Rare disease

Allopurinol-induced hepatomegaly

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Summary

Allopurinol has long been recognised as a cause of hepatotoxicity; however, severe side effects remain rare. We report a case of allopurinol-induced hepatomegaly causing abdominal symptoms in an elderly woman after long-term allopurinol use.

BACKGROUND

Allopurinol has been in clinical use since 1962 for the treatment of hyperuricaemia and its associated complications, most commonly gout. Its use is associated with a number of mild adverse reactions including rash, gastrointestinal upset, fever and arthralgia. More rarely allopurinol causes severe side effects such as hepatotoxicity, presenting as an acute hypersensitivity reaction with fever, arthralgia and eosinophilia. Acute hepatitis and fulminant hepatic failure may also occur.¹

We report a case of allopurinol-induced hepatomegaly found incidentally after admission to hospital following a fall.

CASE PRESENTATION

An elderly lady presented to accident and emergency after a fall at home. Her medical history included atrial fibrillation, hypertension, chronic renal impairment and gout.

Admission haematological investigations showed a normocytic anaemia with a haemoglobin of 7.8 g/dl, mean cell volume 90.2 fl and chronic renal impairment with

creatinine 152 mmol/l and urea 14.2 mmol/l. Haematinics revealed a picture of iron deficiency. The patient complained of long-standing postprandial nausea and abdominal bloating worsening over time. Examination revealed fullness in the epigastrium and hepatomegaly.

INVESTIGATIONS

Investigations were undertaken to reveal any sinister pathology underpinning the anaemia. Upper gastrointestinal endoscopy, myeloma screen and blood film were normal. The patient underwent an unenhanced CT of the abdomen and pelvis as it was felt colonoscopy would be poorly tolerated (see figure 1). CT demonstrated gross hepatomegaly with enlargement of both right and left lobes of the liver (see figure 2). Multiple calcified gallstones but no evidence of associated inflammation were also identified. Spleen, pancreas and adrenals were normal. Ultrasonography was recommended by the reporting radiologist and this corroborated the finding of gallstones and gross hepatomegaly. No masses were identified and the

Figure 1 Axial CT image of abdomen demonstrating hepatomegaly.

Figure 2 Coronal section of CT abdomen and pelvis demonstrating hepatomegaly.

liver contour was normal. No intrahepatic or common bile duct dilatation was seen.

A liver screen demonstrated normal liver function and clotting, and negative serology for viral hepatitis, ferritin, α -feta protein and caeruloplasmin. Echocardiography revealed mild left ventricular hypertrophy with overall good systolic function, normal right ventricle, moderate-to-severe mitral regurgitation and mild tricuspid regurgitation.

Ultrasound-guided liver biopsy was performed, and showed a mild chronic inflammatory infiltrate of mainly lymphocytes and histiocytes. The portal areas showed rounded spaces consistent with fat vacuoles and fibrin-ring granulomas. Further histological testing did not reveal any other hepatic pathology, storage disease or infection, but allopurinol use was specifically suggested in the histology report as a potential cause due to the presence of fibrin-ring granulomas.

OUTCOME AND FOLLOW-UP

The patient had been prescribed allopurinol after an episode of gout approximately 5 years prior to this admission. Allopurinol was subsequently stopped and abdominal symptoms resolved.

DISCUSSION

Allopurinol hepatotoxicity has been recognised since its introduction although it remains a rare side effect. The underlying mechanism of insult remains unknown and indeed the histopathological findings and pathology of each case seems to be variable.² Fibrin-ring granulomas have been associated with allopurinol-induced hepatitis, although other differential diagnoses should be investigated, including infection and malignancy.^{3–4} Classically granulomatous hepatitis takes a more acute course with onset within 2–6 weeks of starting allopurinol. Typically patients are unwell and feverish, with tender hepatomegaly and deranged liver enzymes.⁶ Our patient presented with hepatomegaly and fibrin-ring granulomas on biopsy, but no associated impairment of hepatic function; seemingly a more chronic picture. Lidsky and Sharp⁷ observed increased incidence of allopurinol-induced hepatotoxicity in patients with renal insufficiency, a finding relevant to our case and indeed a large proportion of the elderly population. Allopurinol is commonly prescribed in general

practice and patients suffering adverse effects may present acutely to the hospital. The range of clinical effects and the variable course this rare complication can follow should be borne in mind especially when reviewing elderly patients whose clinical response may often be atypical.

The initial patient presentation with advanced age, anaemia and hepatomegaly seemed highly likely to herald an underlying malignancy. However, on this rare occasion it was less Occam's razor and more Hickham's dictum.

Learning points

- ▶ Allopurinol-induced hepatotoxicity is a rare but potentially modifiable disease.
- ▶ Characteristic histological findings may be present, such as fibrin-ring granulomas.
- ▶ Drug-induced hypersensitivity reactions and side effects should be considered in all patients with metabolic abnormalities, even with longstanding medications, due to the changing metabolism of older people.

Competing interests None.

Patient consent Obtained.

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Please cite this article as follows (you will need to access the article online to obtain the date of publication).

Childs L, Dow C. Allopurinol-induced hepatomegaly. *BMJ Case Reports* 2012;10.1136/bcr-2012-007283, Published XXX

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