Unusual association of Chylomicron retention disease and IRIDA syndrome: case report

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Background and aims:

Chylomicron retention disease (CRD) is uncommon autosomal recessively inherited fat malabsorption syndrome. Previously, about 55 cases were described widespread. The diagnosis is often delayed because symptoms are nonspecific. Iron-refractory iron deficiency anemia (IRIDA) is a rarely diagnosed autosomal recessive anemia. We report uncommon case report of two sisters having undescribed association of CRD and IRIDA.

Results:

- Two sisters from a Turkish family with second degree consanguinity, had two and fourteen years old respectively.
- She had ferropenic, hypochromic microcytic anemia, refractory to oral iron therapy.
- The youngest one had worsen growth, chronic diarrhea, hypocholesterolemia and important deficiency of vitamins E,A,D and K.
- She has undertaken an upper gastrointestinal endoscopy which revealed an extensive fat infiltration with white duodenum.
- The oldest had chronic diarrhea without altered growth, hypocholesterolemia, low levels of vitamins A,D,E, and K with identic result of upper gastrointestinal endoscopy.

Figure 1 and 2: white duodenum with fat infiltration on endoscopy

Figure N°3,4,5 and 6: Fat infiltration of the duodenal epithelioma

- After exclusion of gastrointestinal etiologies of anemia, **IRIDA** diagnosis was suspected and a mutation in the **TMPRSS6** gene was identified.
- A **lipid malabsorption syndrome** associated to **IRIDA** was suspected and the presence of **SAR1B** gene mutation confirms the diagnosis of **CRD in both sisters**.

Figure 7: The family tree

Figure 8 and 9: The genetic study and molecular biology

arr[hg19] 5q31.1(133,942,478-133,944,277)x0 homzygote deletion of 1,8 Kb emported exons 7 et 8 of **SAR1B** gene.

- For both sisters (17CY02260). C 104 Mb of ROH were commun, of this,125 genes were annotated on OMIM entries.
- **The coefficient of consanguinity were 1/16.**
- Both patients were treated with a low fat diet, fat-soluble vitamins and intravenous iron supplementation resulting in significant improvement with 12 months of follow up.

Conclusions:

- **IRIDA** syndrome is due to mutations the **TMPRSS6** gene encoding Matriptase 2, a transmembrane serine protease that plays an essential role in down-regulating hepcidin, the key regulator of iron homeostasis.
- Most IRIDA patients have no major clinical signs, except for pallor, and have normal growth and development.
- Whorsen growth in this cases where due to lipid malabsorption syndrome.
- Thanks to upper gastrointestinal endoscopy which were undertaken to search about digestive bleeding or Iron malabsorption causes , we suspected lipid malabsorption syndrome and looked for **SAR1B** mutation.
- At our knowledge, this association of **IRIDA** syndrome and **CRD** seems to be the first description in literature.
- Consanguinity can lead to an unusual phenotype even with non-contiguous genes. **The coefficient of consanguinity were 1/16 in this case.**
- The youngest had more severe phenotype. So that, despite the same genotype, the clinical presentation changes between individuals.