Focal Nodular Hyperplasia of the Liver

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FOCAL NODULAR HYPERPLASIA OF the liver refers to an uncommon slow-growing benign lesion consisting of liver cells arranged in nodules separated by fibrous tracts within which proliferating bile ducts are included occurring as solitary, sometimes multiple, well-demarcated tumour-like areas in normal livers. This lesion has been found in males and females of all age groups. Most of these lesions have been incidental findings at autopsy or during angiographical studies for other conditions. A minority have become symptomatic. Many names have been given to this lesion such as focal cirrhosis (Benz and Baggenstoss, 1953), hamartoma (Kay and Talbert, 1950), solitary hyperplastic nodule (McBurney et al., 1950), and nodular hyperplasia of the liver (Edmondson, 1958) reflecting the diversity of opinion that exists as to its nature. The aetiology of focal nodular hyperplasia of the liver remains unknown.

One such lesion was an incidental finding in the liver of a 16 year old Malay boy killed in a traffic-accident when autopsy was performed at the University Hospital in Kuala Lumpur. Focal nodular hyperplasia of the liver has not been previously described in Malaysians although this lesion is a well recognised entity.

This case of focal nodular hyperplasia of the liver is being reported because it is important to recognise this lesion and differentiate it from other liver disorders such as cirrhosis, partial nodular transformation of the liver, congential hepatic fibrosis, adenomas and hepatocellular carcinoma.

Case Report

A 16 year old Malay boy was knocked down by a car and died while on the way to hospital.

Autopsy findings

Autopsy was performed four hours after death. Multiple traumatic injuries were present: multiple skin abrasions; a 5 cm. laceration of the occipital scalp; simple fractures of the left clavicle, right femur, right tibia and fibula; and, fracture across the posterior cranial fossae with extensions into the middle cranial fossae resulting in right otorrhoea. As a result of the basal fractures in the skull aspiration of blood into the lungs had occurred.

The brain was swollen with laceration of the inferior parts of the cerebellar hemispheres and focal subarachnoid haemorrhages were present in the cerebral hemispheres. There was bilateral swelling of the cerebellar tonsils and uncal grooving. Coronal sectioning of the brain showed no intra-cerebral haemorrhage or laceration.

In the liver was found a superficial, solitary, 6 x 5 x 5 cm., firm, tan coloured, irregularly nodular, rounded mass which was replacing the caudate lobe and protruding from it (Fig. 1). This lesion was sharply demarcated from the normal liver parenchyma by a distinct fibrous capsule. Some prominent thin-walled engorged blood vessels were present on the surface of the capsule. On sectioning, the cut surface of the mass showed numerous pale, tan coloured, irregular nodules which were separated by small stellate-shaped fibrous scars and fibrous bands. The nodules ranged from 1 to 8 mm. in

diameter. Some dilated blood vessels were present at the interface between the lesion and the liver parenchyma and within the lesion itself. There was no bile-staining. The rest of the liver was smooth, reddish-brown in colour, normal in consistency and shape, and, including the mass, weighed 920 g. A normal lobular pattern was discernible and fibrosis, cirrhosis and cavernous haemangioma were absent.

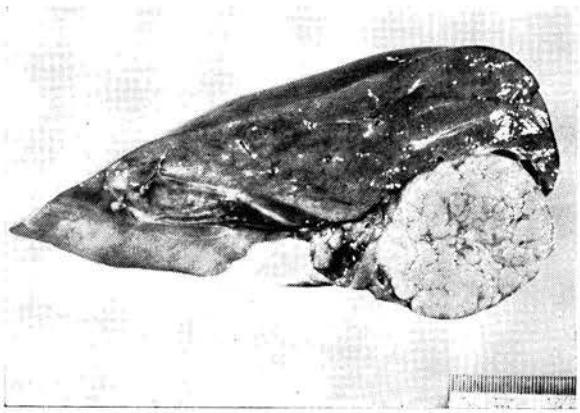

Fig. 1
Focal nodular hyperplasia of the liver. Portion of right lobe of liver showing a well demarcated, solitary, tan coloured, 6 x 5 x 5 cm., irregularly nodular mass replacing the caudate lobe and proturding from it.

The gall-bladder, biliary ducts and pancreas were normal. There was no portal veinous thrombosis or signs of portal hypertension. The spleen was normal. The other organs were normal. The autopsy did not show any metastatic tumour deposits in the organs.

The cause of death was aspiration of blood into the lungs as a consequence of multiple fractures at the base of the skull.

Histology

On histological examination, sections of the hepatic lesion stained with haematoxylin and eosin showed a pattern suggestive of mixed nodular cirrhosis with numerous irregular hyperplastic regeneration nodules of varying sizes surrounded by bands of fibrous tissue, generally thin and narrow, but occasionally rather broad, and separated in many places by small stellate-shaped fibrous scars (Fig. 2). Many of the peripheral scars were continuous with the capsule but the deeper ones interconnected with each other through fibrous bands.

