CASE REPORTS

Whipple's endocarditis

D West BSc MRCS(Ed)[1] S Hutcheon ChB MD[2]
R Kain MD[3] T Reid FRCP FRCPath[4]
S Walton MD FRCP[2] K Buchan ChB FRCS[1]

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The causal organism in Whipple's disease, a rare disorder with characteristic duodenal and jejunal changes, was first cultured in 2000.[1] Although cardiac involvement is common in Whipple's, it is seldom an isolated finding.

CASE HISTORY

A man of 58, with the habit of drinking 80–100 units of alcohol a week, was referred to our hospital with heart failure. Nine months earlier his usual good health had been interrupted by an episode of acute shortness of breath without chest pain. Transthoracic echocardiography had revealed global impairment of myocardial function without a rise in troponin. He was diagnosed as having alcoholic cardiomyopathy with or without coronary artery disease and responded well to an angiotensin converting enzyme inhibitor and a diuretic. Shortly before readmission his shortness of breath returned. He was again in cardiac failure, with peripheral oedema, hepatic congestion, and a raised jugulovenous pressure. There was no fever. Echocardiography showed a dilated left ventricle with global hypokinesis. A coronary angiogram was normal. Over the next eight weeks serial echocardiograms revealed worsening regurgitation at the mitral and aortic valves, with new mobile masses forming on both. Initially, antibiotics were withheld and he remained apyrexial. Seven sets of paired aerobic and anaerobic blood cultures yielded no bacterial growth; C-reactive protein ranged from 36 to 69 mg/L. Broad-spectrum antibiotics were introduced, but his heart failure worsened and surgical intervention was judged necessary. At operation multiple firm, pearly-yellow vegetations were apparent on the aortic and mitral valves and an abscess was found within the posterior annulus of the mitral valve. This was deroofed and swabbed copiously with iodine. St Jude Biocor bioprosthetic valves were inserted in the aortic and mitral positions. Postoperatively he was coagulopathic with high output cardiac failure. Despite blood product replacement, inotrope therapy and intra-aortic balloon pump support he developed peripheral circulatory failure and died 48 hours after surgery.

Departments of [1]Cardiac Surgery, [2]Cardiology, [3]Pathology and [4]Medical Microbiology, Aberdeen Royal Infirmary, Foresterhill, Aberdeen AB25 2ZN, Scotland, UK

Correspondence to: Dr Douglas West

E-mail: dgwest@rcsed.ac.uk

Pathology

Post mortem samples were taken from heart, coronary artery, lung, liver, kidney and duodenum. Valve tissue from surgical specimens was fixed in 4% buffered formaldehyde and embedded in paraffin. 4 μm sections were stained with haematoxylin and eosin, methenamine silver and elastica van Gieson. Periodic acid Schiff reaction was performed with (D-PAS) and without (PAS) prior diastase treatment. Gram and Ziehl–Neelsen stains were performed. For electron microscopy, small areas of chordae tendineae with representative yellow adhesions were fixed in 2.5% glutaradehyde, postfixed in 1.0% osmium tetroxide and embedded in TAAB epoxy resin. Ultrathin sections were stained with uranyl acetate and lead citrate, and viewed in a Phillips EM10 transmission electron microscope.

Macroscopically, small, warty, yellow elevated adhesions were present, particularly on the chordae tendineae (Figure 1*a*). Histological examination showed subendocardial neovascularization (Figure 1*b*) resembling previous descriptions of Whipple's endocarditis.[2] D-PAS positive foamy macrophages, which stained with silver, were found in areas corresponding to the yellow lesions (Figure 1*c*,*d*,*e*). On electron microscopy, large lysosomal inclusions and multivesicular bodies were seen within macrophages, containing microbial structures in various stages of lysis (Figure 1*f*). Within these inclusions electron dense, rod shaped multilamellar structures were clearly visible (Figure 1*g*).

At necropsy there was evidence of global ischaemic changes to the ventricles, kidneys and intestine. No conclusive macroscopic or histological evidence of Whipple's disease was seen. The intestine showed extensive autolysis but no foamy macrophages or PAS positive material. A polymerase chain reaction (PCR) assay performed on the aortic valve tissue, targeting domain III of the 23SrDNA of *Tropheryma whippelii* as described elsewhere,[3] was positive.

COMMENT

Whilst 20–55% of patients with a diagnosis of Whipple's disease have clinically evident cardiac manifestations,[4] in very few reported cases has the initial presentation been valvular heart disease.[5,6] Paravalvular abscess formation, seen in the present case, does not seem to have been reported in Whipple's endocarditis. Once diagnosed, Whipple's disease can be successfully treated with 1–2 years of agents such as cotrimoxazole.

