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Case report

Hepatocellular calcification

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Summary. Autopsy of a twenty year old girl dying from complications of renal and cardiac failure demonstrated severe hepatocellular calcification, a rare finding. The pathogenesis is thought to be a combination of dystrophic calcification caused by severe centrilobular necrosis and metastatic calcification due to secondary hyperparathyroidism.

Key words: Hepatocellular calcification – Renal failure – Cardiac failure

Introduction

It is well-known that chronic renal disease predispose to secondary hyperparathyroidism with metastatic calcification in several organs. The liver is, however, very rarely involved.

A case is presented where a 20 year old female with renal and cardiac failure had severe hepatocellular calcifications. The aetiology and pathogenesis are discussed.

Case report

A 20 year old woman with renal failure was treated with peritoneal dialysis from 1981 to May 1983 when she had a kidney transplant. During the first 2 months following transplantation the graft function was good, however signs of rejection appeared, necessitating haemodialysis. After 2 weeks the patient started peritoneal dialysis because of problems with the arterio venous fistula.

In late August 1983 biochemical investigations provided evidence of hepatocellular damage with raised liver enzymes, especially transaminases. Serological investigations for viral hepatitis A and B were negative. Titers of 30 to 60 were found for cytomagalovirus, herpes virus and *Chlamydia* psittaci, but no titer increase was demonstrated. The patient had hypertension and signs of cardiac dysfunction with pulmonary congestion and cardiac dilatation. Serum levels of phosphate were elevated while the serum level of calcium was within normal levels. The C-terminal parathyroid hormone level was 20 times the upper limit of normal. In September 1983 graft failure progressed and was complicated with a perforation of the sigmoid colon precipitating faecal peritonitis and death.

Autopsy demonstrated slight enlargement of the liver. The cut surface of the liver was primarily characterized by chronic passive congestion but several small greyish dots 2–3 mm in diameter scattered throughout the parenchyma were also seen. The vessels of the transplanted kidney were thrombosed with infarction of the tissue, presumably secondary to chronic vascular rejection. The right kidney was absent. Microscopic examination of the left kidney showed a nonspecific interstitial nephritis. The left side of the heart was hypertrophied with a wall thickness of 16 mm.

Microscopic examination of the liver showed chronic passive congestion with severe centrilobular necrosis and calcification. The calcium-phosphate deposits stained black with the von Kossa method which stain phosphate ions (Fig. 1) and orange red with the Alizarin-Red S method for calcium (McGee-Russel 1958). The hepatocytes near the central vein were totally replaced by calcium-phosphate while the hepatocytes in the peripheral zone of the lobulus contained granules of calcium-phosphate in their cytoplasm (Fig. 2).

Electron microscopic investigation on previously paraffin-embedded tissue confirmed the light microscopic findings with haevy calcium-phosphate crystal formation in the cytoplasm of the hepatocytes.

Calcification was also found in the small vessels of the lungs, in the medullary zone of the transplanted kidney and in the myocardial cells (Fig. 3).

Discussion

Liver calcification is most often seen in metastatic adenocarcinoma from the colon or stomach (Karras et al. 1962, Miele and Edmonds 1963) but calcium deposits may rarely be seen in other metastatic lesions such as osteogenic sarcoma, carcinoid, neuroblastoma, lymphoma and in the Zollinger-El-

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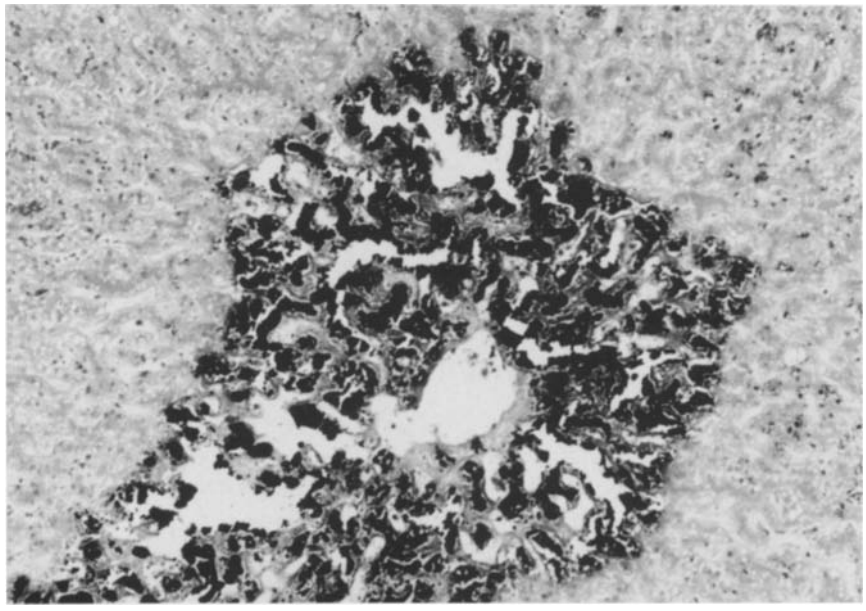

Fig. 1. Central vein surrounded by heavily calcified hepatocytes. (von Kossa ×90)

