

# FDG PET/CT in the Evaluation of a Rare Case of Multisystem Involvement in Newly Diagnosed Rosai–Dorfman–Destombes Disease

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## Abstract

Rosai–Dorfman–Destombes disease (RDD) is a rare histiocytic disorder with a broad spectrum of clinical presentations. The disease typically presents with lymphadenopathy but may involve multiple systems. Usually, RDD lesions demonstrate intense <sup>18</sup>F-Fluorodeoxyglucose (FDG) uptake in positron emission tomography/computed tomography (PET/CT) imaging due to the inflammation and infiltration with high metabolic process of the disease. Here, we describe a rare case of 37-year-old man who presented with multiple systemic symptoms, including fever, weight loss and bilateral cervical, and inguinal lymphadenopathy who underwent FDG PET/CT for detection of disease extension. This case highlights the role of FDG PET/CT in establishing the disease extent in newly diagnosed RDD and guiding the therapeutic recommendations and for follow-up to monitor the disease response to therapy. To the best of our knowledge, this is the first case report from Saudi Arabia highlighting the role of FDG PET/CT in newly diagnosed RDD.

**Keywords:** FDG PET/CT, histiocytes disorders, Rosai–Dorfman–Destombes disease, lymphadenopathy, lymphoma, lymphoma

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## INTRODUCTION

Rosai-Dorfman-Destombes disease (RDD) is a rare non-Langerhans cell histiocytosis characterized by activated histiocytes within affected tissues.<sup>[1,2]</sup> In general, histiocytic neoplasms are rare neoplasms originating from cells with a myeloid lineage and include Erdheim–Chester disease (ECD), Langerhans cell histiocytosis (LCH) and RDD.<sup>[3]</sup> Historically, RDD is known as a self-limited disease, although few patients have poor outcomes.<sup>[4]</sup> RDD is a rare disease with a prevalence of 1:200,000, the disease is more frequent in children and young adults and more common in

male and individuals of African descent.<sup>[5,6]</sup> The etiology of RDD is not well proven. Studies have associated RDD with viral infection such as herpes viruses and Epstein-Barr virus, cytomegalovirus (CMV) and human immune deficiency virus (HIV), although a clear link is not yet established.<sup>[7]</sup>

Most patients with RDD present with bilateral, massive and painless cervical lymphadenopathy with or without fever, and the prognosis has been found to correlate with the number of nodal groups involved by RDD.<sup>[4]</sup> All

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patients with suspected RDD warrant baseline peripheral blood smear analysis and various imaging modalities to determine the extent of the disease. RDD lesions are typically F-Fluorodeoxyglucose (FDG) avid. FDG positron emission tomography/computed tomography (PET/CT) offers whole-body imaging from the vertex to the toes and this case highlights the role of FDG PET/CT in the detection and management of RDD.

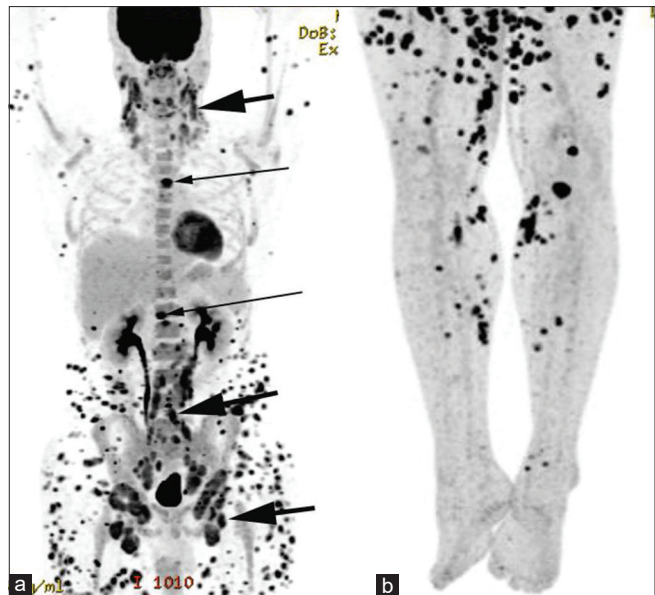
## CASE PRESENTATION

A 37-year-old male patient presented with a 5-month history of an on-and-off fever, weight loss, night sweats, facial rash, subcutaneous nodules, bilateral cervical and inguinal lymphadenopathy. He had no significant past medical history or any other genetic disease.

On physical examination, he had normal vital signs. A skin examination revealed multiple well-demarcated erythematous-inflamed papules and scattered pustules on his face, including the nasolabial folds. In addition, there were numerous subcutaneous non-tender nodules located mainly on the upper back and upper extremities. There was also extensive bilateral, non-tender, mobile, 3 × 3 cm cervical, including internal jugular and posterior compartment chains, and inguinal lymphadenopathy. The chest, cardiac and abdominal examinations were normal, with a normal liver and spleen. The musculoskeletal examination revealed normal joints without tenderness, swelling or a range of motion limitations.

