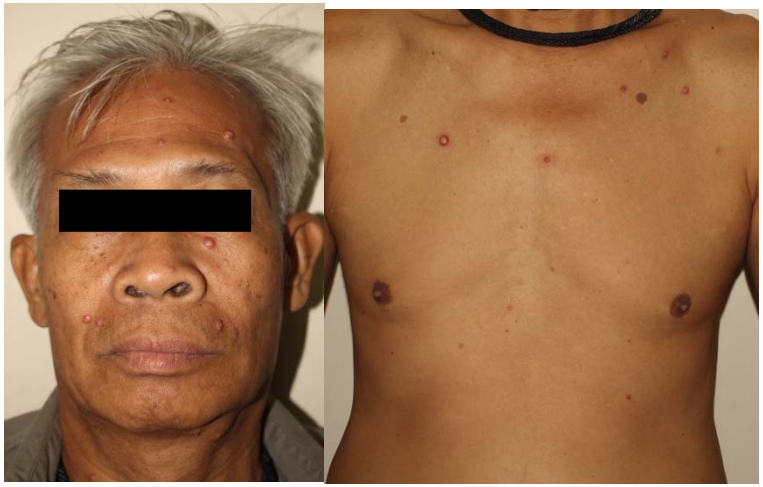
**Case 9.1**
A 63 year-old Thai male from Ayutthaya

**Chief complaint**: multiple discrete erythematous and yellowish papules on face, trunk and both arms for 3 months



(Fig.9.1.1)

**Present illness**: The patient developed asymptomatic erythematous and yellowish papules starting on face and spreading to both arms, chest and back for 3 months. Two months ago he had painless bilateral cervical nodules, fatigue and low grade fever. He denied any history of contact with tuberculosis or leprosy patient.

**Past history:** He was otherwise in good health and never had similar rash before

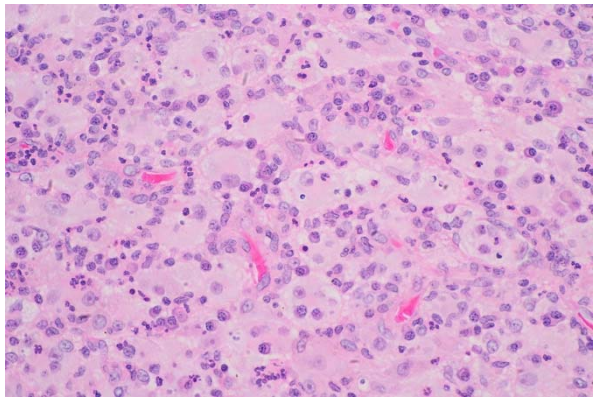
**Underlying disease:** Type 2 diabetes mellitus, dyslipidemia

**Family history:** No family history of similar cutaneous lesions

**Dermatological examination**: Multiple discrete erythematous and yellowish dome shape papules on face, chest, back, and both arms

**Physical examination:**
LN: bilateral, non-tender cervical lymphadenopathies varying in size 1-2 cm in diameter
Other systemic examination revealed no abnormality.

**Histopathology:** (S17-22951, Chest) (Fig. 9.1.2)

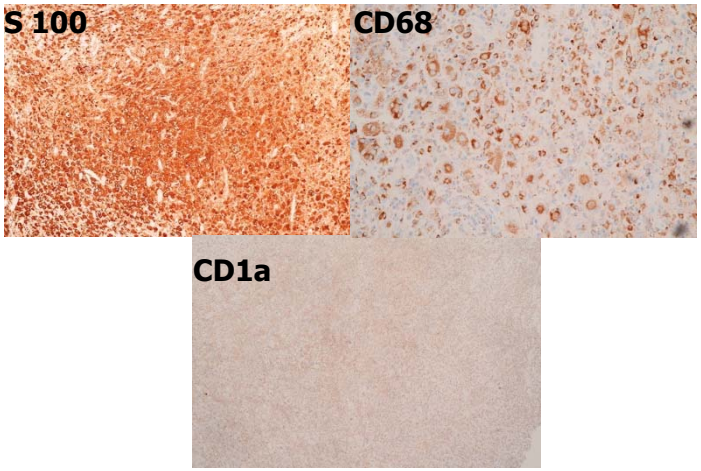


(Fig.9.1.2)