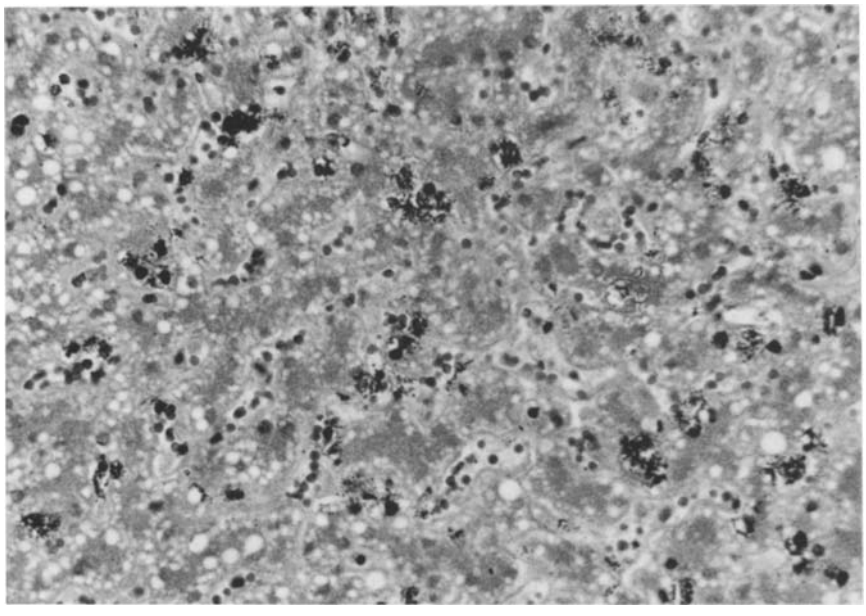

Fig. 2. From the periphery of a hepatic lobulus. Many of the hepatocytes contain granulated calcium deposits in the cytoplasm. (von Kossa ×225)

lisons syndrome (Bozymski et al. 1973). Primary tumours of the liver including liver cell carcinoma, haemangioendothelioma and haemangioma may also cause calcification (Aspray 1945; Margulis et al. 1956; Schrøder 1959). Further, calcium deposits may be seen in connection with syphilis (Karras et al. 1962) and granulomatous lesions in the liver such as tuberculosis and histoplasmosis (Okudaira et al. 1961) as well as in the walls of simple cysts, hydatid cysts and pyogenic abscesses (Karras et al. 1962; Drury 1962). In these kinds of liver calcifications localization of the calcium-phosphate deposits is in connective tissue or degenerate tumour cells.

Chronic renal disease with secondary hyperparathyroidism causes widespread calcification in several organs – but not usually the liver. Diffuse centrilobular calcification in the liver as a consequence of renal failure was first reported by Patrick and McGee in 1980.

Recently Pounder (1985) published a case of hepatocellular calcification in a 65 year old man

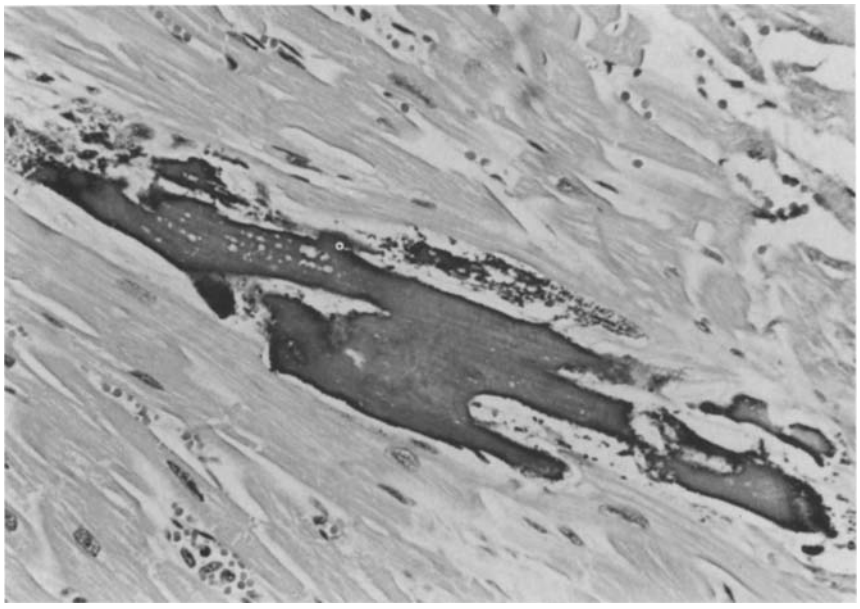

Fig. 3. Calcified myocardial fibres (von Kossa × 225)

suffering from cardiac as well as respiratory and renal failure. In the present case the patient suffered from cardiac and renal failure with hyperphosphataemia. The mechanism of dystrophic calcification is not clear, but it is suggested that denatured proteins bind phosphate ions which in turn bind with calcium to form calcium phosphate.

The raised liver enzymes seen in the present case indicate such damage to the liver cell with increased plasma membrane permeability and denaturation of proteins. This is an extremely common event in the liver but for reasons which are uncertain it does not normally lead to dystrophic calcification. It is characteristic, from the previously described cases with hepatocellular calcification, that the calcium-phosphate product is usually elevated, supplying an additional risk of metastatic calcification, as in the present case. The pathogenesis of hepatocellular calcification in our case is probably due to cardiac failure with severe passive congestion and centrilobular necrosis of the liver combined with raised calcium-phosphate product, causing dystrophic and metastatic calcification in the damaged hepatocytes.

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