

## Case Report

# Extranodal Rosai-Dorfman-Destombes disease mimicking renal cell carcinoma: a case report and review of literature

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## ABSTRACT

Rosai-Dorfman-Destombes disease (RDD) is an uncommon histiocytic disorder of unknown aetiology. Extranodal involvement occurs in a significant proportion of patients but involvement of the kidney is rare. Here we present a case report of extranodal RDD of the kidney. Imaging revealed a heterogeneously enhancing solid mass lesion in left renal hilum infiltrating renal medulla and deeper layers of renal cortex. With the clinical diagnosis of suspected left renal cell cancer, laparoscopic left radical nephrectomy was performed. Macroscopic examination showed specimen covered with Gerota's fascia and perinephric pad of fat. Renal capsule could be easily split off. On cut section, ill circumscribed solid lesion having variegated appearance with areas of necrosis and haemorrhage, involving middle and lower pole, was noted. Renal sinus appeared to be involved. Microscopic examination showed sheets of histiocytes with abundant eosinophilic to vacuolated cytoplasm. There was emperipolesis of intact lymphocytes. Also, seen were sheets of plasma cells, lymphocytes with intervening dense hyalinised stroma. Retro peritoneal lymph nodes and para-aortic lymph nodes also showed similar histological picture. Immunohistochemistry showed that the histiocytes were positive for S100 and CD68. IgG4-positive plasma cells were not seen. These findings showed that the lesion represented and extranodal RDD of the kidney. Although rare, extranodal RDD should also be included in the differential diagnosis of a renal mass and frozen section be advised whenever feasible.

**Keywords:** Rosai-Dorfman, Histiocytic disorders, Non-Langerhans cell histiocytoses, Lymphadenopathy, Extranodal, Renal mass, Rare

## INTRODUCTION

Non-Langerhans cell histiocytoses (non-LCH), are a diverse group of uncommon histiocytic disorders, characterised by the accumulation of histiocytes, but do not meet the criteria for the diagnosis of Langerhans cell histiocytoses (LCH).<sup>1</sup> RDD is a rare non-LCH first described in 1965 by a French pathologist, Pierre Paul Louis Lucien Destombes, who reported 4 cases with the presence of lymphadenopathy and sinus histiocytosis upon histologic analysis.<sup>2</sup> Four years later in 1969, Juan Rosai and Ronald Dorfman analysed 34 cases of the same entity under the name sinus histiocytosis with massive lymphadenopathy.<sup>3</sup> Characteristic lesional histiocytes are

S100 and CD68 positive with negative CD1a and demonstrate emperipolesis in varying frequency.<sup>4</sup> Historically, RDD has been considered self-limited disorder of unknown aetiology, although few patients have poor outcomes. Patients with classical RDD present with bilateral cervical lymphadenopathy, but 43% of with RDD present with extranodal disease.<sup>4</sup> Less than 5% of patients with RDD have renal involvement, whereas isolated localization of RDD as a renal mass is very rare.<sup>5</sup>

## CASE REPORT

A 63-year-old man presented, to urology outpatient clinic at our hospital, with left flank pain associated with fever

and nausea. He had no other complaints, no known comorbidities, no significant past history and no prior surgeries. On clinical examination mild left renal angle tenderness was present, no other local or systemic findings were appreciable. All relevant haematological and urine investigations were normal except rise in ESR (94 mm/hr). Contrast CT of abdomen showed heterogeneously enhancing solid mass lesion measuring 6×7×9.8 cm in left renal hilum, infiltrating renal medulla and deeper layers of renal cortex. Branches of renal artery and tributaries of renal vein were seen coursing through the lesion without obstruction. Few enlarged retroperitoneal lymph nodes in para-aortic region were noted (Figure 1). Laparoscopy showed left renal mass with hilar and left para-aortic lymph node involvement. Single renal vein and artery were noted. Patient underwent laparoscopic left radical nephrectomy along with removal of proximal ureter and para-aortic lymph nodes. The patient had uneventful recovery.