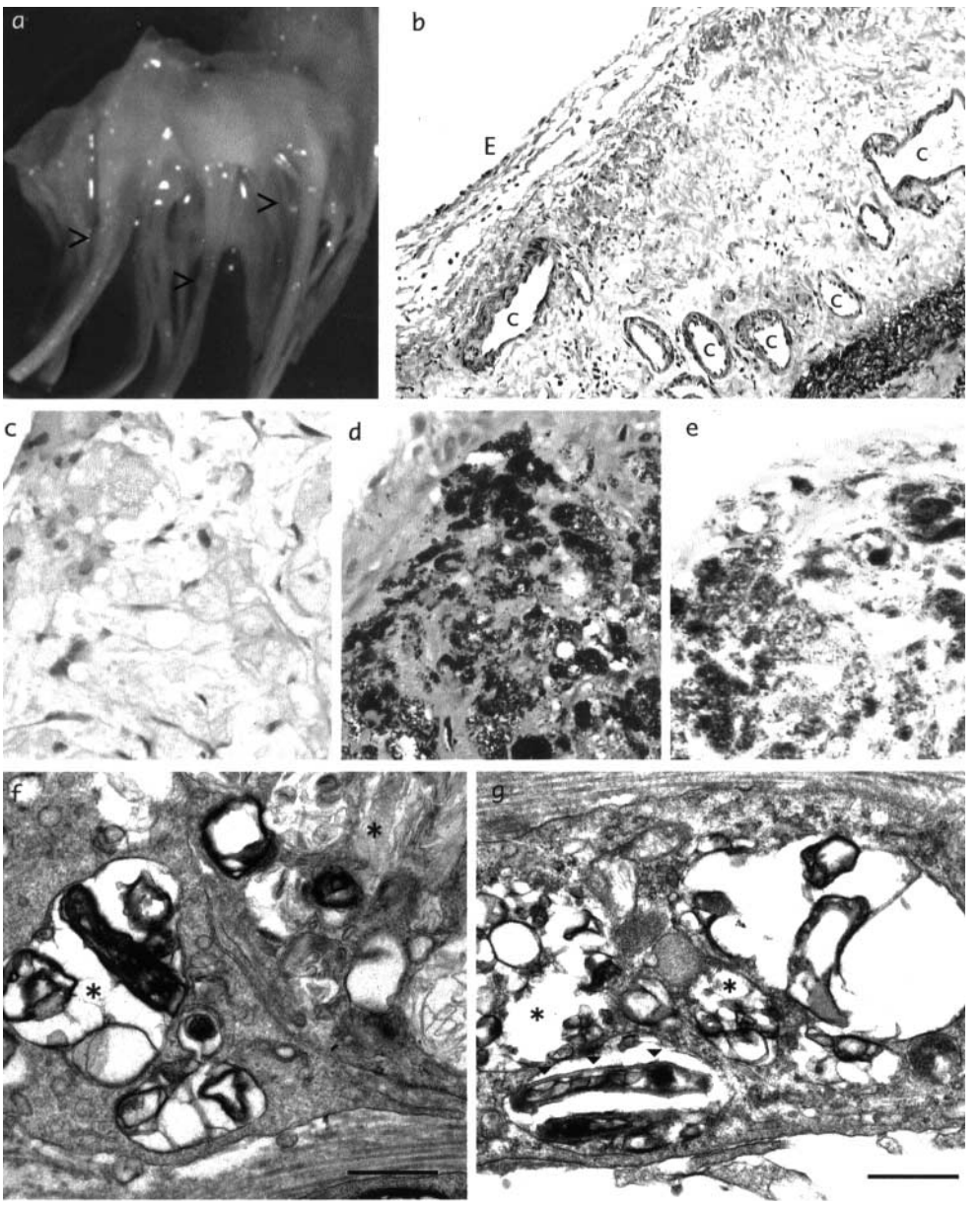

Figure 1 **Surgical and post mortem specimens.** (*a*) Lesions on chordae tendineae; (*b*) capillaries [C] and endocardium [E] ×20; (*c*), (*d*), (*e*) yellow lesions stained with haematoxylin, D-PAS and methenamine silver ×40; (*f*), (*g*) electronmicrograph, showing microbial structures (*) and multilamellar inclusions (▼), bar=0.5 μm. Colour version online

In the past, Whipple's endocarditis was diagnosed solely on light and electron microscopy but specific PCR testing for *T. whippelii* DNA has been commercially available for several years, and tests on valve tissue in culture-negative endocarditis have identified occasional cases of *T. whippelii* infection.[7] However, preoperative testing of blood or intestinal samples could give misleading results, since *T. whippelii* DNA has been found in symptomless individuals and in human sewage; in other words, some people may be colonized without harm. As yet, no sensitive and specific serological test exists. Therefore the diagnosis must be sought as soon as valve tissue is available from operation. Had the present patient survived without diagnosis, his endocarditis might well have returned postoperatively.

