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Case Report

CASE REPORT

Acute liver injury in a patient with adult-onset Still's disease—the challenge of differential diagnosis

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Abstract

In addition to the cardinal symptoms of fever, rash and arthralgia, liver involvement in patients with adult-onset Still's disease (AOSD) has been described. However, acute liver injury in AOSD patients can have various other causes: it can be a result of an AOSD-induced macrophage activation syndrome or be associated to the drugs given for the underlying diseases and symptoms. Differential diagnosis can therefore be challenging. We here present a case of a 32-year-old male with acute liver injury following the initial diagnosis of AOSD to discuss the possible underlying reasons.

INTRODUCTION

Recently, it has been demonstrated that liver dysfunction is one of the most prevalent features of patients with macrophage activation syndrome (MAS) induced by adult-onset Still's disease (AOSD) [1]. Moreover, liver involvement has been described as a direct complication of AOSD [2, 3]. In addition, other differential diagnosis needs to be ruled out.

CASE REPORT

We here report the case of a 32-year-old Caucasian male who was diagnosed with AOSD following presentation with pharyngitis, fever ≥39°C, rash, arthralgia and leucocytosis, all of which belong to the classification criteria for AOSD [4]. He was started on high-dose prednisolone (1 mg/kg/d) and anakinra (100 mg/d). A total of 21 days after the initiation of prednisolone and 9 days after the initiation of anakinra the patient presented at our hospital with acute liver injury. Upon admission, he showed highly elevated aminotransferases (AST 1139 U/l, ALT 2617 U/l, upper limit of normal [ULN] 49 U/l) and lactate dehydrogenase (1920 U/l, ULN 249 U/l) as well as hyperferritinemia(71 900 ng/ml, ULN 400). However, coagulation parameters, as indicators of liver function, were preserved, and no signs of hepatic encephalopathy were present. Following admission, the patient had non-remittent fever and reappearance of the arthralgia. Because drug-induced liver injury (DILI) could not be ruled out, all medications, including ibuprofen, which he had been taking per request for the arthralgia, were discontinued. Other causes for liver injury such as viral hepatitis, autoimmune hepatitis, cholestatic, metabolic or ischemic hepatic disorders were ruled out. The further work-up included liver biopsy and a bone marrow examination. Liver histology showed a mild chronic active hepatic inflammation with perivenously accentuated necrosis and portal inflammation without relevant interface hepatitis and was classified as most likely drug-induced hepatic injury. There were no signs of a relevant infiltration with plasma or eosinophilic cells, no cholestasis and no fibrosis. The bone marrow analysis, however, revealed hypercellularity with a left shift of haematopoiesis and a strongly intensified granulopoiesis. In addition, hemophagocytosis was demonstrated. Based on these findings, AOSD-induced MAS was suspected and the patient was treated with high-dose prednisolone and later on a monoclonal antibody directed against interferon-1ß

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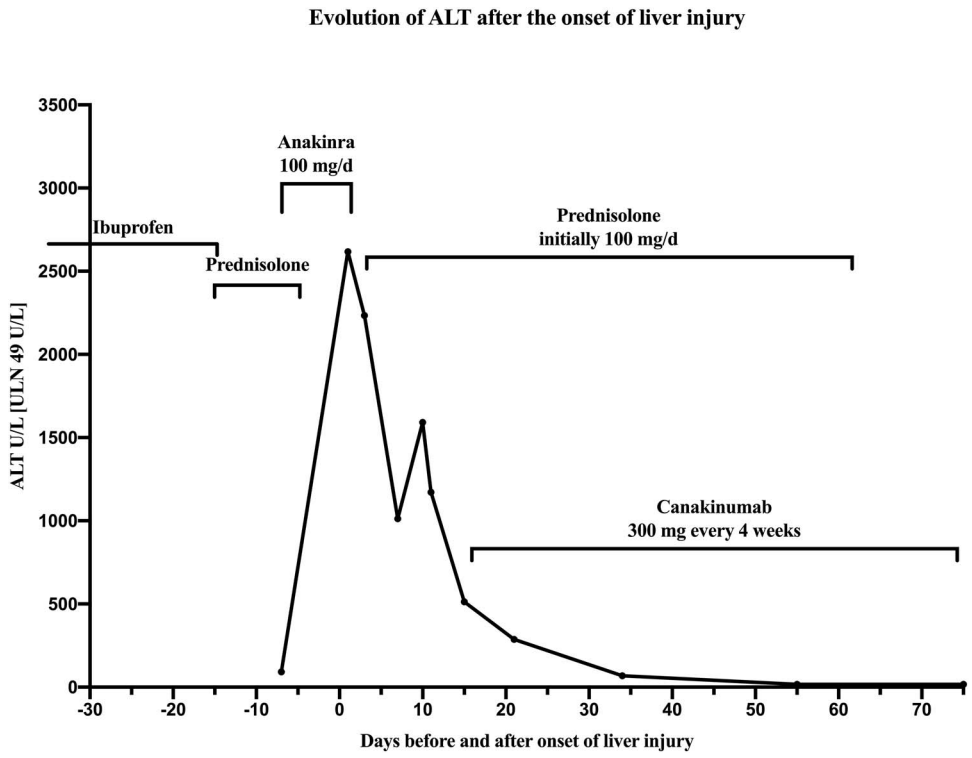

