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A GIANT ANEURYSM OF PROPER HEPATIC ARTERY IN A CRYOGLOBULINEMIC PATIENT ON HEMODIALYSIS: A CASE REPORT.

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Running head: Proper hepatic aneurysm

ABSTRACT

Introductrion. Hepatic artery aneurysms (HAAs) are unusual vascular lesions often associated with many different pathological conditions. Most of reported cases are described in association with connective tissue diseases, such as polyarteritis nodosa and systemic lupus erythematosus.

Case report. We observed a 52-year-old man with hypertension and HCV-related cryoglobulinemia complicated by end stage renal disease on replacement therapy by hemodialysis. He was admitted to our hospital because of the worsening of blood pressure values (170/110 mmHg) associated to new onset abdominal pain. After an initial physical examination, that showed a periumbelical bruit associated to a pulsatile mass in right hypocondrium, an abdominal ultrasound was performed with evidence of aneurysms of both the right branch (diameter max 4,5 cm) and the left branch (diameter max 1.5 cm) of the hepatic artery. An abdominal CT study was also performed and it confirmed the diagnosis of right intrahepatic artery aneurysm with partially thrombosed area in its peripheral distal portion.

Discussion. Many different factors can contribute to the aneurysm formation in this patient. Vasculitic involvement due to cryoglobulinemic disease, therapy with steroid drugs, inflammatory state associated to HCV-related hepatitis, chronic kidney disease and replacement therapy by hemodialysis may all be involved in the development of the aneurysmatic hepatic lesion.

INTRODUCTION

Hepatic artery aneurysms (HAAs) are uncommon vascular lesions accounting for 20% of all splanchnic aneurysms [(1)]. Among the approximately 500 cases reported in literature, HAAs often occur in the common hepatic artery, whereas the proper hepatic artery is rarely affected. Most of reported cases are associated with trauma, infections, liver transplantations or connective tissue diseases with vasculitic involvement, mainly polyarteritis nodosa and systemic lupus erythematosus [(2,3)], but the association of HAA with cryoglobulinemic vasculitis has not been described. In addition, there are few data about the coexistence and the relationship between HAA and chronic kidney disease, especially in hemodialysis [(3)].

We observed a patient with HCV-related cryoglobulinemia and end-stage-renal disease on replacement therapy by hemodialysis who had a large pulsating mass in right hypocondrium due to a giant aneurysm of proper hepatic artery.

CASE REPORT

A 52-year-old man with an history of hypertension and HCV-related cryoglobulinemia complicated by end stage renal disease on replacement therapy since 2008 by hemodialysis was admitted to our hospital because of worsening of blood pressure values associated to new onset of continuous, pulsating abdominal pain (epigastrium and right hypochondrium area) and deterioration of overall clinical conditions.

At first examination, blood pressure was 170/110 mmHg, heart rate 88 bpm, temperature 36,3 °C and BMI 23,6 Kg/m^2. Physical examination revealed a liver protruding 1 cm from the rib and a pulsatile mass in right hypocondrium associated to a systolic periumbilical bruit, while the abdomen was markedly and diffusely painful on palpation, in absence of wall tension or peritoneal impairment. A palpable purpura affecting lower limbs was also present, in the absence of erythema or edema. Laboratory analysis showed hyporegenerative anemia (RBC: 3.290.000 c/mm^3; Hb: 8,1 gr/dl; HCT: 27,8%; MCV 84,5 fl) with lack of leukocytosis (WBC

3.450 c/mm^3), elevated erythrocyte sedimentation rate (60 mm/h), hypocalcemia (7,65 mg/dl), hyperphosphatemia (5 mg/dl) and hyperuricemia (8,30 mg/dl). Elevated serum creatinine values (7,4 mg/dl) and BUN levels (45 mg/dl) in absence of residual diuresis (<100 cc/24 h) were also present, associated with hypoalbuminemia (3,0 g/dl), hypoproteinemia (5,58 g/dl) and slightly increased levels of ALT/AST (64/75 U/L), with no other abnormal liver function test. A condition of compensated metabolic acidosis was also present (pH: 7.356; PCO_2: 33.5 mmHg; PO_2 52.7 mmHg; SO2: 84.3 %; cBase: -6.2 mmol/l, HCO_3^-: 18.3 mmol/l). Based on these examinations, a new antihypertensive therapy was started to reduce blood pressure, and an increased therapy with erythropoietin was established.

