

Acute Ischaemic Hepatitis Secondary to Acute Portal System Thrombosis Triggered by Diabetic Ketoacidosis: Rare Presentation of Acute Ischaemic Hepatitis

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ABSTRACT

Hypotension, hypoxia or hypotension and hypoxia together may lead to ischaemic hepatitis; hypotension is often as a result of cardiovascular diseases. Ischaemic hepatitis not due to the cirrhotic process or malignancy but due to acute thrombosis of the portal venous system is rare. In this article, we present a case of acute ischaemic hepatitis due to an acute thrombus developing after a ketoacidosis coma which was thought to have triggered this event. Other reasons which could have triggered this event, such as a thrombophilia and cirrhosis or malignancy, were excluded.

Keywords: Diabetic ketoacidosis, ischaemic hepatitis, portal thrombus

Hepatitis Isquémica Aguda Sistema Secundaria a la Trombosis Portal Aguda Desencadenada por Cetoacidosis Diabética: una rara Manifestación de la Hepatitis Isquémica Aguda

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RESUMEN

La hipotensión, la hipoxia, o la hipotensión y la hipoxia juntas, pueden conducir a la hepatitis isquémica. La hipotensión suele ser a menudo consecuencia de enfermedades cardiovasculares. La hepatitis isquémica que no se debe a un proceso cirrótico o una malignidad, sino que se produce como consecuencia de una trombosis aguda del sistema venoso portal es una rara manifestación. En este artículo, presentamos un caso de hepatitis isquémica aguda debido a un trombo agudo desarrollado después de un coma de cetoacidosis, que se pensó haber sido la causa desencadenante. Otras razones que pudieran haber desencadenado esta manifestación – tales como una trombofilia, una cirrosis, o una neoplasia – fueron excluidas.

Palabras claves: Cetoacidosis diabética, hepatitis isquémica, trombo portal

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INTRODUCTION

Venous thromboembolism is a rare complication of diabetic ketoacidosis (1). Ischaemic hepatitis is characterized by cir-

culational failure of the liver. Liver enzymes may be elevated up to 75 or 100 times from the normal ranges and these elevations may persist for seven to 10 days. Hypotension, hypoxia or hypotension/ hypoxia together may proceed to ischaemic hepatitis. The reason for hypotension is often cardiovascular diseases (2). Impaired perfusion from decreased cardiac output may be associated with acute hepatocellular necrosis with marked elevations in serum aminotransferases. Cardiogenic ischaemic hepatitis (“shock liver”) may ensue following an episode of profound hypotension in patients with acute heart failure.

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Acute hypoxic hepatitis most commonly arises in the context of profound systemic hypotension from acute cardiopulmonary collapse after myocardial infarction, exacerbation of heart failure or pulmonary embolism (3). Here we report a case with acute ischaemic hepatitis due to portal system thrombosis triggered by diabetic ketoacidosis, which has not been reported in the literature so far according to our knowledge.

CASE REPORT

A 44-year-old woman with a known history of diabetes experienced pruritus and fatigue and attended our hospital emergency department. She was not taking any drugs for diabetes. One month before attending hospital, the patient was advised to go to the endocrinology department for treatment of her diabetes. The patient attended the emergency department with the complaint of nausea and vomiting and was hospitalized with the diagnosis of diabetic ketoacidosis. Her blood pH level was 7.2; blood glucose was 430 mg/dL. Haemoglobin level was 9 g/dL, white blood cell count was 4400/mm³, neutrophil count was 3300/mm³, sedimentation rate 40 mm/hour, platelet count was 450 000/mm³. Thrombophilia factors were negative (Lupus anticoagulant negative, antithrombin III levels were within normal limits, factor 5 Leiden mutation (activated protein C resistance) was negative and the levels of factor 2, 8, 9, 10, and protein C and protein S were normal. Factors which may cause acute viral hepatitis (anti-HAV IgM, anti-HBc IgM, anti-HCV, anti-CMV IgM, antitoxoplasma IgM, Anti-rubella IgM, herpes simplex virus IgM) were all negative. Also, Jak 2 mutation was negative. Here transaminase levels (AST: Aspartate aminotransferase, ALT: Alanine aminotransferase) were within normal ranges at first sight but increased with accompanying abdominal pain (ALT: 2000 IU/mL and AST: 1800 IU/mL). The patient's cholestasis enzymes and direct bilirubin levels were increased slightly. Requested abdominal ultrasonography (USG) revealed gallbladder sludge and minimal dilatation in the proximal choledochal duct. In order to explain the massive increase of aminotransferase levels, a magnetic resonance cholangio-pancreatography examination was requested. There were thrombi in the portal venous system and in the splenic vein.

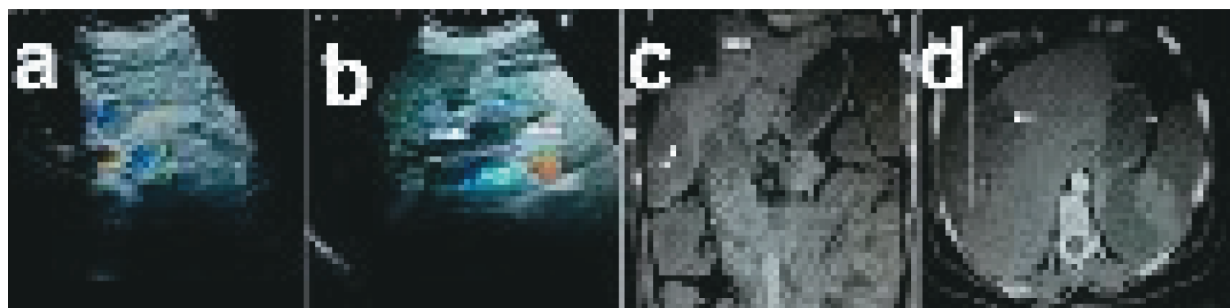
Additionally, multiple hypo-intense areas in the spleen and in the liver were seen. These lesions in the liver parenchyma could be also a sign of multiple metastases. For defi-

