Madelung's disease in a patient with advanced hepatocellular carcinoma☆

Síndrome de Madelung en un paciente con hepatocarcinoma avanzado

We present the case of a 67-year-old patient who came to our department with a two-year history of asthenia and anorexia, having not previously seen any other physician with these symptoms. A slight elevation of liver enzymes indicating cholestasis led us to suspect a liver disorder. Ultrasound showed space-occupying lesions, although without identifying their origin. As we suspected malignancy, we ordered an abdominal computed tomography (CT) scan. The CT was suggestive of hepatocarcinoma, but this required confirmation. Additional findings were tumour-related portal vein thrombosis with cavernous transformation, normal-sized spleen and collateral circulation with oesophageal varices. The liver had areas of impaired perfusion and discrete lobulation of segment I. Ascites made it unfeasible to take samples by biopsy, so a magnetic resonance imaging (MRI) scan was performed and identified the lesion as advanced LDH hepatocellular carcinoma (Fig. 1B–D). The patient had never been screened for hepatocellular carcinoma.

Other tests we carried out were serology for hepatotropic viruses, which were all negative; and blood analysis, showing elevation of GGT with normal ALT and AST, normal bilirubin and glucose, low albumin levels with normal total proteins, mild hyponatraemia, macrocytic anaemia without thrombocytopenia, decreased prothrombin activity and elevation of IgG and IgA.

The ascitic fluid was also analysed, finding a normal amount of polymorphonuclear cells and red blood cells. The albumin gradient was over 1.1 g/dl and the protein concentration in the fluid was 2.6 g/dl, compatible with ascites resulting from portal hypertension.

In view of the spread of the tumour and the patient's poor general condition, with his agreement, it was decided to provide palliative treatment at home.

On physical examination, multiple, hard, rounded subcutaneous lesions were noted on the neck and chest, as well as on the forearms, thighs and abdomen (Fig. 2A–D). The patient had started developing these lesions in his twenties and they had previously been asymptomatic. His alcohol consumption had been at excessive levels of approximately 60 g a day since his youth. Although large in size, the lesions had not been causing any symptoms apart from restricting cervical flexion and extension movements. The patient had no family history of lipomatosis and had never required any medical care prior to this episode. The CT scan performed to study the liver lesion showed the fatty nature of these lesions (Fig. 1A). After reviewing the available literature, we attributed these abnormalities to type I Madelung's disease due to its characteristic distribution and morphology,[1–6] and the diagnosis was supported by the patient's previous medical history.

Madelung's disease or benign symmetric lipomatosis or Launois-Bensaude syndrome, is a progressive disease with usual onset between the ages of twenty and forty, whose main manifestation is the growth of multiple

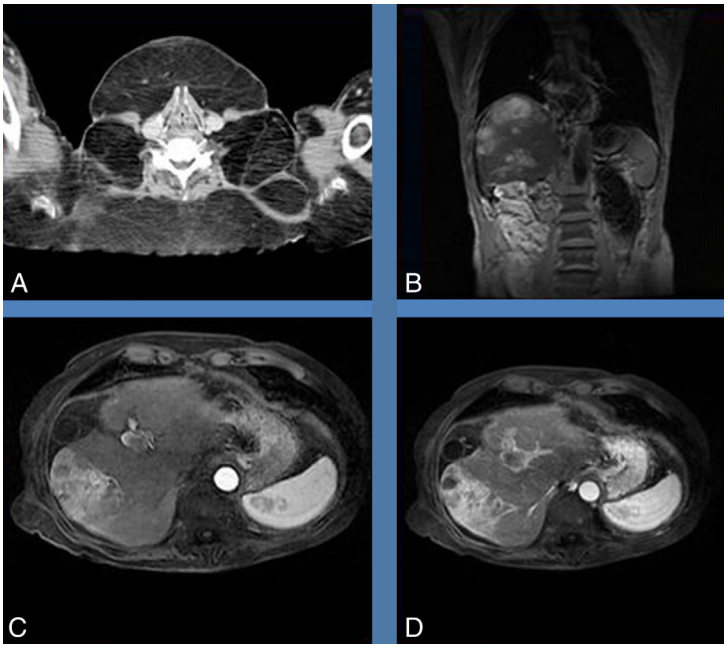

Figure 1 (A) Axial section of the neck, showing the fat content. (B) Coronal section of the MRI. (C and D) Sagittal sections of the MRI.