An abdominal ultrasound was performed in order to better investigate on the presence of periumbelical bruit and pulsatile mass in right hypochondrium. It showed a normodimensional liver with abnormal inhomogeneous echostructure, but aneurysms of both right branch (diameter max 4,5 cm) (*Figure 1*) and left branch (diameter max 1.5 cm) of the proper hepatic artery were found. Moreover, signs of parietal thrombosis were also evident.

For a more accurate study, an angiographic study was planned, but the patient had not given consent. Therefore, abdominal CT studies were carried out by means of a multidetector (64-slice) scanner, with 3D volume rendering, axial and multiplanar reconstructions in portal-venous phase, confirming the aneurysmatic nature of the lesion, its anatomical localizzation in the right hepatic artery (*Figure 2*) and the presence of a partially thrombosed area in its peripheral distal portion. Thus, the patient was sent to the Surgery Unit of our hospital for a further evaluation, in order to remove this hepatic lesion.

DISCUSSION

Several conditions have been associated with the presence of non traumatic HAA, such as infection, liver transplantation or connective tissue diseases [1,2]. However, there is no evidence in literature about the coexistence of HAA and cryoglobulinemia.

Whether this association is casual or causal it is still to be established. However, there are many evidences supporting the latter hypothesis.

First, numerous data emphasize the importance of vasculitic process to aneurysm formation, regardless of localization of the affected artery. In fact, HAA has been classically described in microscopic polyangiitis/panarteritis nodosa as expression of the underlying vasculitic phenomenon, and several studies have more recently shown increased association with systemic lupus erythematosus (SLE), Wegener's granulomatosis, Takayasu's arteritis and other pathological conditions such as Wiskott-Aldrich syndrome. This stresses a possible pathogenetic role of the vascular inflammation itself, especially when it involves small vessels, regardless of kind of vasculitis: arteritic process, in fact, would result in fibrinoid degeneration of collagen and destruction of tunica media, therefore promoting aneurysm formation [2,3]. These changes could also occur in cryoglobulinemia, in which it has been widely described an inflammatory involvement of small vessels [4].

Another mechanism of vascular wall damage, which leads to aneurysmal dilatation, might be represented by anti-inflammatory and immunosuppressive treatment required by cryoglobulinemia and other vasculitides [5], although conflicting data still exist in literature [6]. In fact, a sustained steroid therapy could result in medial necrosis because of connective tissue disintegration, therefore contributing to the creation of a *minoris resistentiae* area (more susceptible to local hemodynamic injury) and to the growth of the aneurysm itself [3,5].

Besides, an important aetiopathogenetic role in the HAA genesis could be played by the concomitant presence of chronic kidney disease, especially in hemodialysis treatment: in this condition, many classical factors are associated with vessel wall damage and vascular remodeling, in particular hypertension and widespread atherosclerosis.

Furthermore, it is well known that an increased systemic inflammatory status is found in patients with end stage renal disease: in this regard, several studies have underlined in this condition an increase of inflammatory cytokines and growing factors such as epidermal

growth factor (EGF) and, above all, hepatocyte growth factor (HGF), which has shown important new antifibrotic properties on the kidney and has been related with the development of arterial dilatation [7,8]. Systemic pro-inflammatory status seems to be directly implicated in cardiovascular system modification and vessels wall remodeling, having been repeatedly associated to aneurysm development in many arteries [9].

However, an augmented inflammatory status is also a feature of chronic inflammatory hepatic diseases, such as HCV-related hepatitis complicated by cryoglobulinemia: in these conditions, augmented release of inflammatory cytokines and growth factors, in particular HGF, seems to improve hepatic cellular regeneration and revascularization process [10], but unfortunately it may result in a vessel wall weakening, therefore promoting aneurysm development.

