Recurrent gastrointestinal bleedings in MNGIE patients

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BACKGROUND

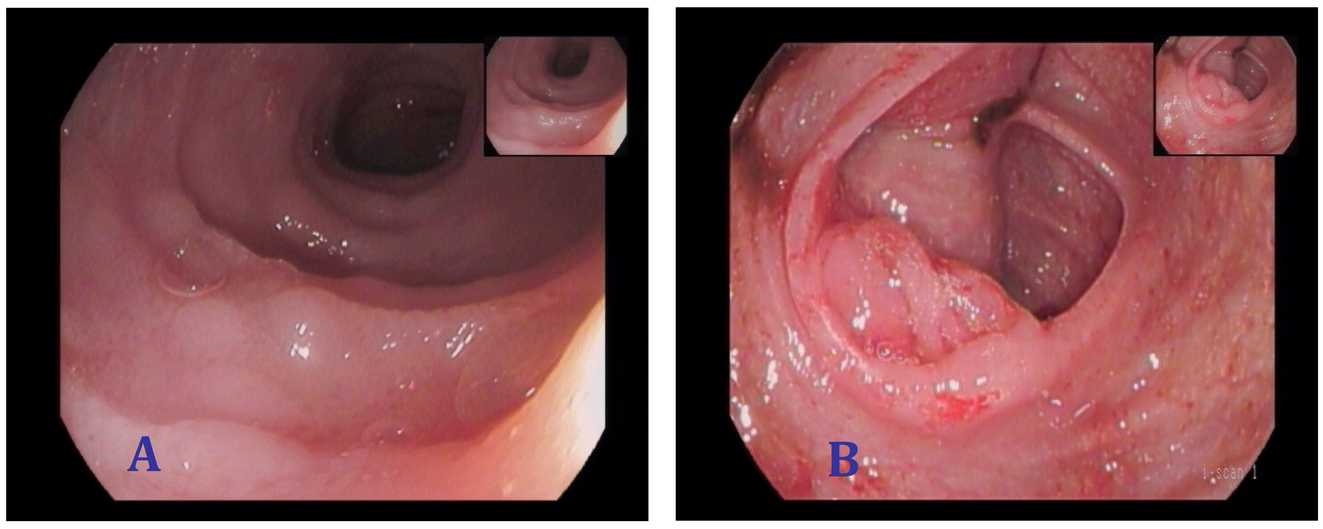
Mitochondrial neurogastrointestinal encephalomyopathy (MNGIE) is a rare autosomal recessive disorder due to thymidine phosphorylase (TP) deficiency. Typically, MNGIE phenotype is characterized by gastrointestinal dysmotility, cachexia, opthalmoplegia, muscle wasting, peripheral neuropathy and leukoencephalopathy. Gastrointestinal (GI) symptoms occur virtually in all individual with MNGIE, representing the earliest and often fatal manifestations. They include early satiety, nausea, postprandial emesis, episodic abdominal pain, episodic bowel distention and diarrhoea (1). To our knowledge, GI bleeding has not be reported in association with MNGIE (2).

OBJECTIVE

Here we report MNGIE patients with recurrent episodes of gastrointestinal bleeding responsible of a significant worsening of clinical conditions.

CASE REPORTS

The first case, whose clinical details have been already extensively reported (3, 4) is a 25 year-old female who five years ago underwent allogenic hematopoietic stem cell transplantation (HSCT) followed by normalization of biochemical parameters and remission of gastrointestinal symptoms. Nevertheless, three years after transplant she presented repeated episodes of severe anaemia requesting blood transfusion due to heavy GI bleeding. Screening for infectious and autoimmune disorders resulted normal. GI endoscopy and biopsies ruled out the common causes of digestive bleeding and, in particular, a chronic rejection after transplantation, showing, on the other hand, the presence of a marked vascular fragility.



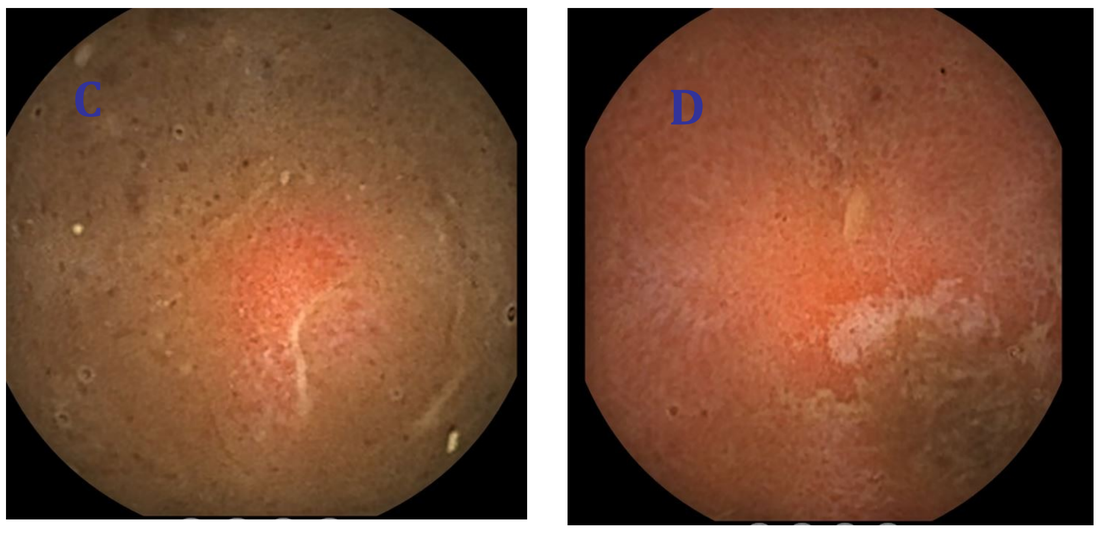


Fig. A,B: Colonoscopy images: the mucosa was normal (A) until the ascending colon which, on insertion, appeared diffusely haemorragic with blood oozing from the colonic wall (B),

Fig. C,D: Small bowel video capsule endoscopy showing ulcer in the terminal ileum.

The second case is a 20-year old female, carrying two heterozygous *TYMP* gene mutations, a c.215-11_223del in exon 3 (p.(Gly72_Leu75delinsVal)) and a c.977G>A mutation in exon 8 (p.G326D), with a mild phenotype characterized by thin body habitus, bilateral palpebral ptosis and diffuse weakness, in the absence of gastrointestinal symptoms. Her affected brother, with a predominant gastrointestinal phenotype, at the age of 21y presented an abrupt clinical worsening for the occurrence of recurrent episodes of copious digestive bleeding leading to death in a few months. A GI workup failed to clarify the cause of the haemorrhage.

CONCLUSIONS

Digestive bleedings have an high incidence and prevalence in the general population. In spite of the extensive and severe GI involvement in MNGIE, digestive haemorrhages have not been reported in the classical phenotype. Nevertheless, our cases suggest that intestinal tract haemorrhages may present and complicate the clinical course of the disease. Their pathogenesis is unclear, possibly related to the presence of intestinal vascular fragility (5). In conclusion, gastrointestinal bleeding could be considered a previously unreported and potentially life-threatening manifestation of MNGIE phenotype. Further studies are needed to clarify its pathophysiological mechanism.

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