### Pathological examination

The left radical nephrectomy specimen was measuring 15×11×8 cm with ureter measuring 8 cm. Gerota's fascia and perinephric pad of fat were noted. Renal capsule was easily split off. Cut section showed ill circumscribed solid lesion, having variegated appearance, with areas of necrosis and haemorrhage, involving middle and lower pole, measuring 7×6 cm (Figure 2). Renal sinus appeared to be involved. Left para-aortic lymph node was measuring 5×4×3 cm. Histopathological examination revealed lesion composed of sheets of histiocytes with abundant eosinophilic to vacuolated cytoplasm. Many of them showed emperipolesis of intact lymphocytes. Also, seen were sheets of plasma cells, lymphocytes with intervening dense hyalinised stroma (Figure 3 and 4). Renal hilar and para-aortic lymph nodes also showed similar histological picture. Renal vessels and ureteric resected margin were normal and uninvolved. No evidence of malignancy was seen. Immunohistochemistry showed that the histiocytes were positive for S100 (Figure 5) and CD68 (Figure 6), but negative for CD1a and IgG4. Final diagnosis of the lesion was extra-nodal RDD of the kidney.

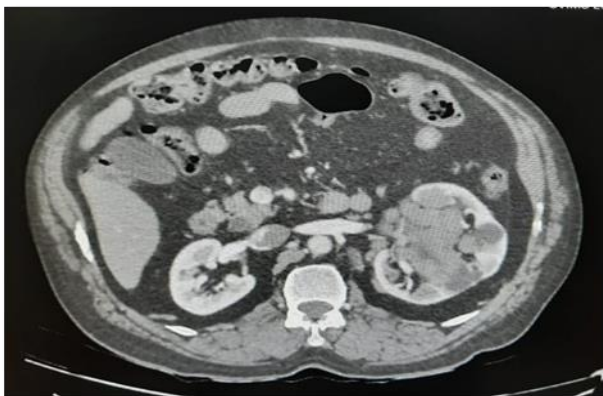


Figure 1: CECT abdomen-axial cut.



Figure 2: Left radical nephrectomy specimen cut section.

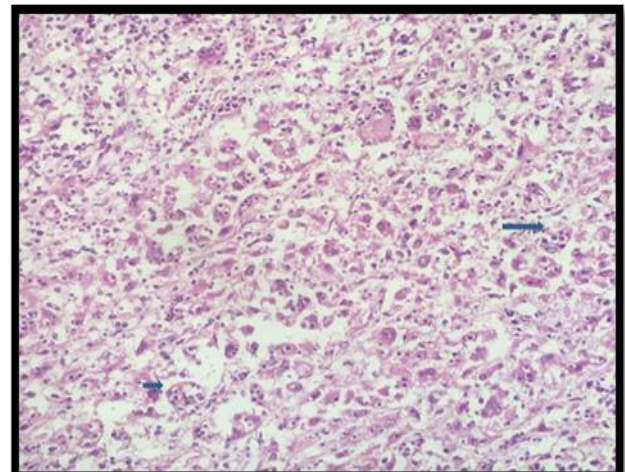


Figure 3: Haematoxylin and eosin stain-10x.