The laboratory tests showed normal hemoglobin level and leukocytosis, white blood cells count of 15,860 cells/mcL (normal 8,600–11,000 cells/mcL) and normal chemistry. C-reactive protein was 122 mg/L. The results of human immunodeficiency virus (HIV) screening, Epstein–Barr virus (EBV) serology and the serological diagnosis of cystic echinococcosis (CE) were negative.

Interferon-gamma assays (IGRAs) for mycobacterium tuberculosis were negative. CT of the neck, chest, abdomen and pelvis revealed extensive cervical lymphadenopathy (largest: 2 cm × 2 cm), no significant mediastinal or hilar adenopathy, extensive abdominal, retroperitoneal, pelvic and inguinal lymphadenopathy (up to 3 cm × 2 cm), with innumerable subcutaneous nodules. Subsequently, <sup>18</sup>F-FDG PET/CT was performed, which revealed intense FDG-avid lymphadenopathy corresponding to the lymphadenopathy noted on CT, innumerable intense FDG-avid subcutaneous nodules, and there were multiple hypermetabolic lesions in the thoracolumbar spine [Figures 1 and 2]. Bone marrow

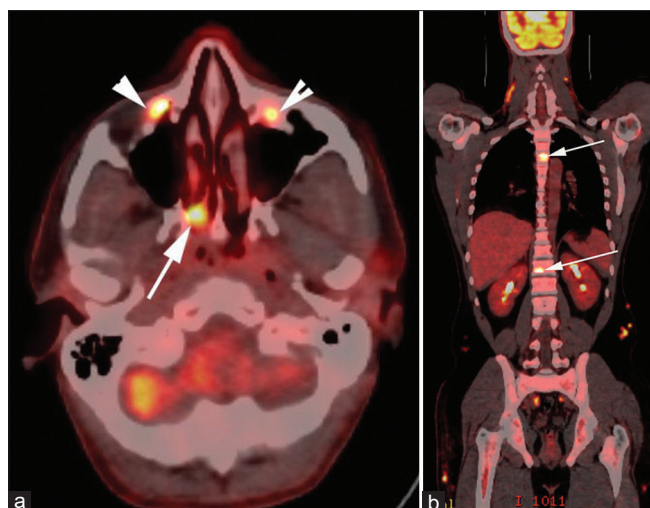


**Figure 1:** (a) Whole body maximum intensity projection positron emission tomography Image A (from the skull to the mid-thigh) revealed extensive soft tissue disease involving multiple nodal stations including; cervical, retroperitoneal, and inguinal regions (thick black arrows) and upper and lower thoracic spine bone lesions (thin black arrows). Extensive intensely fluorodeoxyglucose-avid subcutaneous nodules were also noted all over the body. (b) Whole body Maximum Intensity Projection positron emission tomography image (from the mid-thigh to the foot) revealed extensive soft tissue intensely fluorodeoxyglucose-avid subcutaneous nodules

aspirate showed cellular marrow with extensive trilineage hematopoiesis consistent with reactive changes. The excisional right cervical lymph node biopsy showed reactive lymphoid hyperplasia, with preservation of the lymph node architecture with positive large histiocytes, which was consistent with RDD [Figure 3a and b]. The immunohistochemical staining was positive for S100 and CD68 (KP-1), and negatively stained with CD1a. The patient was started on high-dose oral prednisone and a topical mometasone cream for his systemic symptoms and facial rash, respectively. At the 4-week follow-up visit, the patient reported no fever or other symptoms, a decreased number of subcutaneous nodules and a mild improvement of the facial rash. He was referred for hematology service for follow up and reevaluation. At the time of reporting this case, his medications included 60 mg prednisone and topical mometasone. The follow-up FDG PET/CT demonstrated complete metabolic resolution of abnormal FDG avid tissue and documented complete disease remission. He was off therapy for 5 months with continued observation and regular outpatient follow up.