In conclusion, HAA presence in our patient seems to have pathogenetic and pathophysiological connections with the various diseases of the patient. Further studies are necessary to confirm the mechanisms we proposed to explain this unusual and abnormal vascular finding.

CONFLICT OF INTEREST

The authors declare that they have no conflict of interest

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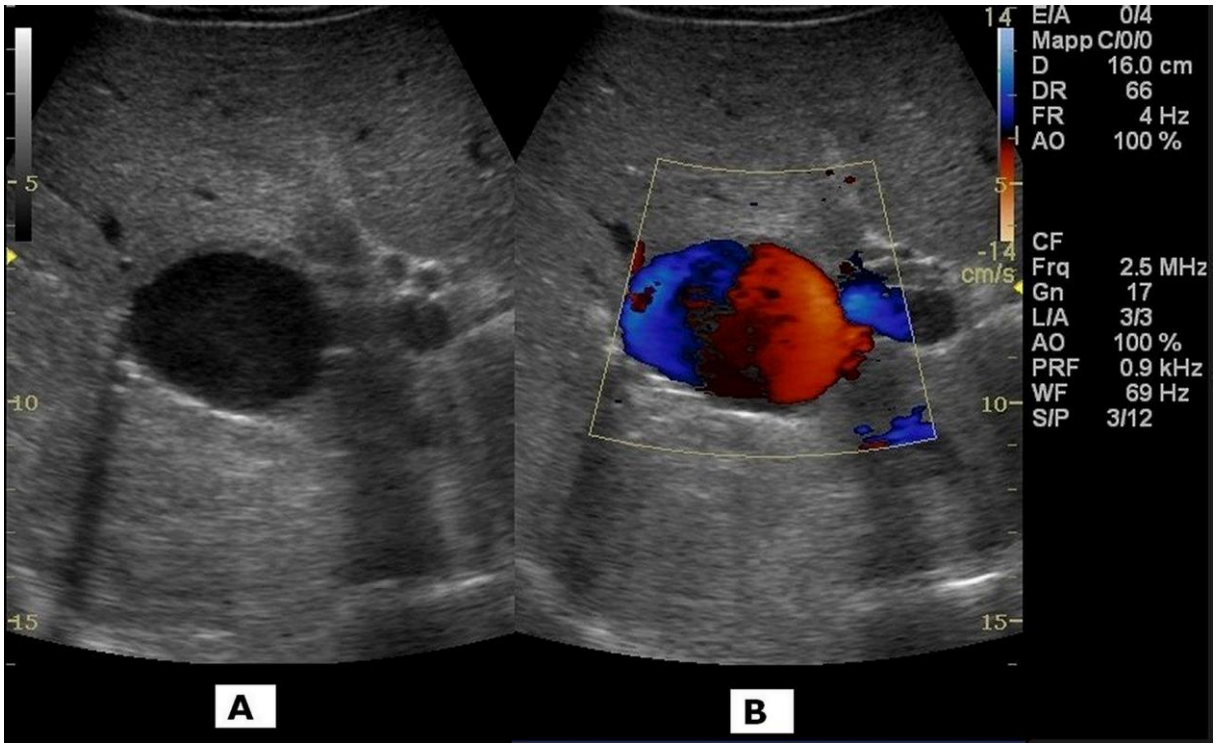

Figure 1. Ultrasonographic examination of the upper abdomen (GE Logiq P5 PRO instrument with a 4 MHz transducer, operating at 2.5 MHz for Doppler analysis) detected an anechoic space-occupying lesion of the liver, with parietal enhancement, measuring 4 x 4.5 cm (*Figure 1a*). Color-Doppler integration of this mass showed a "korean-flag pattern" suggestive of a low-flux aneurysm (*Figure 1b*).