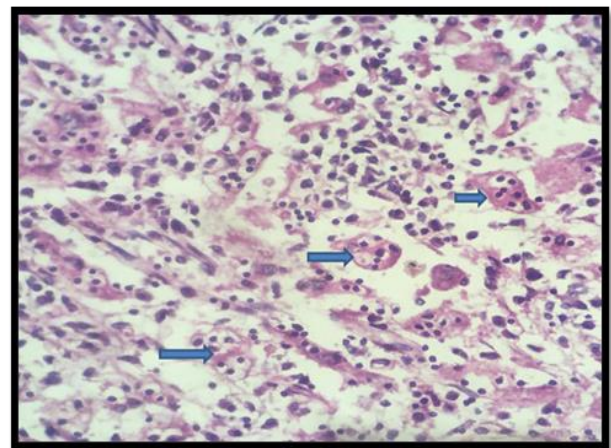
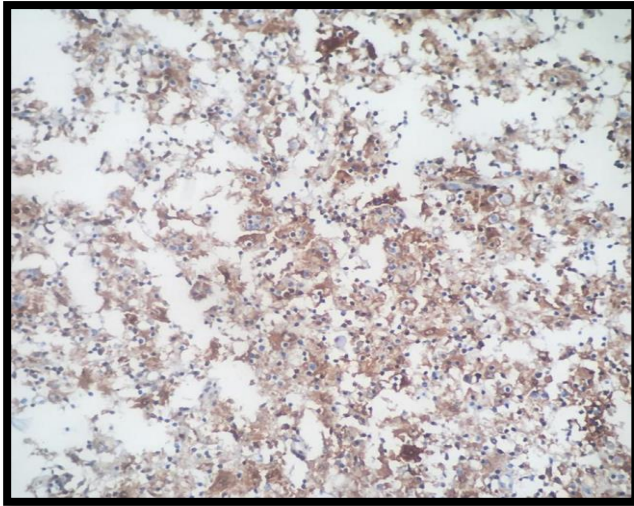
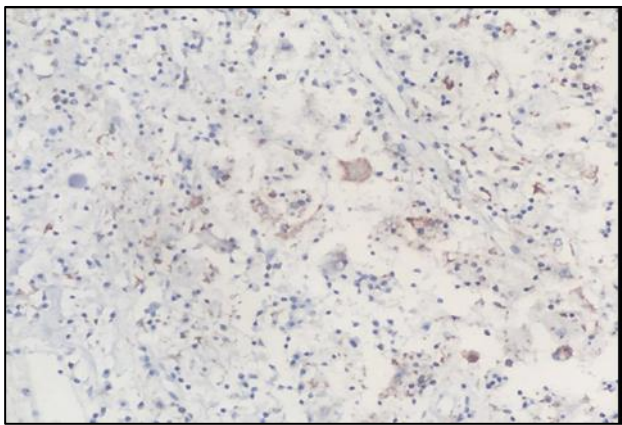


Figure 4: Haematoxylin and eosin stain-10x.

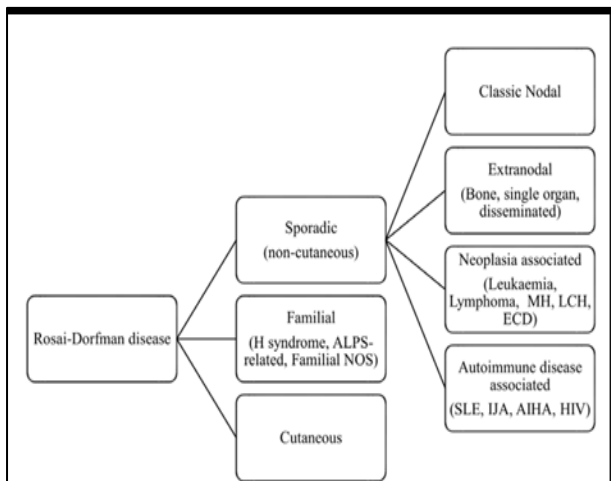




**Figure 5: Immunohistochemistry-S100.**



**Figure 6: Immunohistochemistry-CD 68.**



**Figure 7: Schematic classification of RDD according to the histiocyte society.<sup>6</sup>**

AIHA, autoimmune haemolytic anaemia; ALPS, autoimmune lymphoproliferative syndrome; ECD, Erdheim-Chester disease; IJA, idiopathic juvenile arthritis; LCH, Langerhans cell histiocytosis; MH, malignant histiocytosis; NOS, not otherwise specified; SLE, systemic lupus erythematosus.

## DISCUSSION

DD is a rare disease with a prevalence of 1:2,00,000.<sup>6</sup> It is more frequently seen in children and young adults, although it has been reported in individuals in their eight decade. RDD is more common in males and in individuals of African descent, with the cutaneous form more common in female Asians.<sup>7</sup> The aetiology of RDD is not well defined and is likely not uniform across the spectrum of phenotypes. Prior clonal studies suggested that RDD cells were polyclonal, reactive, and non-neoplastic.<sup>8</sup> Studies have also associated RDD with viral infections such as herpes viruses, Epstein-Barr virus, cytomegalovirus, and HIV, although a clear link has not yet been proven.<sup>9</sup>