- Diffuse inflammatory cell infiltrate composed of macrophages with large pale cytoplasm
- A variable number of inflammatory cells including lymphocytes,

neutrophils, eosinophils and plasma cells are present
- Some macrophages ingest lymphocytes, demonstrating emperipolesis

**Immunohistochemistry:**




- Positive CD68, S100 staining
- Negative CD1a staining

**Laboratory investigations:**
- CBC: Hct 34.1%, WBC 12,610 cells/µL (N 59%, L 28%, Mono 8%, Eo 4, Baso 1%), Platelets 333,000 cells/µL
- LFT: AST 28 U/L, ALT 22 U/L, ALP 58 U/L, GGT 46 U/L, TP 88.4 g/L, Alb 29.2 g/L, TB 0.5 mg/dL, DB 0.2 mg/dL
- BUN/Cr: 10/0.76 mg/dL
- LDH: 125 U/L (normal)
- Serum Kappa: 84.5 mg/L (3.3-19.4)
- Serum Lambda: 48.4 mg/L (5.71-26.3)
- Kappa/lambda: 1.746
- Albumin/globulin ratio: 0.73
- Immunofixation: No paraprotein detected
- IgA, IgG, IgM: Normal level
- Anti-HIV: Negative, Hepatitis profile: Negative all

**CT neck, chest and abdomen with contrast:**
- Fixed irregular tracheal wall thickening, no tracheobronchial obstruction
- Multiple tiny pulmonary nodules at both lungs, nature may follow by tracheobronchial lesions
- Multiple cervical, axillary and intraabdominal lymphadenopathies: hepatic, perigastric, mesenteric, both groins
- Multiple osteolytic bony destruction at both ischium, pubic bones, Rt. femoral head, both ilium, manubrium, Lt. clavicular head, Rt. scapula, both ribs, and multivertebral levels

**Bronchial nodule biopsy**: Consistent with Rosai-Dorfman disease

**Diagnosis:** Rosai-Dorfman disease

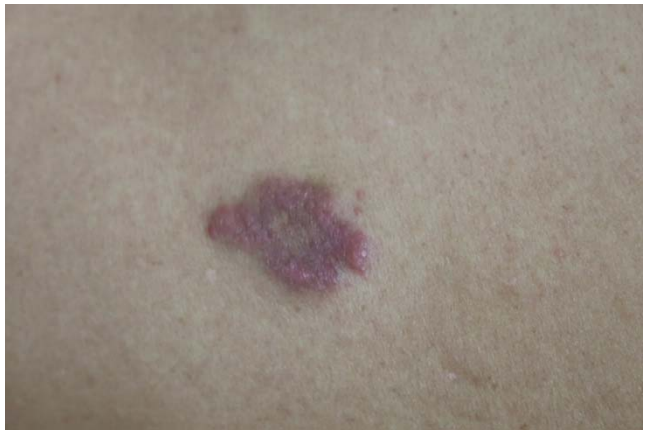
**Treatment:** Oral prednisolone 0.5 mg/kg/day

**Presenter:** Jutamas Tankunakorn, MD

**Consultant:** Silada Kanokrangsri, MD

**Case 9.2**
A 55 year-old Thai male from Bangkok

**Chief complaint**: solitary progressive painless erythematous to violaceous papules confluent to form plaque on back for 2 years


(Fig. 9.2.1)

**Present illness:** The patient developed asymptomatic progressive erythematous to violaceous papules confluent to form plaque on back for 2 years. No prior history of ulcers before. He denied history of fever, weight loss or previous trauma.