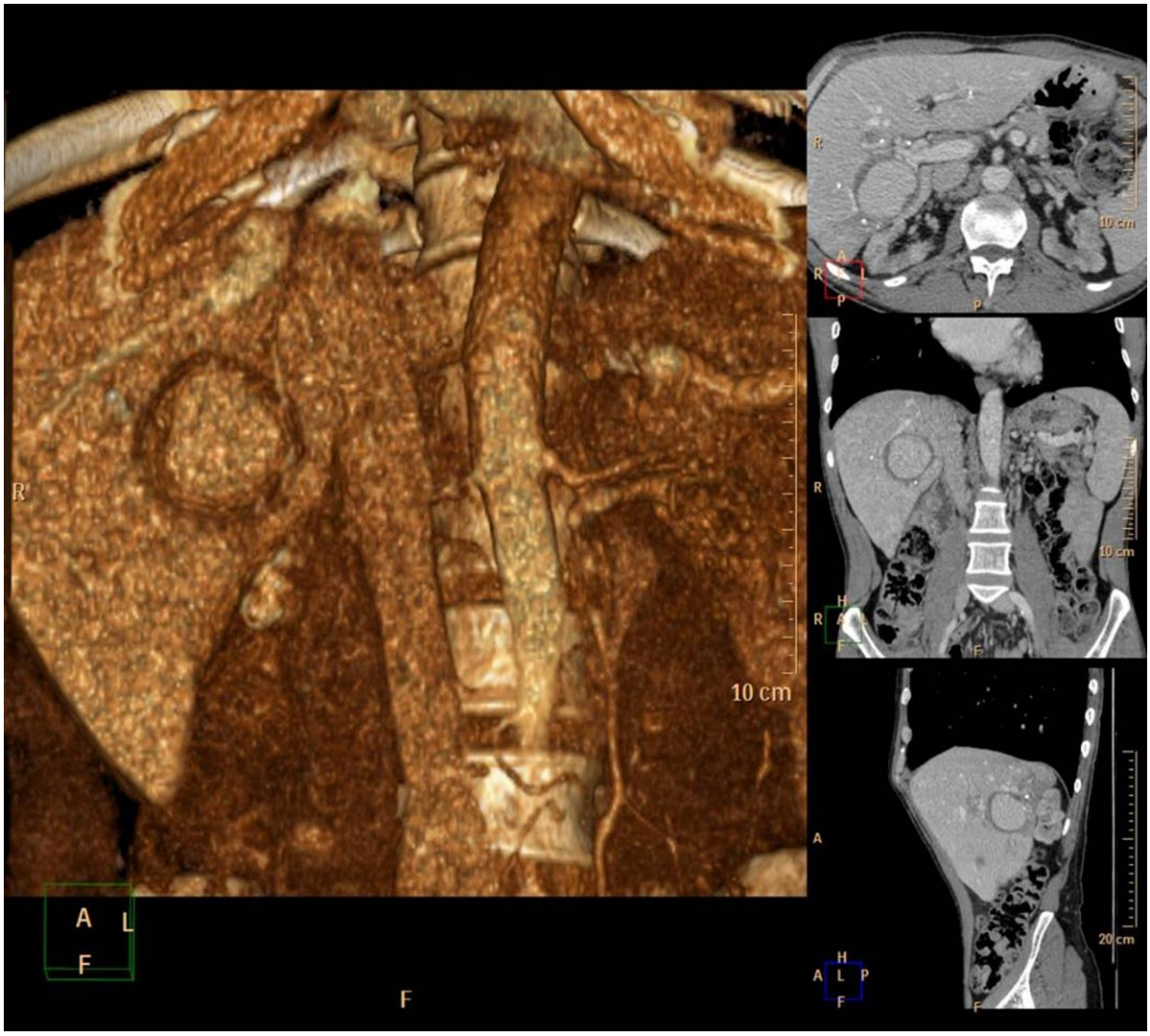

Figure 2. CT studies were performed by means of a multidetector (64-slice) Philips Brilliance scanner (Royal Philips Electronics, Andover, MA, USA) with the acquisition of non-enhanced and contrast-enhanced images and subsequent 3D volume rendering, axial and multiplanar reconstructions in portal-venous phase. See text for further explanations.