Figure 1: Evolution of ALT after the onset of liver injury. The figure demonstrates the evolution of aspartate aminotransferase (ALT) in this patient with acute liver injury after the diagnosis of AOSD. Treatment with anakinra had been started 9 days before the onset of liver injury and was continued until the onset of liver injury. Concomitant medication before liver injury was prednisolone with an initial dosage of 75 mg daily from Days 16 to Day 3 before liver injury and Day 41 to Day 13 before liver injury. After the onset of liver injury he received a pulse therapy with prednisolone and then was started on canakinumab.

(canakinumab). After the initiation of prednisolone, aminotransferases started to decline together with a significant reduction of ferritin (Fig. 1). However, the patient experienced persisting symptoms, in particular fever, which decreased upon the initiation of canakinumab accompanied by a further decline of aminotransferases. A total of 54 days after, the onset of liver injury the patient reached remission.

DISCUSSION

This case demonstrates the challenge of differential diagnosis of acute liver injury in patients with AOSD. Liver injury can be due to the underlying disease itself or to AOSD-induced MAS [2, 5]. Moreover, DILI due to the immunosuppressive treatment is another diagnosis to be considered. In this respect anakinra, an interleukin 1 receptor antagonist, has been associated with acute hepatic injury [6]. Identifying the cause of liver injury has major implications for the individual patient: intensifying immunosuppressive treatment is necessary in the case of MAS-induced liver injury, whereas suspending all unnecessary medication is the consequence in the case of DILI. As for the reported case, DILI was initially suspected due to the temporal association with the institution of anakinra and the histopathological features present in the liver biopsy. However, hyperferritinemia, persisting fever and the finding of hemophagocytosis in the bone marrow analysis directed the diagnosis towards MAS [5, 7]. Since the patient was initiated on corticosteroid treatment shortly after the onset of liver injury, which can have beneficial effects on the evolution of DILI patients as well [8, 9], the final diagnosis remains equivocal. Importantly, DILI secondary to newer biologicals used for immunosuppression is still not well understood and clinical pictures may vary from DILI due to conventional medication, and thus DILI is often not identified until liver injury has become severe. In conclusion, acute liver injury in patients with AOSD can have various reasons including DILI, which should be considered in such patients, especially if immunosuppressive or anti-inflammatory treatment has already been initiated.

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AUTHORS' CONTRIBUTIONS

All authors contributed to the study conception and design. Material preparation, data collection, analysis and writing of the first draft were performed by Sabine Weber. All authors read and approved the final manuscript.

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CONFLICT OF INTEREST STATEMENT

None declared.

ETHICS APPROVAL

All procedures were in accordance with the ethical standards of the responsible committee on human experimentation (Faculty of Medicine, LMU Munich; project number 55–13) and with the Declaration of Helsinki.

CONSENT TO PARTICIPATE

Written informed consent for participation and publication was obtained from the patient.

GUARANTOR

Sabine Weber and Alexander L. Gerbes.

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