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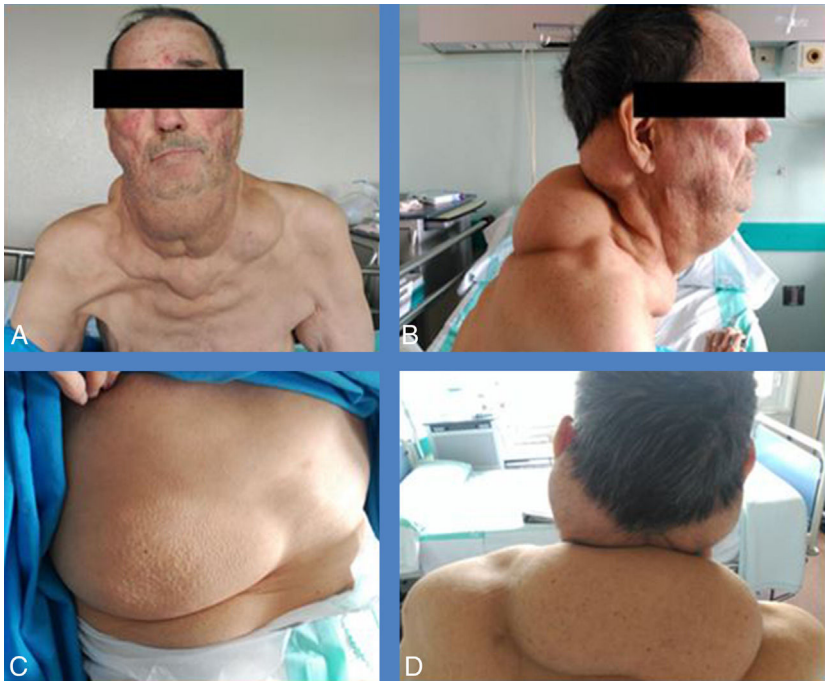

Figure 2 (A–D) Different views of the patient, where lipomas can be seen with special emphasis, but also on the chest (C).

benign non-encapsulated lipomas, typically on the neck, but also on the chest, abdomen, arms up to the elbow, thighs[1] and, on occasion, on the tongue, in some cases causing macroglossia.[7] The presence of multiple lipomas but with the distal parts of the extremities remaining unaffected is highly suggestive of Madelung's disease. It can be divided into two types: type I if the distribution is circumscribed; and type II when lipomatosis takes on the appearance of conventional obesity.[1,2,5] The lipomas do not become malignant, with the main complication being limitation of mobility, especially of the neck. However, an increase in morbidity and mortality rates has been reported due to other causes, cardiac and cancer-related in particular, and the concept of benign disease is now under discussion. Other complications described are gynaecomastia, fatty liver disease, peripheral neuropathy and dyslipidaemia.[1]

The incidence is higher in males (15:1) and 90% of cases are related to alcohol abuse.[1,2,8] Most of the cases reported are from countries in the Mediterranean area (mainly Spain, Italy and Greece).[1] Madelung's disease is also associated with liver disorders,[1,2,9] mainly steatosis, although here we have the important confounding factor of alcoholism, given that it is the main risk factor.[5] Giving up alcohol is the only non-surgical treatment found to have any effect in reducing the size of the lesions; intra-lesional therapy with beta-blockers was no better than placebo.[2] Lipomas should not be operated on unless they are causing compression or cervical mobility problems, because they will recur.[2]

The main genetic aetiopathogenic theory involves mitochondrial DNA, and there is a form with a maternal inheritance.[1]

Although the relationship between Madelung's disease and fatty liver disease is clearly described in the literature, there are no previous reports of associated hepatocarcinoma. Our case could therefore be the first example of such an association and, despite the alcohol being a confounding factor, it may have been a predisposing factor for the development of the patient's liver tumour.