The hepatic cells were swollen with clear cytoplasm devoid of lipofuscin pigment, and were arranged in one to three cell thick slightly disorganised plates separated by dilated sinusoids. There was slight increase of binucleated hepatic cells. Fatty change in hepatic cells was present focally, but other degenerative changes and necrosis were absent,

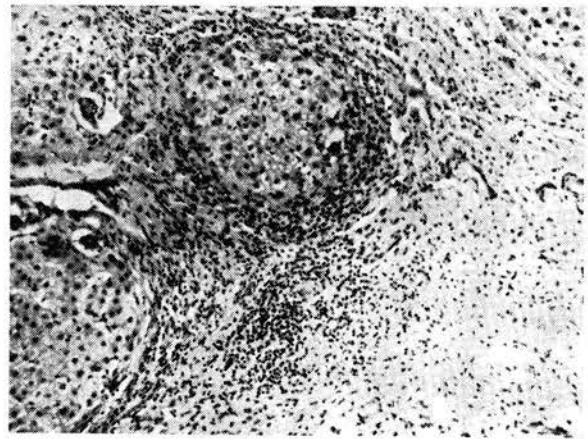

Fig. 2
Focal nodular hyperplasia of the liver showing a pattern suggestive of cirrhosis with regeneration nodules surrounded by fibrous bands and separated by small fibrous scars. Aggregates of lymphocytes with histoicytes are present within the bands and scars. H. & E. stain x 32.

and there was no cellular anaplasia or pleomorphism. The Kupffer cells were normal. Central veins were generally absent in the nodules. Many clusters of proliferating bile ducts were present at the periphery of the nodules but no cholestasis was noted. Focal aggregates of lymphocytes admixed with some histiocytes were present in the areas of scarring and fibrous bands (Fig. 3).

In the thick fibrous capsule were compressed clusters of normal hepatic cells, proliferating bile ducts and focal aggregates of mononuclear inflame atory cells.

Focal groups of dilated engorged blood vessels were present at the interface between the lesion and normal liver, within the fibrous capsule, and in the scars and fibrous bands within the lesion. Most were thin-walled, but a few showed fibroblastic proliferation of media and intima with mural thickening. There was no necrosis or inflammation of vessel walls and no thrombosis. Whether these blood vessels were arteries or veins was difficult to ascertain. Elastic stain showed no clearly definable elastic tissue in the thickened walls.

In the macroscopically normal liver tissue the hepatic cells were histologically normal and there

were no abnormal vascular changes. Focal nodular hyperplasia of the liver was the final diagnosis.

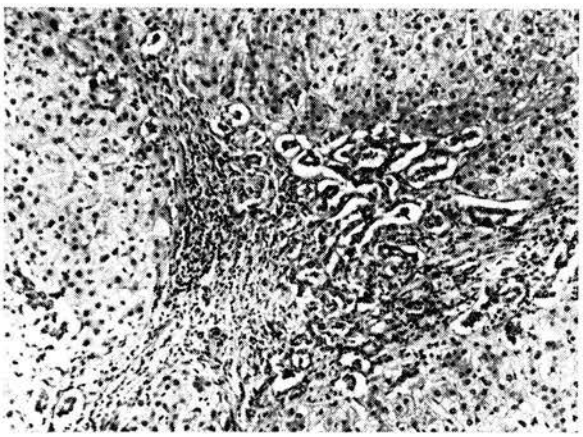

Fig. 3
Focal nodular hyperplasia of the liver. The regeneration nodules are composed of hepatic cells with clear cytoplasm arranged in one to three cell thick slightly disorganised plates separated by dilated sinusoids. Many clusters of proliferating bile ducts are present at the periphery of the nodules. Focal aggregates of lymphocytes with histoocytes are present within the fibrous bands. H. & E. stain x 125.

Discussion

Focal nodular hyperplasia of the liver is a well recognised entity of which about 300 cases have been reported in the literature over the past 30 years. There have been several large series of cases (Benz and Baggenstoss, 1953; Begg and Berry, 1953; Edmondson, 1956). The pathological features of this lesion are well documented. Amongst Malaysians this hepatic lesion has never been previously reported. Morphologically, the hepatic mass in this present case is one of focal nodular hyperplasia of the liver.

