Polyarteritis nodosa (PAN) is a systemic necrotising vasculitis that affects the small- and medium-sized arteries. Multifocal aneurysmal formation in the renal, hepatic, and mesenteric vasculature is a hallmark of this condition, and spontaneous aneurysmal rupture may occur, resulting in life-threatening haemorrhage. We describe a 42-year-old man who initially presented with fever of unknown origin. A diagnosis could not be reached at that time despite extensive investigations. The fever subsided spontaneously after 8 weeks, and the patient remained well for 6 years until he was admitted again for evaluation of fever. During his hospital stay, he developed a spontaneous massive intra-hepatic haemorrhage resulting in hepatic rupture and a haemoperitoneum. The bleeding was controlled at emergency laparotomy. An abdominal angiography demonstrated multiple microaneurysms in the hepatic and mesenteric arterial vasculature. The clinical findings suggested polyarteritis nodosa, and the source of bleeding was probably a ruptured intra-hepatic artery aneurysm.

Case report

In July 2006, a 42-year-old Chinese man was admitted to United Christian Hospital with a 10-day history of swinging fever. He also complained of malaise, but denied having any other symptoms. He had been extensively investigated for fever of unknown origin 6 years earlier, in May 2000. At that time, routine blood tests revealed anaemia (haemoglobin, 88 g/L [reference range, 130-175 g/L]), neutrophilia (neutrophil count, 10.8 x 10^9/L [1.8-7.5 x 10^9/L]), elevated levels of alkaline phosphatase (395 IU/L [30-125 IU/L]), and alanine aminotransferase (287 IU/L [reference level, <41 IU/L]), and an erythrocyte sedimentation rate of 107 mm/h (<10 mm/h). All bacteriological cultures and extensive serological tests for infectious agents, including hepatitis B virus (HBV), hepatitis C virus (HCV), and the human immunodeficiency virus (HIV), were negative. Tests for anti-nuclear antibody (ANA), anti-double stranded DNA antibody, anti-neutrophilic cytoplasmic antibody (ANCA), and rheumatoid factor were negative. Chest radiography, abdominal ultrasonography, a computed tomographic scan of the thorax and abdomen, gallium scintigraphy, endoscopic retrograde cholangiopancreatogram, and an echocardiogram were all unrevealing. He had transient maculopapular rashes over both shins, but a skin biopsy was not diagnostic. A bone marrow aspirate and trephine and a liver biopsy demonstrated normal histology only. The fever subsided without specific therapy within 8 weeks, and the laboratory abnormalities gradually returned to normal within 4 months. He remained well until the 2006 presentation.

Upon admission, he had a temperature of 39.5°C and a blood pressure of 107/70 mm Hg. There were no skin rashes or signs of peripheral neuropathy, and a physical examination of the abdomen was unremarkable. Laboratory test results showed a mild anaemia (haemoglobin,
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114 g/L), neutrophilia (neutrophil count, 12.9 x 10^9/L), elevation of urea (12.2 mmol/L [reference range, 3-8 mmol/L]) and creatinine (152 µmol/L [62-115 µmol/L]), elevation of liver enzymes (alkaline phosphatase, 154 IU/L; alanine aminotransferase, 116 IU/L), and a C-reactive protein of 270 mg/L (reference level, <5 mg/L). Blood cultures were negative. Tests for ANA, ANCA, HBV, HCV, and HIV were repeated and were negative. Four days after admission, he developed sudden abdominal pain associated with hypotension and a drop in his haemoglobin level to 50 g/L. An abdominal ultrasound performed only a few hours before the onset of this abdominal pain showed a fatty liver only. On physical examination he had a tender and distended abdomen. An emergency laparotomy for suspected intra-abdominal bleeding and haemoperitoneum was performed and a haemoperitoneum from two sources of hepatic bleeding was identified. The first bleeding point was located in the right liver lobe causing formation of a large haematoma within the hepatic parenchyma. The second was a laceration of the liver capsule over the right lobe caused by the large subcapsular haematoma. Haemostasis was attained using radiofrequency cauterisation (DS3.0 Dissecting Sealer; TissueLink Medical Inc, Dover NH) and abdominal packing. A repeated laparotomy for removal of the abdominal packs was performed the next day, and haemostasis was further secured using radiofrequency cauterisation. The patient recovered uneventfully. A histological examination of a liver specimen obtained intra-operatively demonstrated steatohepatitis only. A coeliac and mesenteric angiography performed postoperatively revealed the classical changes of PAN with multiple microaneurysms along branches of the right hepatic artery, gastroduodenal artery, and mesenteric arteries (Figs 1 and 2). Treatment with prednisolone and cyclophosphamide was then commenced. At the 3-month follow-up, the patient was well, his serum biochemical abnormalities had returned to normal, and his C-reactive protein was less than 1 mg/L. A follow-up coeliac and mesenteric angiography was suggested but the patient refused.