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Hepatic epithelioid haemangioendothelioma

Elizabeth Haydon BSc[1] Geoffrey Haydon MD MRCP[2]
Simon Bramhall MD FRCS[2] A David Mayer MS FRCS[2]
Desley Niel MB MRCPath[3]

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Primary liver tumours have a varied prognosis. Orthotopic liver transplantation has the potential to cure some of these cancers, and these cases need to be identified.

CASE HISTORY

A woman of 47 reported a dull ache in her right shoulder which, over the next few months, worsened and moved to her abdomen; it was associated with epigastric fullness, nausea, anorexia and tiredness. Fifteen months from symptom onset she had lost 5 kg and was experiencing a grabbing right upper quadrant and epigastric pain on deep breathing and coughing. She was unable to lie flat because of the pain. Initially, dietary treatment for gallstones slightly lessened the symptoms, but at twenty-three months the pain was incapacitating—severe, though fluctuating, and now extending to the left upper quadrant. She was admitted for investigation.

On examination there were no stigmata of chronic liver disease, masses or organomegaly. Ultrasound showed no abnormalities, and ultrasound-guided liver biopsy at this stage was inconclusive. Her alcohol history was 1–2 units per week. The differential diagnosis included acute-on-chronic cholecystitis, peptic ulceration and recurrent acute pancreatitis. A second ultrasound-guided liver biopsy then showed hepatic epithelioid haemangioendothelioma (Figure 1). CT revealed several focal lesions, each up to 3 cm in diameter. She was referred to the regional liver unit, where orthotopic liver transplantation was performed nine months later. Figure 2 shows a slice of the explanted liver, with several discrete and coalescing pale lesions. Serum aspartate aminotransferase was normal by day 8 and the patient returned to work after ten weeks. Sixteen months postoperatively she was in good health, and on ultrasound scanning the liver was normal in shape and echotexture, with no focal lesions or biliary dilatation. There was no free fluid in the abdomen, the spleen and kidneys were of normal size and liver function tests were within the normal range.

COMMENT

Hepatic epithelioid haemangioendothelioma is a rare multifocal vascular tumour[1] that can develop at any age, with a female preponderance. The aetiology is unclear, although vinyl chloride, liver trauma and exogenous hormones[1] have come under suspicion. Survival of affected individuals has ranged from a few months to many years. On the spectrum of malignancy haemangioendothelioma lies between benign haemangioma and malignant angiosarcoma.[1,2] There are several diagnostic difficulties. First, the presentation is non-specific; second, liver function tests may not become abnormal until the disease is advanced; third, ultrasound scans of the liver can be inconclusive; and, finally, CT may lead to a misdiagnosis of metastatic disease because of the tumour's multifocal nature. On CT, multiple angiogenic lesions, 1–3 cm in diameter,[3] are a common feature. The peripherally placed lesions are hypodense in the centre and cause enhancement of contrast media at the

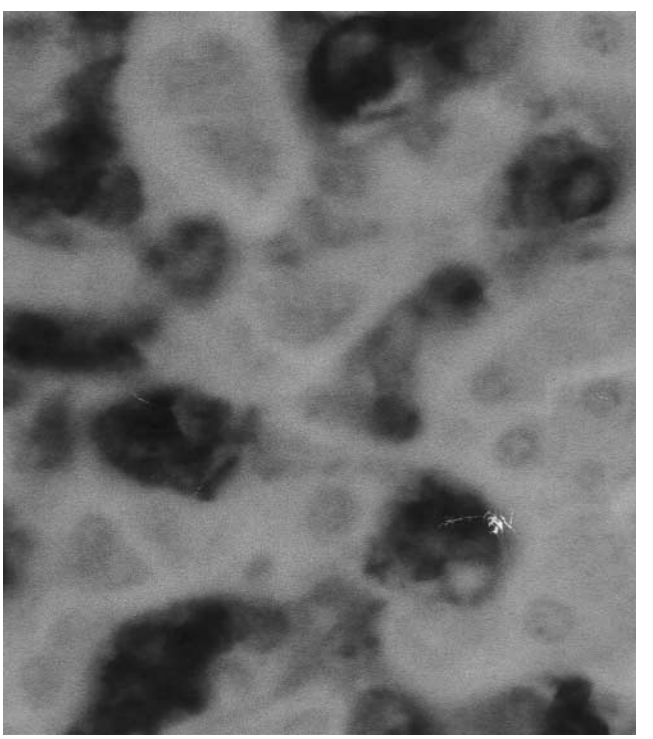

Figure 1 **Sample of tumour obtained by ultrasound-guided liver biopsy.** A proliferation of atypical endothelial cells is seen with CD31 immunostaining. Original magnification ×40

[1]Medical School, University of Birmingham; [2]Liver Unit and [3]Department of Pathology, Queen Elizabeth Hospital, Birmingham B15 2TH, UK

Correspondence to: Mr Simon Bramhall FRCS