nite diagnosis portal, venous Doppler USG and dynamic liver computerized tomography (CT) scan were requested. With the Doppler USG examination, a widespread thrombosis was detected in the portal venous system. Moreover, there were multiple hypo-intense lesions which were consistent with multiple infarct areas in the liver and spleen (Fig. 1a, b). In order to clarify whether there were intestinal infarcts, and to understand the extensiveness of thrombosis in the portal venous system, the patient underwent a dynamic (triphasic) liver CT scan. The dynamic CT scan revealed that there was no sign of intestinal infarcts, there were multiple infarct areas in the liver and spleen. There was widespread multiple thrombi in the portal system and collateral vascularity in the portal confluence (Fig. cd).

With the diagnosis of ischaemic hepatitis, parenteral anticoagulation was started. The patients activated partial thrombin time, international normalized ratio (INR) and liver enzymes were monitored. Her liver enzymes returned to normal values and symptoms resolved within next two weeks. No relapse was observed in the three consecutive monthly checks of the patient. The patient is still on follow-up with oral anticoagulant.

DISCUSSION

Abdominal pain is a frequent symptom in patients with diabetic ketoacidosis. Often, it is attributed to metabolic acidosis, but other reasons may also trigger abdominal pain. Pant and colleagues reported in a patient with visceral vein thrombosis which has been triggered by diabetic ketoacidosis (4). Also, Gill and colleagues reported on a patient with axillary vein thrombosis during diabetic ketoacidosis (5). Our patient had experienced abdominal pain and had been treated in the endocrinology department for diabetic ketoacidosis. Despite normalization of glucose and metabolic parameters her abdominal pain persisted and liver enzymes increased. She was diagnosed with ischaemic hepatitis. Ischaemic hepatitis, a relatively infrequent disorder often follows episodes of hypotension or acute heart failure. Diseases which may cause hypotension like myocardial infarction, arrhythmia, sepsis, trauma and extensive burn reactions may lead to ischaemic hepatitis (6). Our patient did not experience any heart failure, myocardial infarction, arrhythmia, sepsis, trauma or burn reactions before developing ischaemic hepatitis. The only accompanying rea-



Figs: (a,b,c,d): Doppler USG images (a,b), and CT images (c,d) of the patient.

son was diabetic ketoacidosis coma. First line choice for diagnosing portal venous thrombosis is Doppler USG (7). The absence of flow partially or complete and cavernous transformation can be observed by Doppler USG (8), and the differentiation of benign or malignant lesions can also be observed (7).

Tessler and colleagues have reported that the sensitivity and specificity of this imaging technique for diagnosing portal venous thrombosis are 89 and 92 %, respectively (9). Negative predictive value has been reported as 0.98 and positive predictive value as 0.62. Doppler USG is a valuable technique for evaluating the portal vein patency, and if the portal vein flow can be seen, no other techniques are required (8). Our patient's Doppler USG images revealed heterogeneous-patchy areas (infarct areas) in the periphery of the liver parenchyma and no flow could be detected in the portal vein, superior mesenteric vein and in the splenic vein. There were echogenic thrombi in the lumens of the portal system and branches. There were collateral vascular images in the portal hilus and all these findings were consistent with the literature. Acutely developed ascites and minimal splenomegaly were also observed. These findings can be observed in all hepatitis patients. Our patient had also gallbladder sludge on ultrasound examination. The second choice for diagnosing portal venous thrombosis is CT in the portal phase (6). Our patient's dynamic CT revealed extensive hypodense areas in the liver which were especially dominant on the anterior segment of the right lobe. There were no mass lesions. There was no contrast uptake in these areas, and hypodense areas in the portal vein and splenic vein which may be consistent with thrombi were observed. The splenic central area showed normal pattern while medial and lateral areas showed hypodense areas with contrast phase imaging. These CT findings in the liver and spleen suggested multiple infarct areas and were consistent with the literature. Acute portal thrombosis is a severe clinical picture which may lead to fulminant liver insufficiency and death. Other reasons for thrombophilia and hypercoagulable states should be kept also in mind in such patients. All possible causes for thrombophilia and hypercoagulable states were excluded in our patient. Also, other "shock liver" (hypoxia and ischaemic

causes), acute viral hepatitis, acute toxic hepatitis and reasons for intra/extrahepatic cholestasis were also excluded.

The optimum treatment is anticoagulation for these patients. We have also used first parenteral and then oral anticoagulants as described in the literature. In conclusion, diabetic ketoacidosis is a severe clinical picture which may cause a lot of pathophysiologic disturbances and multiple organ failures. Our patient experienced an acute ischaemic hepatitis due to portal vein thrombosis which may have been triggered by diabetic ketoacidosis. Especially if poorly controlled, diabetic patients can develop diabetic ketoacidosis and experience an acute abdomen from a portal vein thrombosis, and subsequent developing acute ischaemic hepatitis. If physicians are alert to this, it may allow early diagnosis and thus, improve patient survival. To the best of our knowledge, this patient is the first case of ischaemic hepatitis due to portal vein thrombosis triggered by diabetic ketoacidosis.

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