**Past history:** He was otherwise in good health and never had similar rash before

**Underlying disease:** Adenocarcinoma of lung stage I status post Rt. Lobectomy

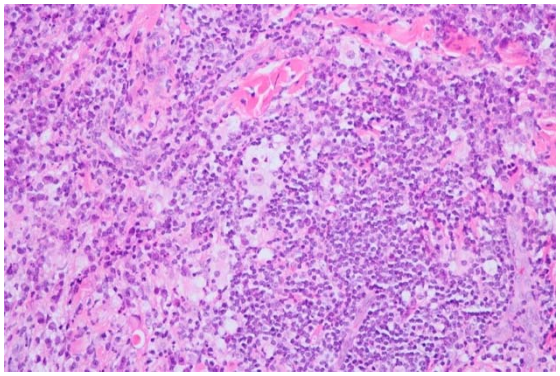
**Family history:** There was no family history of similar cutaneous lesions

**Dermatological examination:** (Fig. 9.2.1)
Solitary well-defined, non-tender, erythematous to violaceous papules confluent to form plaque about 3 cm in diameter on back

**Physical examination:** Other systemic examination revealed no abnormality.

**Laboratory investigations:**
- CBC: Hct 41.6%, WBC 7,240 cells/µL (N 72%, L 20%, Mono 7%, Eo 1%, Baso 0%), Platelets 340,000 cells/µL
- BUN/Cr: 7/0.96 mg/dL
- Immunology: Alpha1, 2, beta, gamma globulin: normal

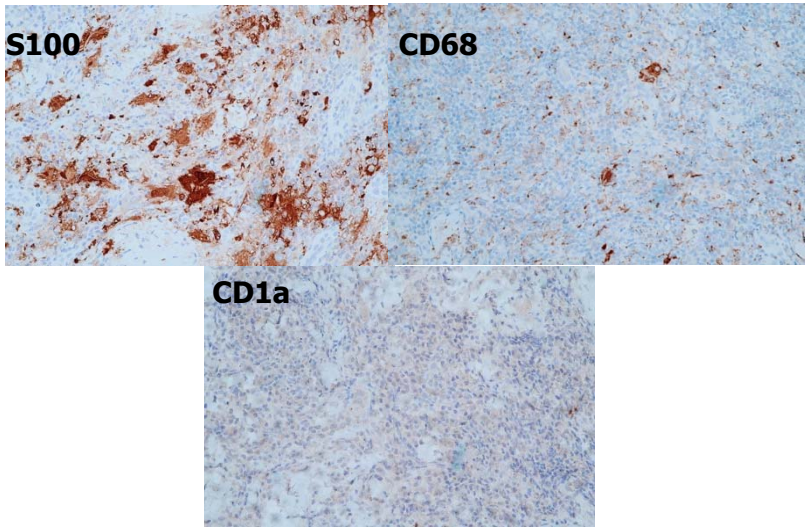
**Histopathology:** (S17-25166, Back) (Fig. 9.2.2)


(Fig. 9.2.2)

- Diffuse inflammatory cells infiltrate composed of mainly lymphocytes admixed with some large macrophage with pale abundant cytoplasm.

- A variable number of inflammatory cells including lymphocytes, neutrophils, eosinophils, and plasma cells are present.
- Some macrophages ingest lymphocytes, demonstrating emperipolesis.

**Immunohistochemistry:**




- Positive CD68, S100 staining
- Negative CD1a staining

**Diagnosis:** Cutaneous Rosai-Dorfman disease

**Treatment:** *Surgical excision*

**Presenter:** Jutamas Tankunakorn, MD

**Consultant:** Silada Kanokrangsri, MD

**Discussion:**

Rosai-Dorfman disease (RDD), also known as sinus histiocytosis with massive lymphadenopathy, is a rare self-limited and benign disease described by Rosai and Dorfman[1] just over 40 years ago. Children, adolescents, and young adults are more frequently affected by this disorder, but it may also occur in older adults.[2, 3]

The etiology of the disease is unknown but several theories have been suggested. Some infectious agents have been suspected, including Epstein-Barr virus[4], Parvovirus B19[5], Herpes virus type 6 and 8 and Polyomavirus.[6] Other proposed mechanisms include immune dysfunction or an aberrant exaggerated immune response to an infectious agent or an antigen that causes a proliferation of histiocytes.

The most common presentation is bilateral painless massive cervical lymphadenopathy associated with fever, night sweats, fatigue, and weight loss while other lymph node sites, such as the axillary, inguinal, and mediastinal lymph nodes, may also be involved.[7]

Although originally described as a nodal disorder, extranodal involvement by sporadic RDD has been documented in 43% of cases with the most frequent sites being skin (10%), nasal cavity, bone, soft tissue, and retroorbital tissue. Bone RDD may be responsible for isolated lytic lesions, or associated with other localization and most lesions are attached to the dura.[8]

The first our patient presents as typical case of Rosai-Dorfman disease with multiple lymphadenopathy. He also had bone involvement that CT show multiple osteolytic bony destruction.

