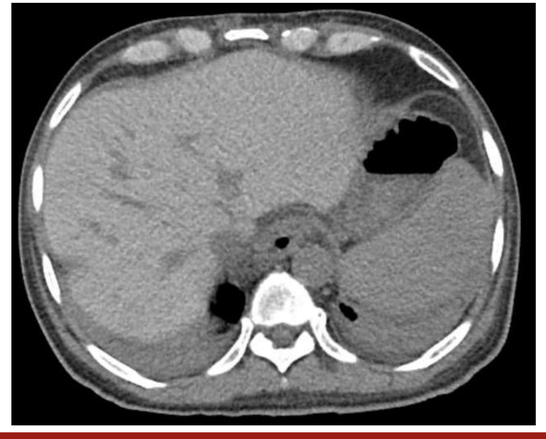
A Rare Case of X-Linked Recessive Sideroblastic Anemia (XLSA) Masquerading as Myelodysplastic Syndrome-Refractory Anemia with Ringed Sideroblasts (MDS - RARS)

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Background

- Sideroblastic anemia is categorized as a rare type of anemia by National Organization for Rare Disorders.
- Fewer than 200 cases with less than 100 unrelated probands have been described for X-linked recessive sideroblastic anemia (XLSA).
- XLSA is the most common type of non-syndromic congenital sideroblastic anemias (CSA)
- Almost 40% of all CSA cases involving mutations in the ALAS2 (δ- aminolevulinic acid synthase) gene.
- Male patients (two-thirds of known cases) usually present in childhood or adolescence with symptoms of anemia, while female patients present in middle age. **(1)**



Case Report

- 63 y/o M with PMHx of MDS, iron overload – hemochromatosis, developmental delay, BPH, portal HTN and gastric varices, urinary/renal calculi presented with symptoms of anemia which have been ongoing for the last 10 years intermittently. History of multiple blood transfusions over a period of 10 years.
- Subsequent bone marrow biopsy showed a hypercellular bone marrow with erythroid hyperplasia, increased iron and ringed sideroblasts consistent with refractory anemia with ringed sideroblasts, no abnormal karyotype in cytogenetics, and normal flow cytometry results.
- A liver biopsy showed hemosiderotic changes, and he was initially considered to have myelodysplastic syndrome-refractory anemia with ringed sideroblasts(MDS - RARS).
- The patient was then started on iron chelating agents and pyridoxine, folic acid with improvement in anemia and did not require any further transfusions with significant improvement in his symptoms.
- A hereditary anemia NGS (Next-Generation Sequencing)and Deletion/Duplication panel was then done which showed presence of pathogenic X-linked recessive hemizygous mutation involving ALAS2 gene – OMIM 301300 **(5)**
- No SF3B1 gene mutation was detected, which is the gene mutation commonly associated with MDS-RARS. **(4)**
- JAK2, HFE gene mutations were not detected.

Discussion

- Treatment for XLSA is mostly supportive with frequent monitoring of Hemoglobin and iron levels with lifelong Vit B6 and Folic acid supplementation.
- Anemia responsiveness to pyridoxine varies from case to case and is almost never complete.
- Occasional prophylactic phlebotomy might be needed to avoid iron overload, in pyridoxine-responsive anemia.
- However, if iron overload has already manifested as in our patient, regular phlebotomy and/or use of iron chelating agents is indicated to normalize iron levels.
- Prognosis is good with almost a normal life-expectancy in patients with pyridoxine responsive XLSA with early diagnosis and maintenance of low levels of iron stores in the body by avoiding unnecessary blood transfusions. **(5)**



Conclusion

- This case report highlights the necessity for extensive workup in patients with sideroblastic anemia, given the rarity of XLSA and similarity in its clinical symptoms to MDS-RARS, and the need for its early diagnosis.
- Response to the pyridoxine treatment, absence of SF3B1 gene mutation, and presence of ALAS2 gene mutation helped confirm the diagnosis of XLSA in our patient. **(2), (3), (4)**
- In our patient, iron overload and subsequent liver cirrhosis developed due to multiple transfusions for refractory sideroblastic anemia which was treated as MDS-RARS and could have been avoided if XLSA had been suspected earlier in the course of the disease.



References

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