## DISCUSSION

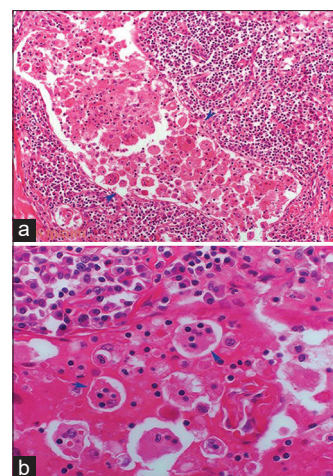
Most patients with RDD present with bilateral painless cervical lymphadenopathy with fever, night sweats and



**Figure 2:** Selected fused fluorodeoxyglucose positron emission tomography/computed tomography image (at the level of the nasal sinus) shows multiple Fluorodeoxyglucose-avid soft tissue lesions in the bilateral anterior maxillary sinus wall (arrow heads) and right posterior nasal cavity extending to the sphenoid foramen (arrow). (b) Selected fused coronal fluorodeoxyglucose positron emission tomography/computed tomography image demonstrates upper and lower thoracic spine lesions (arrows). Again, multiple Fluorodeoxyglucose-avid subcutaneous nodules and cervical lymphadenopathy were noted

weight loss. Multiple lymph node groups, such as the mediastinal, axillary, inguinal and retroperitoneal nodes, are involved. Extranodal RDD has been reported in 43% of cases, and multisystem involvement occurs in 19% of cases. Prognosis is controlled based on the number of extranodal involvements. Cutaneous manifestations occur in 10% of extranodal RDD patients, and isolated skin lesions are rare. These lesions are typically painless nonpruritic nodules and plaques.<sup>[8]</sup> Involvement of the central nervous system (CNS) occurs in less than 5% of cases, and its symptoms include headache, seizure, gait difficulty and cranial nerve deficits.<sup>[9]</sup> Only 2% of RDD patients develop intrathoracic symptoms such as interstitial lung disease (ILD) and pulmonary nodules that may mimic primary lung cancer, sarcoidosis and rheumatoid arthritis-related lung disease.<sup>[10]</sup> Gastrointestinal involvement is rare and reported in less than 1% of RDD cases.

RDD can be solitary or segmental and mostly affects the ileocecal area, appendix and colon.<sup>[11]</sup> Bone manifestations occur in 5%–10% of RDD cases. The paranasal sinuses are the most common extranodal site of involvement after skin, patients often present with nasal obstruction, epistaxis or anosmia.<sup>[12]</sup> Bone lesions typically occur in the metaphysis and the diaphysis, and can take the form of osteolytic or mixed lytic/osteolytic lesions. The main differential diagnoses of bone lesions in RDD are osteomyelitis, fibrous dysplasia and lymphoma.<sup>[12]</sup>



**Figure 3:** (a) Low power view showing expansion of lymph node sinuses (between 2 arrowheads) by large pale pink histiocytic cells with emperipolesis. H and E  $\times 200$ . (b) High power view depicting the emperipolesis (phagocytosis of lymphocytes and plasma cells) by large histiocytes, indicated by arrow heads H and E  $\times 500$

The diagnostic evaluation of newly diagnosed RDD in adult patients includes CT of the neck, chest, abdomen and pelvis is recommended. RDD lesions are known to be FDG avid, including in extranodal disease.<sup>[13]</sup> The differential diagnoses of clinical disorders mimicking RDD on FDG PET/CT are numerous and include intermediate and high-grade lymphoma, infections like HIV, inflammation such as granulomatous disease, autoimmune diseases such as systemic lupus erythematosus, as well as other benign lymphoproliferative diseases.

The FDG avidity of RDD lesions is attributable to the intense glucose dependence of the proliferating histiocytes and other infiltrating inflammatory cells. FDG PET/CT offers an accurate evaluation of increased glucose metabolism and contributes to understanding the disease extent. In one study, FDG PET/CT was used for the accurate initial evaluation of the disease and included an assessment of the nodal and extranodal extent of the disease. Furthermore, PET/CT may be used to assess the disease response to therapy and the disease progression.<sup>[14]</sup> Recently, some studies have suggested that PET/magnetic resonance imaging (PET/MRI) could provide comparable results to PET/CT for detecting metabolically active disease and monitoring in the pediatric population to ensure radiation-dose saving.<sup>[15]</sup> The FDG PET/CT performed on our patient demonstrated more accurately the extent of the disease and showed several new unexpected lesions in the subcutaneous tissue, especially in the thighs and lower legs, multiple bone lesions in the thoracolumbar spine and multiple paranasal sinus lesions. A 6-month follow-up FDG PET/CT documented a complete response to therapy with no identified FDG lesions, highlighting the importance of



FDG PET/CT imaging in the accurate detection of the disease extent initially and monitored response to therapy.

## CONCLUSION

This case demonstrates the role of FDG PET/CT imaging in the accurate evaluation of multisystem involvement in RDD. In addition, FDG PET/CT may be used to assess the disease progression and determine the response to therapy. In imaging of patients with suspected RDD, FDG PET/CT is considered the modality of choice.

## Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent forms. In the form, the patient has given his consent for his images and other clinical information to be reported in the Journal. The patient understands that his name and initials will not be published, and due efforts will be made to conceal his identity, but anonymity cannot be guaranteed.

## Peer review

This article was peer reviewed by two independent and anonymous reviewers.

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## Conflicts of interest

There are no conflicts of interest.

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