Proven: The causative role of homozygous H63D mutation in hereditary haemochromatosis

Se demuestra el papel causal de la mutación H63D en homocigosis en la hemocromatosis hereditaria

Dear Editor:

We have read with interest the scientific letter by Pinto-Pais et al.1 ‘Is H63D a ‘minor’ HFE polymorphism?’ They have studied 230 consecutive patients with hypferferritinaemia and they have retrieved 16 H63D homozygotes. They have searched for the possible causes of hypferferritinaemia, and in all the studied cases but in one there was a possible cause to explain the hypferferritinaemia (NAFLD, chronic alcohol consumption, HBV, HBV). No liver iron concentration determination was determined in these patients and this was a very important point to know because of the possible causative role for hereditary hemochromatosis of this polymorphism.2 Only in one patient, the study for other liver diseases was negative. Recently, we have published a work developed in 132 consecutive patients referred to a secondary hospital because of hypferferritinaemia.3 Only 5% presented high liver iron overload (>80 µmol/g) and 33% of patients had liver iron surcharge (>36 µmol/g). The genotypic frequency of the H63D/H63D mutation was 21.56% in our series (6.96% for the Pinto-Pais et al. group),4 and we concluded that H63D/H63D genotype and H63D allele predispose in our Region individuals to hypferferritinaemia. Effectively, the H63D polymorphism is highly prevalent in Caucasian population (15–20%). The highest allele frequency (>30%), has been reported in the Basque Country, Spain.4 The significance of this mutation was in doubt and the EASL consensus do not consider it as a predisposing mutation, but there is evidence that contradicted this: (a) excess of H63D alleles among Hemochromatosis patients; (b) C282Y/H63D have been found to express hemochromatosis with less penetrance that C282Y homoygotes; (c) in vitro evidence has been found; (d) murine evidence of H63D contributing to murine hemochromatosis. There is evidence that H63D mutation contributes to iron overload, increasing serum iron and transferrin, and also it has been demonstrated an independent relationship with hemochromatosis from the presence of C282Y,3,5 The H63D/H63D genotype is responsible for hyperferritinemia.2,3,6 It has been shown that H63D produces liver iron overload in homocygosis or in compound heterocygosis with C282Y. The causative role of H63D/H63D mutation in hereditary hemochromatosis or iron overload was demonstrated,4,7,8 but with less penetrance and a considerable variation of phenotypic expression. Mutations in other genes, gene penetrance, and environmental factors (alcohol abuse, steatosis, etc.) have been shown to explain the variable phenotypic expression of C282Y/H63D and H63D/H63D mutations. The search for other mutations in other genes or other unknown nongenetic factors will explain the development of hemochromatosis in these patients.4

Conflicts of interest

None declared.

References


DOI of original article:
http://dx.doi.org/10.1016/j.gastrohep.2015.12.004
Small bowel perforation by an intrauterine device

Perforación del intestino delgado por dispositivo intrauterino

To the Editor:

The intrauterine device (IUD) is a highly effective, inexpensive, generally well tolerated and widely used contraceptive method. A serious but rare complication is perforation of the uterus and migration to the abdomen. The risk of uterine perforation (UP) is reported to be between 1 in 350–2500 women, although the actual incidence could be higher, since many of these cases are asymptomatic. While most IUD uterine perforations do not involve other organs, a small percentage cause erosion and perforation of other abdominal organs, among them the small intestine, for which fewer than 10 cases have been described. The following case of small bowel perforation by an IUD describes this rare complication.

A 29-year-old patient came to the emergency department for moderate intensity hypogastric pain associated with amenorrhoea and negative pregnancy test. She had a history of irregular menstruation and insertion of a T-shaped IUD 14 months previously. She did not report any complications at the time of placement and denied expulsion. Abdominal examination revealed moderate intensity pain on deep palpation in the hypogastric region with no guarding, normal size intrapelvic uterus, and no palpable tumours. During the gynaecological examination, the threads of the IUD were not observed in the external cervical orifice. Rectal examination was normal.

Plain abdominal X-ray identified the IUD in the pelvic cavity. Ultrasound revealed normal uterus and ovaries, with the IUD near the fundus of the uterus, without confirming the intrauterine position; computed tomography showed the IUD in the abdomen, outside the uterus, with no evidence of free air or fluid collection (Fig. 1).

Laparoscopy was performed, finding the IUD embedded in the small bowel 10 cm from the caecal valve, with the vertical portion exiting through the intestinal wall (Fig. 2). Laparoscopic resection of the affected bowel portion was carried out to completely remove the IUD, with terminal-anastomosis and no complications. The UP site did not require repair. Histopathological examination revealed the IUD embedded completely in the bowel wall, surrounded by granulation tissue and fibropurulent exudate, consistent with an erosion and perforation of the small bowel wall. The patient was treated conservatively, with no evidence of bowel obstruction or perforation.

Figure 1  Computed tomography images, in which the arrows indicate the location of the intrauterine device in the abdominal cavity.

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