This hepatic lesion has been reported in all age groups from infancy to old age and it has been found to be more frequent in females than males (Benz and Baggenstoss, 1953; Begg and Berry, 1953; Garancis et al., 1969; Whelan et al., 1973). Clinically, focal nodular hyperplasia of the liver may be symptomatic or asymptomatic Individuals may harbour this lesion without complications for many years and be noted as an incidental finding at autopsy. Benz and Baggenstoss (1953) reported a series of 34 such lesions which were incidental findings at autopsy and had not produced symptoms. Conversely, these lesions may become symptomatic (Begg and Berry, 1953): by virtue of size, as an abdominal mass; by torsion if the lesion is pedunculated, producing infarction and pain; or by rupture of capsular veins resulting in intraperitoneal haemorrhage. Such symptomatic lesions have usually occurred in children (Edmondson, 1956). In the present case, focal nodular hyperplasia of the liver is an incidental finding at autopsy in a 16 year boy killed in a traffic-accident.

Most authors consider focal nodular hyperplasia of the liver to be a benign lesion. The lesions reported by Benz and Baggenstoss (1953) were noted as incidental findings at autopsy which is suggestive of their benign nature. In some cases in which the lesion could not be surgically removed, patients had remained in good health (Edmondson, 1958). Whelan et al., (1973) reported two cases followed up 5 and 6 years after hepatic lobectomy and showed no evidence of recurrence. Histologically, these lesions have not been reported to show cellular anaplasia or other signs of malignancy such as invasion of the liver capsule and surrounding liver tissue, lymphatics and blood vessels, and no distant metastases have been found. The present lesion shows no evidence of such malignant features and is histologically graded as benign.

The aetiology of these lesions remains an enigma. They have been variously regarded as hamartomas (Kay and Talbert, 1950; Gerding et al., 1951), benign neoplasms (Hoffman, 1942; Christopherson and Collier, 1953; Garancis et al., 1969) and regenerative lesions (Begg and Berry, 1953; Edmondson, 1958). Recent authors (Thomas et al., 1966; Palubinskas et al., 1967; Garancis et al., 1969; Whelan et al., 1973) have stressed the importance of vascular anomalies in the lesions of focal nodular hyperplasia of the liver such as dilated blood vessels (Thomas et al., 1966; Palubinskas et al., 1967), mural thickening of the walls of small blood vessels (Whelan et al., 1973), dilatation of sinusoids (Whelan et al., 1973) and a somewhat frequent association of these lesions with cavernous haemangiomas in the same livers (Benz and Baggenstoss, 1953). Arteriographical studies, during life (Palubinskas et al., 1967; Aronsen et al., 1968; Whelan et al., 1973), have demonstrated increased anomalous arterial supply to the lesion. Accumulated evidence suggests that an anomalous and increased arterial supply is an important factor in the development of focal nodular hyperplasia of the liver.

The exact mechanism for the parenchymal changes in the liver leading to focal nodular hyperplasia is at present unknown. Whelan et al., (1973) have theorized on two possible mechanisms; first, the lesion may be due to injury secondary to increased pressure in the sinusoids and portal vein branches from chronic exposure to arterial pressure. Occlusive lesions of the small blood vessels may

produce ischaemia, followed by atrophy and compensatory regenerative nodules; second, the lesion may be explained by the fact that the vascular anomaly is, in fact, a focal arteriovenous malformation. Shunting of blood away from a localized area of liver may produce ischaemia with its previously noted effects.

Morphologically, the present lesion can be described as a "focal cirrhosis' 'as most of the features of cirrhosis of the liver are present: the prominent nodularity due to regenerative nodules separated by fibrous bands and scar tissue; the disorganisation of the normal lobular pattern of the liver; the marked proliferation of bile ducts; and the presence of aggregates of lymphocytes and histiocytes within the fibrous bands and scar tissue which would suggest that this lesion is regenerative rather than neoplastic in nature. The nature of the aetiological agent cannot be ascertained although the findings of an increase in vascularity around and within the lesion, mural thickening of small blood vessels and the dilatation of sinusoids within the regenerative nodules would support the current hypothesis that anomalous vascularization in a portion of liver is an important factor in the pathogenesis of this condition.

Focal nodular hyperplasia of the liver is an eminently treatable lesion which is of excellent prognosis. Therefore, it is important to distinguish between this lesion and other liver disorders such as cirrhosis, partial nodular transformation (Sherlock et al., 1966), congenital hepatic fibrosis (Kerr et al., 1961), adenomas and hepatocellular carcinoma as these entities commonly simulate focal nodular hyperplasia clinically but, prognostically, they are very different. Differentiation is mainly morphological rather than clinical.

Summary

A case of focal nodular hyperplasia of the liver which was an incidental finding at autopsy in a 16 year old Malay boy killed in a traffic-accident is reported. The autopsy and histological findings are described. Morphologically, this lesion can be described as a "focal cirrhosis" and therefore is suggestive of a regenerative rather than a neoplastic lesion. Vascular anomalies present around and within the lesion would support the current hypothesis that anomalous vascularization in a portion of liver is an important factor in the pathogenesis of this condition. It is important to differentiate this lesion from other liver disorders as it is eminently treatable and of excellent prognosis.

Acknowledgements

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