

Title:

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Paraneoplastic acquired hemophilia A associated with hilar cholangiocarcinoma arising in an intraductal papillary neoplasm of the bile duct

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Dear Editor,

A 74-year-old female was admitted due to painless jaundice. Laboratory tests showed hyperbilirubinemia, cholestasis, normal coagulation and Ca 19-9: 163 U/l. The computed tomography (CT) scan reported dilation of the intrahepatic and extrahepatic bile ducts secondary to a 24-mm tumor in the intrapancreatic common bile duct. The magnetic cholangioresonance showed multiple endoluminal polypoid lesions, suggestive of intraductal papillary neoplasm of the bile duct (IPNB). The endoscopic bile duct brushing was non-conclusive.

After an initial study, surgery was indicated. However, during preoperative evaluation, she developed new onset isolated partial thromboplastin time (aPTT) lengthening without hemorrhagic complication. Therefore, surgery was contraindicated. The hemostasis tests showed factor VIII: 15.7 U/dl (NV: 50-150) and inhibitory activity against factor VIII

(Bethesda: 2 UB), consistent with acquired hemophilia A (AHA). Immunosuppressive treatment with prednisone and cyclophosphamide was started. Six weeks later, with coagulation and factor VIII within normal range, the patient underwent surgery. A bile duct resection, lymphadenectomy and Roux-en-Y hepaticojejunostomy were performed. The postoperative period was uneventful, and the patient was discharged maintaining descending corticosteroids. The pathology study reported an extrahepatic cholangiocarcinoma with foci of dysplasia (pT2pN0). After one-year follow-up, there was no evidence of recurrence nor aPTT lengthening.

Discussion

The incidence of AHA rises among patients in their 60s and young women (1). In recent years, AHA has been diagnosed more frequently, due to greater recognition in association with some diseases, such as cancer (2). Typically, AHA is diagnosed in the setting of bleeding that quickly compromises the patient's life, as recently reported by del Pino et al. in which multiple attempts were needed in order to acutely control bleeding (4). However, few asymptomatic cases with a prolonged aPTT have been reported (3). It is suggested that AHA is caused by the interaction between genetic and environmental factors affecting immunological tolerance, producing autoantibodies (2-4). There is still no way to predict the risk of AHA, since 50 % of cases have unknown associations (1). Few reports show an association between AHA and bile duct neoplasms. However, none have been linked to a IPNB (5). IPNB is a premalignant neoplasm characterized by intraductal papillary growth of biliary-type epithelium and may be associated with invasive carcinoma (6).

The patient received immunosuppressive treatment, allowing surgical treatment. The treatment of AHA is based on hemostatic drugs as recombinant factor VII and activated prothrombin complex, and immunosuppressants (1). Immunosuppressive treatment can exert its action by preventing T-mediated activation of B-lymphocytes, cytotoxicity or blocking antibodies (1). The treatment with three immunosuppressants allows a rapid rise of factor VIII in four weeks, with a remission rate up to 80 %, avoiding cancer treatment delay (2).

AHA is caused by factor VIII autoantibodies and usually presents with hemorrhage. In this unusual case, AHA presented as a paraneoplastic syndrome associated with IPNB.

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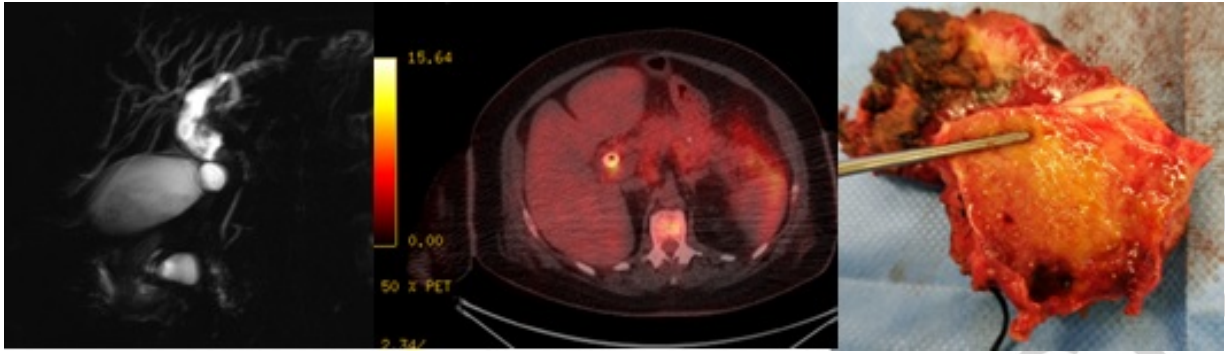


Fig. 1. A. Magnetic cholangioresonance showing multiple endoluminal polypoid lesions, suggestive of foci of intraductal papillary neoplasia. B. Positron emission tomography-computed tomography (PET-CT) scan showed no suspicious focal uptake. C. Common bile duct surgical specimen showed the presence of an endoluminal lesion.

Figure 2. Trends of protrombin time and aPTT from diagnosis up to 1 year follow-up

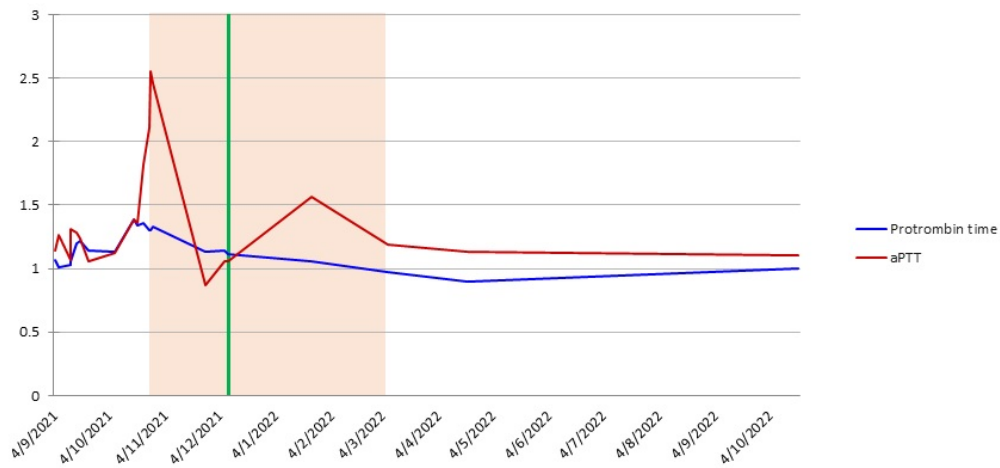


Fig. 2. Trends of prothrombin time and activated partial thromboplastin time (aPTT) from diagnosis up to one-year follow-up. The orange interval represents the immunosuppressive treatment duration and the green bar represents surgery.