Recent studies identified NRAS, KRAS, MAP2K1, and ARAF mutations in patients with features of RDD.<sup>10,11</sup> Further research is needed to investigate the cell of origin of neoplastic forms of RDD.<sup>12</sup>

Histiocyte society classification of RDD in Figure 7.<sup>13</sup>

Coming to retroperitoneal and genitourinary manifestations of RDD, the kidneys are affected in 4% of RDD cases, with a discrete mass or diffuse infiltration.<sup>14,15</sup> Symptoms include haematuria, flank pain, abdominal fullness, renal failure, hypercalcemia, or nephrotic syndrome caused by amyloidosis or renal vein thrombosis.<sup>16-18</sup> Hydronephrosis and ureteral obstruction can also occur.<sup>19</sup>

Isolated localization of RDD as a renal mass is difficult to diagnose preoperatively.<sup>15</sup> In our case, CT findings resembled those of renal malignancy with nodal spread.

The differential diagnosis of renal RDD includes Xanthogranulomatous pyelonephritis (XGP), renal cell carcinoma, Erdheim-Chester disease, leukaemia, lymphoma, tuberculosis, IgG4-related disease, storage diseases or metastatic tumour. In XGP, fibrosis and chronic granulomatous inflammatory infiltrate with lipid-laden macrophages are observed, but histiocytes with emperipolesis are absent. Patients with renal involvement have a poor prognosis, with 40% mortality rate.<sup>4</sup>

Testicular involvement in RDD is rare and manifests as a testicular or epididymal mass with or without pain mimicking epididymitis or tumour.<sup>4</sup> Adrenal gland involvement is also possible but rare.<sup>7</sup>

Evaluation of RDD includes a thorough physical examination of all systems and a wide range of investigations to rule out multifocal involvement. In our case a full body PET-CT was done (RDD lesions can have appearance and avidity on FDG-PET similar to those of intermediate- and high-grade lymphomas) after the pathology report and showed some residual uptake (apart from physiological uptake) in the retroperitoneal region with no other system involvement. Also, no

cutaneous manifestations were noted. Patient was not willing for any further evaluation and management but was followed up till 15 months post-surgery and was asymptomatic.

Treatment options for RDD in general include:<sup>20,21</sup> Observation (because 20% to 50% of patients with nodal/cutaneous disease will have spontaneous remissions), surgical resection (curative for unifocal disease), corticosteroids, sirolimus, chemotherapy (Sustainable remissions after regimens containing vinblastine/MTX/6-MP and 6-thioguanine, vinblastine/prednisone/MTX/6-MP or vinorelbine/MTX have been reported), immunomodulatory therapy (TNF- $\alpha$  inhibitors like thalidomide and lenalidomide), targeted therapies (like Imatinib mesylate- tyrosine kinase inhibitor), radiotherapy (doses between 30 and 50 Gy have been employed).

Available data is insufficient to characterize the prognosis of RDD. Outcomes are usually favourable, particularly in patients with nodal and cutaneous disease, as these are often self-limited. Some patients experience an unpredictable clinical course, with alternating periods of remission and reactivation that may last for years. Patients with multifocal and extra-nodal RDD, particularly those with kidney, liver, or lower respiratory tract disease, seem to have an unfavourable prognosis. Thus, intensive systemic chemotherapy, targeted therapies, and investigational agents may be justified in this context. Further elucidation of the role of these therapies in refractory RDD may mitigate the poor prognosis of some of these cases.

## CONCLUSION

RDD is a rare and heterogeneous disorder presenting many diagnostic and therapeutic challenges. Extra-nodal RDD of kidney is rare occurrence but should be included in differential diagnosis of renal mass evaluation and if there is suspicion frozen section should be advised whenever possible to avoid radical surgery. Multidisciplinary collaboration is often needed to the evaluation and management of patients with RDD. Many cases of RDD can be managed with observation alone, whereas other patients require variety of immunomodulatory and antineoplastic agents. Surgical resection may be considered in localised/organ confined disease. But usually, it is unexpected finding on histology after resection done for some other suspected diagnosis.

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