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CASE REPORTS

Cholangiocarcinoma, renal cell carcinoma and parathyroid adenoma found synchronously in a patient on long-term methotrexate

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Abstract
Cases of patients developing lymphoma and cutaneous neoplasms after long-term methotrexate therapy are well documented in the literature; however, there are no reported cases of other neoplasms resulting from methotrexate therapy. A 52-year-old woman who had been on methotrexate for 9 years for psoriatic arthritis was found to have abnormal liver function tests on screening. Investigation with ultrasound, CT scanning and MRCP showed a hilar cholangiocarcinoma and a synchronous right renal tumour. A left hemi-hepatectomy extended to segments 5 and 8 with the formation of a hepaticojejunostomy was performed for a poorly differentiated infiltrative hilar cholangiocarcinoma. This was combined with a right radical nephrectomy for a T1 renal cell adenocarcinoma. Postoperative vomiting was subsequently found to be due to hypercalcaemia and primary hyperparathyroidism. A parathyroid adenoma was later excised. It seems likely that treatment with methotrexate was causal in the development of these three non-cutaneous neoplasms-two malignant and one benign.

Key Words: *Methotrexate, cholangiocarcinoma, renal cell adenocarcinoma, parathyroid adenoma*

Case report

An asymptomatic 52-year-old woman was found to have abnormal liver function tests (LFTs) on screening after 9 years' treatment with methotrexate (15 mg/week) for psoriatic arthritis. Physical examination was unremarkable. Ultrasound scanning showed dilated intrahepatic ducts in the left liver. Her LFTs revealed: bilirubin 14 μmol/L (normal <17), alkaline phosphatase 141 U/L (normal 25–120), AST 60 U/L (normal <40) and CA 19–9 66 U/L (normal 0–60). CT scanning showed dilated left-sided and right anterior section ducts. In addition there was a lesion in the right kidney. Magnetic resonance cholangiopancreatography was suggestive of a hilar cholangiocarcinoma (Figure 1). Percutaneous biopsy of the right kidney revealed a renal cell adenocarcinoma.

At operation a Klatskin tumour involving the left hepatic and right anterior section duct was found which was also invading the right branch of the portal vein. A left hemi-hepatectomy with sleeve excision of the right portal vein (Figure 2) was performed. Reconstruction included a right posterior section duct hepaticojejunostomy. Roux-en-Y and a right radical nephrectomy were carried out.

Persistent postoperative vomiting and abdominal pain were investigated extensively, looking for a surgical cause. Eventually it was attributed to an elevated calcium of 3.5 mmol/L (normal 2.10–2.55) associated with an elevated parathyroid hormone level of 17.8 pmol/L (normal 0.5–5.5). Treatment with intravenous pamidronate was commenced. A nuclear medicine scan showed a large left inferior parathyroid gland which was excised. The calcium level decreased from 3.15 mmol/L to 2.5 mmol/L on the first postoperative day.

Histological examination showed a T1 renal cell adenocarcinoma, a poorly differentiated infiltrative hilar adenocarcinoma and a parathyroid adenoma. Chemotherapy with combination epirubicin, cisplatinin and 5-fluorouracil was given for the cholangiocarcinoma. She remains well 24 months later.

Discussion

The use of methotrexate in the second-line treatment of psoriasis [1] may be limited by hepatotoxicity [1,2]. Coleiro and Mallia [3] studied patients on