More rarely, cutaneous lesions are the sole manifestation, with purely cutaneous-RDD (CRDD) representing a small minority (3%) of RDD described cases. Such as in our second patient he had only limited cutaneous lesions, no systemic involvement. CRDD is considered a distinct entity, based on the exclusive involvement of the skin, different demographic features and better prognosis, compared with systemic RDD.[9]

In reported cases of CRDD, patients with CRDD are 45 years older compared with patients who have RDD.[10] Women with CRDD appear to be more affected than men, and most cases have been seen among Caucasian and Asian populations. In CRDD, patients typically present with normal laboratory data and no adenopathy. Lesions in CRDD can vary, ranging from less than 1 cm to 30 cm or more at their greatest dimensions. Multiple lesions are generally present and are typically red-brown papules or nodules. Rarely, patients can develop extensive confluent infiltrates. The most common site of skin involvement is the trunk followed by the head and neck region[10], like in our patient that lesion developed on back.

As the cutaneous lesions are clinically nonspecific, the diagnosis of CRDD is histological, and essentially relying on the presence of an infiltrate containing large pale histiocytes, commonly displaying emperipolesis, accompanied by lymphocytes and abundant plasma cells. In the setting of no lymphadenopathy, the histopathological features of RDD are commonly misinterpreted, and it is important to consider that histological features vary in correlation with the cutaneous lesions duration.[11]

The classical histology of Rosai-Dorfman disease is characterized by distorted nodular architecture with marked dilation of lymphatic sinuses, partial effacement of follicles and germinal centers, as well as capsular and pericapsular fibrosis.[7] Lymphatic sinuses are occupied by numerous lymphocytes and histiocytes with vesicular nucleus and abundant clear cytoplasm with phagocytized lymphocytes or plasma cells, also known as 'emperipolesis'.[1]

Immunohistochemically, histiocytes react positively to S-100 protein, CD68 but negatively to CD1a and HLA-DR antigens.[12]

The workup of patients with suspected RDD is similar to that of lymphoma. A detailed history and physical examination should be performed to exclude other causes of the adenopathy. It is worth nothing that hepatosplenomegaly is rare in RDD, while it is commonly seen in other histiocytic disorders.[3,5] Staging should include contrast computed tomography (CT) scans of the neck, chest, abdomen, and pelvis to look for distant disease. The role of bone marrow biopsy is unclear but is usually obtained because primary bone marrow disorders are included in the differential diagnosis of RDD. Laboratory findings include anemia, leukocytosis with neutrophilia, an elevated erythrocyte sedimentation rate, and hypergammaglobulinemia. A reversal in peripheral CD4:CD8 ratio has also been observed.[13] Imaging manifestations of RDD are also nonspecific, but FDG-PET/CT can be used to evaluate the exact extent of dissemination.[14]

Typically, most RDD patients can achieve spontaneous remission after a protracted clinical course.[13] However, a widely disseminated nodal disease and involvement of vital organs, such as the kidney, lower respiratory tract, and liver, can lead to an aggressive, fatal course. Additionally, immune dysfunction, either preceding or following the onset of RDD, usually indicates a poor prognosis, sometimes even a fatal outcome. While CRDD has a benign course and is self-limiting, although patients may experience local relapse or persistent disease. For patients requiring treatment, surgery is an appropriate option for disease that can be excised, including single nodal areas, primary CNS involvement, or localized primary CRDD. Remissions with surgery alone have been reported in CNS-only disease.[15]

Our first patients with RDD requires systemic treatment, systemic steroids are first-line therapeutic option that produces responses in both classical RDD and extranodal disease. However, the reliability and durability of these responses is unpredictable. Radiation can be used as a palliative option for symptomatic disease. For patients with CRDD, therapy is not typically required; however, surgical excision remains the most effective option for treating solitary or small numbers of lesions like in our patient. Radiotherapy, cryotherapy, topical chemotherapy, and topical isotretinoin have also been used but with varying success.[10]

## References: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