sinusoids and their subsequent migration to more distant regions, such as the umbilical cord, while the connection with the main liver may be maintained through the umbilical vein.

The differential diagnosis of umbilical cord masses is complex and must include cyst and pseudocyst, haematoma, umbilical artery aneurysm, haemangioma, teratoma, angiomyomyxoma, patent urachus, ectopic liver, as well as the most common diseases of the umbilical cord, which are umbilical cord hernia, gastroschisis and omphalocoele.

Ectopic liver in the newborn is usually diagnosed by chance following imaging tests or surgical procedures performed for unrelated reasons. However, it may be diagnosed due to complications like torsion, which manifests with abdominal pain, gastric outlet obstruction and respiratory distress syndrome, caused by the presence of hepatic tissue in supradiaphragmatic locations.

Only eight other cases of hepatic tissue in the umbilical cord have been described in the literature[2–6] (Table 1), and the diagnosis of the umbilical cord mass was made prenatally in three of the nine cases, with the definitive diagnosis being made by anatomical pathology. On rare occasions it can be accompanied by symptoms of infection and be associated with other abnormalities, such as utrachal or biliary atresia, ectopic pancreas and heart and lung malformations. In our case, as happened in the one described by Horn et al.,[2] we observed an intraperitoneal connection with the liver that may correspond to the round ligament, a vestige of the left umbilical vein.

To conclude, we would like to highlight that when ultrasound examination reveals a mass in the umbilical cord we should consider the possibility of rare conditions, like the one described here, along with more common diseases.

Doppler ultrasound of the mass can be helpful to this end, although as we mentioned above, in most cases the definitive diagnosis will be made postnatally. At any rate, the histological characteristics of the lesion should not change the obstetric approach in the absence of intestinal or vascular involvement in the foetus, and the surgical approach will depend on the suspected diagnosis after birth.

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Bone marrow toxicity secondary to a primary Epstein–Barr infection in a patient with Crohn's disease on thiopurines treatment☆

Toxicidad medular secundaria a primoinfección por virus de Epstein-Barr en paciente con enfermedad de Crohn en tratamiento con tiopurínicos

Dear Editor:

The efficacy of thiopurine immunosuppressants in the treatment of inflammatory bowel disease (IBD) has been demonstrated, and thiopurines are the most commonly used drugs to maintain remission induced by exclusive enteral nutrition or steroids in paediatric patients with Crohn's (EC) disease. Their long-term use may facilitate the development of opportunistic infections by viruses such as Epstein–Barr virus (EBV). Thiopurine blocking of regulatory T cells enhances the cytotoxicity of EBV, leading to B-cell lymphoproliferation. In immunosuppressed patients, the manifestation of EBV may range from an infectious mononucleosis to a haemophagocytic lymphohistiocytosis (HLH).[1]

We present the case of a 14-year-old male patient with CD in clinical and laboratory remission following combined treatment with infliximab (IFX) and azathioprine (AZA) since diagnosis. In order to reduce the risk associated with dual immunosuppression, IFX was discontinued 10 months after initiating treatment, and the patient developed a high fever, odynophagia, submandibular lymphadenopathy and splenomegaly. Laboratory analysis revealed pancytopaenia and elevated levels of transaminases, triglycerides and ferritin (Table 1). Intravenous empirical antibiotic therapy was initiated due to the presence of febrile neutropaenia (500 cells/mm^3) and was suspended after 72 h following a negative blood culture and a positive Paul-Bunnell test. Epstein–Barr virus was detected by polymerase chain reac-

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Table 1 Diagnostic criteria for haemophagocytic lymphohistiocytosis.

5 of the following 8 criteria must be met:

1. Fever $\geq$ 38.5 °C
2. Splenomegaly
3. Cytopaenias (affecting at least 2 or 3 lineages in the peripheral blood)
   Haemoglobin < 9 g/dL (in infants younger than 4 weeks, haemoglobin < 10 g/dL)
   Platelets < 100×10^3/mL
   Neutrophils < 1×0^3/mL
4. Hypertriglyceridaemia (fasting triglycerides, >265 mg/dL) and/or hypofibrinogenaemia (<150 mg/dL)
5. Haemophagocytosis in bone marrow, spleen, lymph nodes or liver

Adapted from the Histiocyte Society HLH-2004.

Table 2 Laboratory parameters of the patient.

Parameter	Before antiviral treatment	After antiviral treatment
Leukocytes (neutrophils)	3000 cells/μL (600 cells/μL)	6000 cells/μL (1200 cells/μL)
Haemoglobin	9.8 g/L	11 g/L
Platelets	114 000 cells/μL	123 000 cells/μL
Triglycerides	187 mg/dL	193 mg/dL
Ferritin	1.572 μg/L	730 μg/L
ALT/AST	135/178 IU/L	140/122 IU/l
PT/fibrinogen	66.7%/2.7 g/l	75.9%/2.8 g/l
EBV PCR (copies)	7650 copies/mL	1095 copies/mL

tion (quantitative PCR), with a viral load of 7650 copies/mL. An incipient HLH in association with primary infection by EBV (initial test was negative at the time of CD diagnosis) was suspected, leading to discontinuation of AZA and initiation of empirical antiviral treatment with ganciclovir. At 72 h, the clinical manifestations had improved, with a reduction in lymphadenopathy, improvement of pancytopaenia and a decrease in the viral load. Ganciclovir treatment was discontinued on the fifth day, when the patient had been afebrile for 48 h. The patient was discharged seven days after admission after ruling out HLH, as he did not meet the full laboratory criteria[2] (Table 2). Thirty-two days following the diagnosis of primary infection by EBV, the viral load was undetectable and monotherapy with IFX was resumed on an outpatient basis, and at present, 20 months after discontinuation of AZA, the patient remains in clinical and laboratory remission and has not developed any complications from the medication.

It is known that children with IBD have certain characteristics that increase the risk of opportunistic infection (immunosuppressive treatment, malnutrition...). There are cases of infection by EBV with a fatal outcome in patients with CD during treatment with AZA. Biank et al.[3] described four cases of HLH secondary to primary infection with EBV in EC. N'Guyen et al.[4] reported a case of primary infection by EBV in which the patient was receiving treatment with AZA for EC and developed infectious mononucleosis, HLH and a B cell lymphoproliferative disorder. Francolla et al.[5] published the first paediatric case of HLH secondary to EBV in EC during treatment with IFX and AZA. While there is no evidence of the beneficial effect of discontinuing immunosuppressants therapy in these cases, the European Crohn's and Colitis Organization (ECCO) recommends that, in patients that develop severe infection by EBV during treatment with thiopurines, antiviral therapy should be combined with the discontinuation of immunosuppressant therapy, which could lead to the spontaneous improvement of the process without any other intervention.[6] This consensus document states that EBV IgG screening should be considered before initiation of immunomodulator therapy with thiopurines.

In our case, the early diagnosis and management with antiviral therapy and discontinuation of thiopurine treatment probably prevented the development of a haemophagocytic lymphohistiocytosis, which has the potential to become fatal.

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