Discussion

Polyarteritis nodosa is an uncommon disease with...
an estimated incidence of 2 to 3 cases per million. Immune complex-mediated injury to the vessel walls is believed to play a pathogenetic role in PAN and, in most cases, the aetiology is unknown although systemic infection appears to be an important triggering factor in some. An association between HBV infection and PAN has been reported, predominantly in western countries where HBV infection is typically acquired later in life. In Asia, where HBV infection is acquired during the perinatal period, an association with PAN has not been observed. Other infections, such as HCV and HIV infections, have also been found in patients with PAN-like syndromes.

Patients with PAN usually present with a variable combination of non-specific constitutional symptoms. Fever, weight loss, and malaise are more than 50% of cases. Rarely, fever can occur in isolation and the patient may present with fever of unknown origin. Specific complaints related to vascular involvement of a particular organ system may also dominate the clinical picture, including hypertension and renal failure from renal artery disease, myalgias and neuropathy reflecting arteritis in skeletal muscle and along nerves, abdominal pain secondary to mesenteric arterial disease, and skin lesions due to cutaneous vasculitis. Polyarteritis nodosa is a chronic disease, which is characterised by exacerbations and remissions. As in our patient, cases of spontaneous resolution of disease activity and a prolonged period of remission have been reported in the literature.

Although PAN often affects the hepatic arteries with hepatic artery involvement found in over half the cases examined at autopsy, clinical consequences are rare. Spontaneous intra-hepatic or peri-hepatic haemorrhage from a ruptured hepatic artery aneurysm is a rare and life-threatening complication of PAN. More rarely, a hepatic artery aneurysm may rupture into the bile ducts resulting in haemobilia. Erosion of an aneurysm in the extra-hepatic hepatic artery into the duodenum, causing massive gastrointestinal bleeding, has also been reported. Hepatic arteritis in PAN can also present with abnormal liver function tests, hepatic infarction, and nodular regenerative hyperplasia.

The diagnosis of PAN is difficult and often delayed because of the paucity of specific signs and symptoms, and the lack of a diagnostic serological marker. Ideally, the diagnosis of PAN is based on the demonstration of the characteristic findings of a necrotising vasculitis in biopsy material from involved organs. Nonetheless, biopsy of the skin, muscle or testes, or percutaneous biopsies of liver or kidney can establish the diagnosis in only 70% of cases due to focal and segmental disease involvement. Angiography can demonstrate aneurysms in small- and medium-sized arteries in the renal, hepatic, and visceral vasculature in 60 to 80% of patients. The role of angiography is to help confirm or support the clinical impression when a suitable biopsy site is lacking or when the biopsy results are inconclusive. Arterial aneurysms are not pathognomonic of PAN, and other recognisable causes of systemic necrotising vasculitis, such as Wegener’s granulomatosis, Churg-Strauss syndrome, Kawasaki disease, systemic lupus erythematosus, and arteritis of rheumatoid arthritis, that may be associated with aneurysmal formation, should be excluded.

Mild cases of intra-hepatic haemorrhage from a ruptured hepatic artery aneurysm may be treated conservatively, while patients with severe or uncontrolled bleeding should be managed by angiographic embolisation or surgery. A combination of prednisolone and cyclophosphamide should be initiated once the diagnosis of PAN has been made. Cases of complete resolution or regression in the size of aneurysms have been reported after aggressive immunosuppressive therapy. Untreated PAN has a poor prognosis, with a reported 5-year survival rate of between 10 and 20%. Treatment with immunosuppressive agents has increased survival rates to 75-80%, underscoring the importance of a rapid and accurate diagnosis.

In essence, this case illustrates the potential difficulty of making a diagnosis of PAN. The clinical manifestations of PAN are heterogeneous and a high index of suspicion is important to ensure timely diagnosis. Lastly, a negative tissue biopsy does not rule out the condition, and abdominal angiography should be considered in cases where it is suspected.

References