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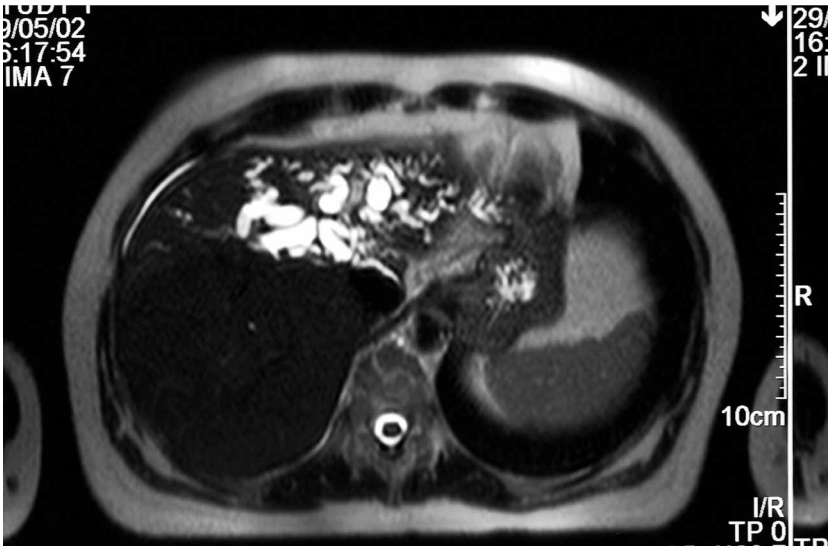

Figure 1. MRCP scan showing dilatation of the left intrahepatic ducts.

methotrexate and found asymptomatic elevation of liver enzymes in 57%.

Such elevations are often transient, do not predict liver damage and frequently return to baseline levels even if methotrexate is continued. Dufour and Kaplan [4] feel that such elevations are not a reason to stop treatment and that consideration should be given to a liver biopsy only in those patients whose serum aminotransferase values remain elevated for more than 2 months.

Several studies have documented the development of squamous cell carcinomas in psoriatic patients on psoralen with ultraviolet A (PUVA) and methotrexate [5]. Zumtobel and co-workers [6] showed that methotrexate was an additional factor independent of PUVA that contributed to squamous cell carcinoma development, and they advised caution in starting methotrexate in patients who had been exposed to high doses of PUVA. While lymphoma resulting from methotrexate treatment is well documented in the literature [7], a Medline search did not reveal any reports of non-cutaneous methotrexate-induced carcinogenesis other than lymphoma. The case described appears to demonstrate the development of multiple neoplasms with long-term methotrexate use.

