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Takayasu arteritis and primary sclerosing cholangitis: A casual association or different phenotypes of the same disease?

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ABSTRACT

Takayasu arteritis and primary sclerosing cholangitis are two rare disorders. The pathogenesis of Takayasu arteritis involves immune-mediated mechanisms, and corticosteroids represent the mainstay for treatment. Conversely, the aetiology of primary sclerosing cholangitis remains elusive, even if dysimmunity seems to be one of the contributors to bile duct damage. Despite this, immunosuppressants do not alter disease course. In this paper we describe the association of these two rare disorders, with an unexpected normalization of cholestatic enzymes following steroid treatment. This might hint a novel subtype of sclerosing cholangitis with a prevalent immunebackground, or a local manifestation of Takayasu arteritis.

1. Introduction

We describe here the unusual association between two rare disorders of unknown aetiologies: primary sclerosing cholangitis (PSC) and Takayasu arteritis (TA). The former is a chronic and progressing disorder of the bile ducts, the latter is a systemic vasculitis mostly affecting large arterial vessels. They can be both associated with Crohn disease, possibly suggesting an underlying immune-related aetiology. Immunosuppressive agents do not modify disease course in PSC but are fundamental for the treatment of TA [1]. In our clinical case we found an unexpected normalization of the liver function tests (LFTs) after starting immunosuppressive treatment for TA despite no improvement of the bile duct irregularities. To our knowledge, the association of TA and PSC is described in a single case report; however, information on the hepatic disease course after treatment begin are lacking [2].

1.1. Case description

A 38-years-old woman referred to our liver unit in 2013 after five years of unexplained chronic cholestasis (alkaline phosphatase (ALP) x 4–5 upper limit of normal (ULN), y-glutamyl transpeptidase (GGT) 3–4 x ULN) with normal bilirubin and mild transaminases increase (alanine aminotransferase (ALT) x 1.5ULN). Common causes of liver and biliary disease were ruled out and abdomen ultrasound did not show any sign of acute or chronic disease. For the persistence of the liver damage, in February 2015, the patient performed a magnetic resonance cholangiopancreatography (MRCP) and liver histology (Fig. 1) which were consistent with PSC. Specific IgG4 histologic staining was negative, as well as serum IgG4 concentration (0,18 g/L). Transient elastography revealed abnormal liver stiffness (10.4 kPa, IQR 0.99). A screening colonoscopy revealed typical histological features of ulcerative colitis with moderate activity in the descending colon treated with 5-aminosalicilates. She started ursodeoxycholic acid (20 mg/kg/day) after PSC diagnosis without any improvement of the cholestatic markers. After three years of UDCA therapy, an off-label attempt of add-on fenofibrate therapy (200 mg per day) did not show any improvement on biochemical cholestasis at 18 months and has been withdrawn.

In 2020, a thyroid ultrasound examination performed as follow-up for an episode of thyroiditis, showed a narrowing of carotid artery caliber. Thus, computed tomography angiography (CTA) was performed confirming vascular disease with ectasia of the ascending aorta, occlusion of 70% of the mid tract of subclavian artery and of 40–50% of the internal and external carotid arteries, respectively. Echocardiography evaluation showed aortic wall thickening and ectasia, mild pulmonary hypertension, and interatrial aneurysm. Positron emission tomography revealed an enhanced uptake along the whole wall of ascending aorta, thus making the diagnosis of TA. She was then started with prednisone (1 mg/kg/die), azathioprine (1.5 mg/kg/die), and acetylsalicylic acid

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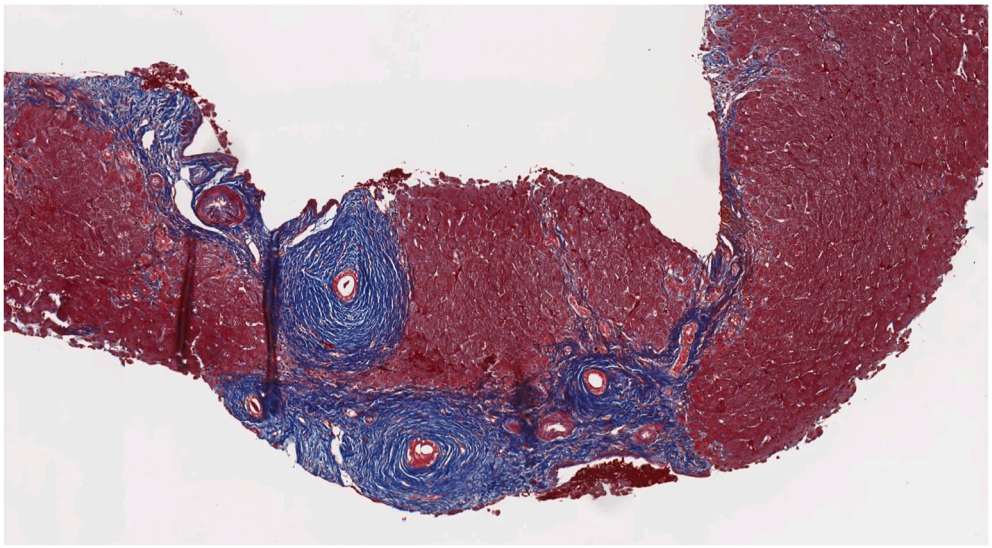

Fig. 1. A medium-sized portal tract with bile ducts surrounded by periductal onion skin concentric fibrosis (Masson's trichrome stain).

(100mg/die). After two months of immunosuppressant therapy both transaminases and ALP levels normalized from 559 UI/L to 49UI/L and remained persistently within range, while GGT significantly decreased to 1.5xULN, reaching normality one year later. Both transaminases and cholestatic markers remained within the normal range during follow-up, which is currently of nine months. No choleretic drugs were introduced. MRCP performed at seven months reported a substantial disease stability.

2. Discussion

We describe here a case of PSC associated to TA and with an unexpected response to steroid therapy. The coexistence between PSC and ANCA-associated vasculitis such as the Churg Strauss syndrome was described [3,4]. In addition, PSC diagnosis was already described in a patient with TA [2]. However, in this case we firstly describe a LFTs normalization under immunosuppression, which is not typical of PSC. Even if response to steroids primarily suggests an IgG4-related cholangiopathy, the negativity of biochemical and histological samples excluded this entity. Further, the coexistent of IBD supports the diagnosis of a PSC. The absence of radiological improvement may have occurred secondarily to irreversible fibrotic alterations as the natural consequence of chronic inflammation. Within this background, we might speculate that this represented a rare case of PSC responding to immune suppressants or a local manifestation of a systemic vasculitis. These findings might suggest that bile duct injury and inflammatory bowel disease might have the same etiological trigger of vasculitis (as shown in IgG4-related disease) and, when presented with this phenotype, immunosuppressive therapy may improve the LFTs. Of note, no signs of disease have been found in the arteries of the liver both in CT and at histology. However, a microvascular involvement of biliary tree causing ischemic fibrosis responsive to immunosuppressive therapy cannot be excluded.

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Specific author contributions

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Potential competing interests

None.

Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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