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Irritable Bowel Syndrome with predominant diarrhea and giardiasis: Is it one or the other?☆

Síndrome del intestino irritable con predominio de diarrea y giardiasis: ¿es uno u otra?

Diarrhea-predominant Irritable Bowel Syndrome (IBS-D) is where more than a quarter (25%) of bowel movements are type 6 or 7 on the Bristol Stool Form Scale, and less than a quarter are type 1 or 2. The symptoms must meet the corresponding Rome IV criteria: recurrent abdominal pain, at least one day per week (on average) in the last three months, associated with at least two of the following criteria: (1) Related to defaecation; (2) Associated with a change in stool frequency; and (3) Associated with a change in stool form (appearance).[1]

Giardiasis is a common cause of infectious gastroenteritis worldwide, being associated with poverty, with a prevalence that varies from 2% (high-income countries) to 30% (low-income countries).[2]

The typical symptoms of giardiasis which include diarrhea, often explosive, especially in the morning, without blood or mucus, flatulence, abdominal pain and swelling,[2] often suggest IBS-D, with which a differential diagnosis must be made. However, with certain frequency, this can become difficult with the usual procedures and end up going unnoticed.

We present the case of a 29-year-old woman who reported having travelled to Mexico over a year beforehand, where she had acute gastroenteritis that took a long time to resolve. She reported weight loss, abdominal distension and pain, and chronic explosive diarrhea, with numerous soft-liquid stools, urgency and relief of pain when expelling wind and/or faeces, since her return from the trip. All tests, including coeliac serology, thyroid function, serial stool cultures/ova and parasite exams and a colonoscopy, were completely normal, and her symptoms were interpreted as a post-infectious-type IBS-D, probably in relation to some viral or parasitic infection acquired in Mexico.

The conventional treatment provided no improvement. With the abdominal pain and diarrhea persisting, treatment was recommended with paroxetine 20 mg/day.

As there was only slight improvement after several months of treatment, the patient was advised to increase the dose to 50 mg/day (30-0-20). After another two months, still with no improvement, further stool cultures/ova and parasite exams were performed, which were again negative, and it was decided to try treatment with rifaximin (400 mg/twice daily, one week a month, repeating for another month), with no results.

Finally, an endoscopy was performed with duodenal biopsies to rule out another malabsorption disorder (biochemically, there were no data to suggest that), and possible duodenal giardiasis, although the stool cultures/ova and parasite exams had been repeatedly negative, with no eggs or trophozoites detected. Duodenal biopsies were also normal, with no evidence of atrophy or giardiasis. We requested that a PCR for *Giardia duodenalis* also be performed on the biopsies and this came back positive, clarifying a diagnosis which had been eluding us for months. The patient was treated with tinidazole 50 mg/kg body weight, in a single oral dose, which led to rapid improvement in symptoms within a few weeks.

There are studies[3] that find a strong association between giardiasis and post-infectious IBS (PI-IBS) in young people. D'Anchino et al.[4] studied 100 patients with symptomatic giardiasis and found that in 82 of them IBS had previously been identified, suggesting that the symptoms attributed to giardiasis may, in fact, be the result of pre-existing IBS, exacerbated by *Giardia* infection.

Moreover, individuals with giardiasis are approximately four times more likely to be diagnosed with IBS 90 days after the diagnosis of giardiasis than those without giardiasis.[3]

In terms of the relationship between the two disorders, giardiasis may be a trigger for the exacerbation of IBS, but the parasitic infection is no longer necessary for the symptoms to persist once they have become established.[4]

From our experience, we recommend performing a PCR assay on a stool sample in patients with symptoms suggestive of IBS-D who have travelled abroad, particularly to low-income areas (risk factor for giardiasis), who have persistent diarrhea, even if stool investigations, including stool cultures and ova and parasite exam, are persistently negative.

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