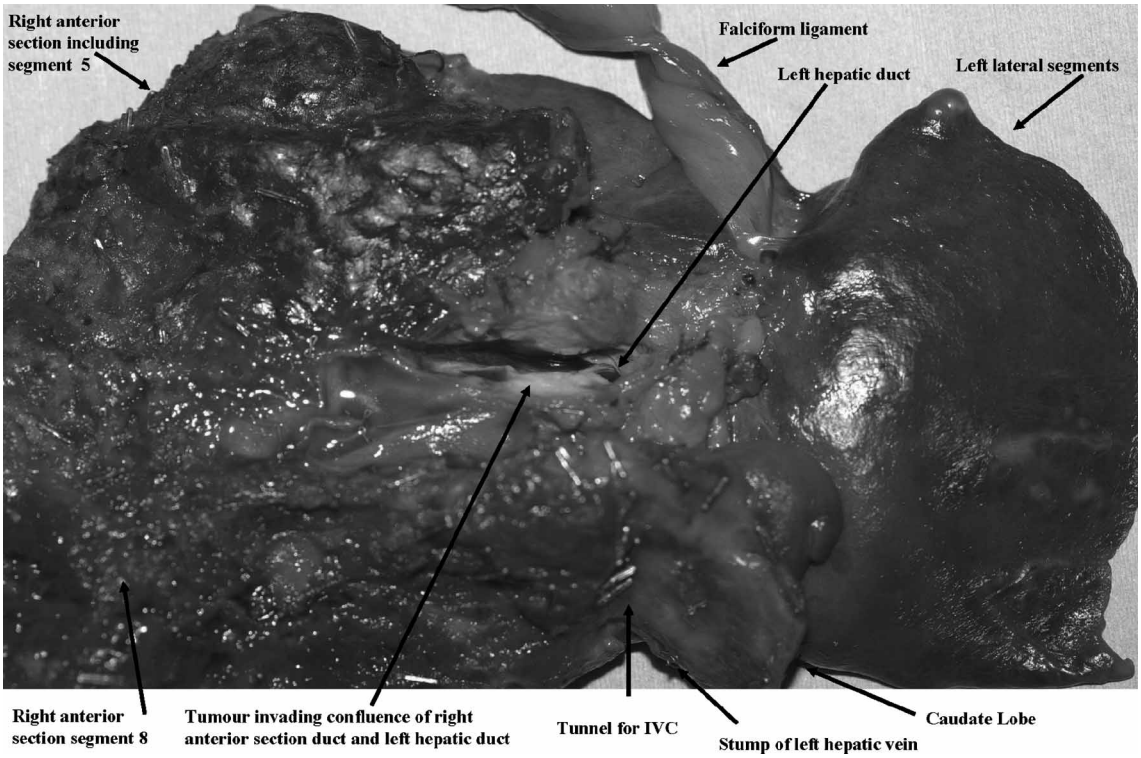

Figure 2. Hilum and underside of extended left hepatectomy specimen.

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Idiopathic fibrosing pancreatitis associated with ulcerative colitis

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Abstract
Idiopathic fibrosing pancreatitis has been associated with Sjögren's syndrome, primary biliary cirrhosis and primary sclerosing cholangitis. This condition frequently develops in childhood and youth, and has also been related to ulcerative colitis and pericholangitis. Pancreatic complications have been rarely described as systemic complications of ulcerative colitis. A 25-year-old man presented with epigastric pain and jaundice. Abdominal ultrasonography, computed tomography (CT), magnetic resonance cholangiopancreatography (MRCP) and endoscopic retrograde cholangiopancreatography (ERCP) revealed a diffuse enlargement of the pancreas, filiform distal stenosis of the common bile duct and intrahepatic bile ducts, and pancreatic duct dilatation. At operation, a rock-hard and nodular pancreas was noted. Cholecystectomy and Roux-en-Y hepaticojejunostomy, with an access loop, was successfully performed. Idiopathic fibrosing pancreatitis should be considered in young patients with obstructive jaundice, especially those affected with chronic inflammatory or autoimmune diseases. Glucocorticoid therapy would be the first-line treatment, although many patients require operation.

Key Words: *Idiopathic fibrosing pancreatitis, autoimmune pancreatitis, chronic pancreatitis, ulcerative colitis*

Introduction

Extra-colonic complications of ulcerative colitis can involve many organs, including liver, biliary tract, joints, eyes and skin. We present a case of obstructive jaundice secondary to a fibrosing pancreatitis associated with ulcerative colitis; complete symptomatic recovery followed surgical treatment.

Case report

A 25-year-old man was admitted with epigastric pain and jaundice. He had a 4-year history of ulcerative colitis demonstrated by colonic biopsy. Acute attacks of colitis had been treated with 5-aminosalicylate. There was no family history of pancreatic disease, hepatic disorders or inflammatory intestinal disease. Laboratory data revealed a total bilirubin of 195 μmol/L (normal <18), an alkaline phosphatase of 1010 U/L (normal <129), a gamma-glutamyl transpeptidase of 214 U/L (normal <61), SGOT of 184 U/L (normal <37) and SGPT of 502 U/L (normal <40). Hepatitis serology was negative. IgG levels were normal.

Ultrasonography revealed dilatation of the main bile duct and pancreatic duct. An ill-defined nodule was seen at the pancreatic head. Abdominal CT revealed intrahepatic and extrahepatic dilatation of the upper biliary tract, plus pancreatic duct dilatation and a homogeneous enlargement of the head of pancreas (Figure 1). The patient underwent endoscopic retrograde cholangiopancreatography (ERCP) (Figure 2) and magnetic resonance cholangiopancreatography (MRCP) (Figure 3), which revealed a filiform distal

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