A case of Rosai-Dorfman Disease, associated with KRAS 13C, POLE, and NDE1 mutations, masquerading as chronic myelomonocytic leukemia: complex management paradigm

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Introduction

- RDD is a rare myeloproliferative disorder of histiocytes with an incidence of 1:200,000, with around 100 new cases diagnosed annually in the United States.
- Initial management includes steroids and rituximab. Lenalidomide is considered second line.
- Rosai–Dorfman disease (RDD) might cause a diagnostic and treatment challenge due to its rarity, overlap, and cooccurrence with other hematologic neoplasms.
- Here we report a patient with initial partial response to rituximab, and steroids subsequently treated in combination with lenalidomide.

Case presentation

A 57-year-old apparently healthy gentleman presented with progressive fatigue of six months duration and painful progressive lymphadenopathy of 1 year. He had normal complete blood count and LDH.

Exam was remarkable for 2 cm left cervical and 4 cm right inguinal lymph nodes; diffuse rash in the trunk and upper extremities.

Biopsy of the inguinal lymph node showed sinus histocytosis suggestve for RDD.

Case presentation

- Flow cytometry was unrevealing for any immunophenotypic abnormalities. Positron-emission tomography showed hypermetabolic lymphadenopathy above and below diaphragm, hypermetabolic bone marrow.
- Patient was started on rituximab with subsequent addition of steroids. He had a partial response, with resolution of rash and lymphadenopathy.
- However, restaging scans 2 years later showed worsening lymphadenopathy and splenomegaly. Lenalidomide was initiated, with complete resolution of lymphadenopathy on restaging scans after almost 2 years.
- However, splenomegaly persisted, and the patient developed significant pancytopenia, despite holding lenalidomide for > 4 weeks.
- The patient had 2 episodes of respiratory failure, in the setting of diffuse bilateral lung infiltrates, responding to high dose steroids within 24 hours, strongly suggestive for lung involvement with RDD.
- Peripheral blood smear showed 67% monocytes, rare phagocytized RBCs. Ferritin was 420, LDH within normal limits, inconsistent with hemophagocytic syndrome.
- Bone marrow biopsy showed hypercellular marrow with erythroid hyperplasia, mild granulocytic and megakaryocytic atypia. NGS showed somatic KRAS G13C, high frequency NDE1 and POLE mutations. Rituximab was added to lenalidomide and prednisone.

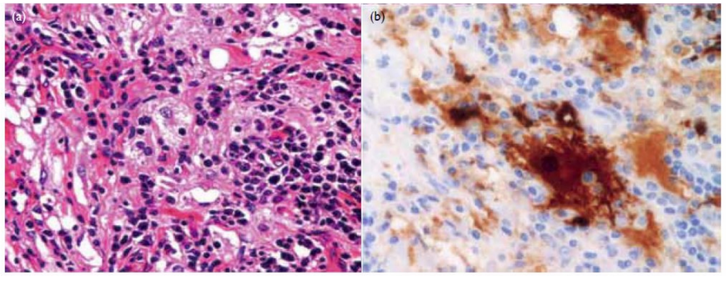


Figure 1. Pale areas of histiocytes with emperipolesis and adjacent areas rich in lymphocytes and plasma cells are evident (haematoxylin and eosin, × 400). (b) Histiocytes are S100-positive on immunostaining. Emperipolesis can also be demonstrated (immunostain for S100, × 600).
Credit: Hong Kong Med J 2019 Apr;25(2):149–51 https://doi.org/10.12809/hkmj164921

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NGS showed somatic KRAS G13C, high frequency NDE1 and POLE mutations.

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Given the patient clinical picture and CT findings, we favored the diagnosis of histiocytic neoplasm or sinus histiocytosis with massive lymphadenopathy that progressed on previous treatment.

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Rituximab was added to lenalidomide and prednisone

Conclusion

Patients with metastatic colon cancer and POLE mutation have high response to immunotherapy. Consideration could be given to treating our patent with immunotherapy, especially if high tumor mutational burden is confirmed.

Our case of a 57-year-old man with RDD, developing worsening cytopenias and respiratory distress, after initial response to rituximab, steroids, and lenalidomide.

NGS is likely to be helpful for the work-up and management of RDD. In our care there were presence of potential novel therapeutic targets in RDD, such as KRAS G13C and POLE mutations.

References

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