Focal nodular hyperplasia of the liver: a link with sickle cell disease?

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Abstract
Focal nodular hyperplasia is a benign liver tumour that is rare in children. We report the second case of a child with sickle cell disease presenting with symptomatic focal nodular hyperplasia. The possible pathogenesis of focal nodular hyperplasia and the association with sickle cell disease are discussed.

Focal nodular hyperplasia of the liver is a rare benign lesion found predominantly in women during their reproductive years.1 It consists of a well circumscribed area of hyperplastic liver parenchyma that may contain a stellate fibrous scar. The lesion is usually asymptomatic and is an incidental finding. We describe a patient with sickle cell disease presenting with a symptomatic lesion of focal nodular hyperplasia. This is the second description of such an association2 and we discuss whether sickle cell disease is a pathogenetic mechanism for the development of focal nodular hyperplasia.

Case report
A 6 year old West Indian girl with homozygous SS sickle cell disease presented with abdominal pain, headache, and night sweats. She had been admitted one year previously with a chest infection and sickle crisis. She was taking prophylactic antibiotics. Apart from sickle cell disease there was no other significant medical or family history.

On examination she appeared anaemic but was not jaundiced. A firm non-tender mass was palpable in the epigastrum. The results of biochemical investigations were haemoglobin concentration 72 g/l, white cell count 8.1×10⁹/l, platelet count 213×10⁹/l, albumin 38 g/l, bilirubin 30 µmol/l, and activities of alkaline phosphatase 201 IU/l, aspartate transaminase 111 IU/l, and γ-glutamyltransferase 146 IU/l. A test for serum α fetoprotein was negative. An ultrasound scan showed a 6 cm well defined mass in the left lobe of the liver. The lesion had a similar density to normal liver on computed tomography (fig 1) and was shown to be avascular on hepatic angiography (fig 2).

At operation, after exchange transfusion, the solid mass was found to be restricted to segments 2 and 3 of the left lobe and was resected. She was discharged home on the ninth postoperative day.

The cut surface of the tumour was smooth with focal areas of haemorrhage, but there was no stellate scar. The microscopic appearance of fibrous bands transecting liver tissue with expanding portal tracts that contained dilated vascular channels and numerous bile ductules was typical of focal nodular hyperplasia (fig 3).

Discussion
Focal nodular hyperplasia is a rare benign liver tumour with fewer than 20% of cases presenting in children.3 The majority are asymptomatic and usually arise on the surface of the liver beneath the capsule. Their aetiology is unknown, although an association with oral contraceptives has been reported.4

The radiological diagnosis depends on identification by ultrasound or computed tomography of a central scar. Angiographic findings of a hypervascular spoke wheel pattern of feeding vessels and numerous small feeding arteries and veins is unusual.5 6

Figure 1 Computed tomogram without contrast showing the mass in the left lobe of the liver (arrow).

Figure 2 Venous phase of an hepatic digital subtraction angiogram showing an avascular mass in the left lobe of the liver (arrow).
vessels which produce a dense capillary blush
are diagnostic but uncommon.5

The management of asymptomatic lesions
should be to confirm the diagnosis of focal
nodular hyperplasia by liver biopsy, excluding
benign lesions such as hepatic adenoma,
mesenchymal hamartoma, or haemangio-oma. Ultrasound follow up has been suggested.
Symptoms may settle by withdrawal of oral con-
traceptives, but in other patients symptomatic
lesions should be resected or if this is not possible they can be emboled.1

The pathogenesis of focal nodular hyperplasia
has been considered to be neoplastic, hamarto-
matous, or a response to ischaemia or other focal injury. It has been suggested that the
lesions arise as a hyperplastic response of liver
parenchyma to differential blood flow caused by
a pre-existing arterial malformation.6 Poorly
perfused areas undergo atrophy and well-per-
 fused areas develop regenerative nodules. Whelan et al suggested that increased blood
flow and turbulence caused platelet disruption
with thrombosis of smaller arterial vessels that
lead to a release of platelet derived growth factor
which may stimulate hepatocellular hyperplasia.7
Oral contraceptives may affect the hepatic
vasculature and influence the development of
focal nodular hyperplasia.8 Patients taking oral
contraceptives tend to have larger, symptomatic
lesions sometimes associated with haemangio-
matas. 1 8

Oclusive lesions in small arteries and veins
may also cause ischaemia followed by atrophy
and regenerative nodules. In sickle cell disease
blockage of small vessels by deformed red blood
cells leads to tissue damage. Sequestration of sickled cells also lead to infarction. The result-
ing ischaemia and necrosis may provide an ex-
planation for the development of focal nodular hyperplasia. Markowitz et al suggested that the
primary abnormality may still be an underlying
vascular anomaly and that ischaemia from sickle
cell thrombosis acts as a stimulant to the
development of focal nodular hyperplasia.2

Figure 3 Section showing regenerative nodules of liver parenchyma (thin arrow) transsected by fibrous bands with expanded portal tracts (thick arrow) containing dilated vascular channels and bile ductules (magnification x 100).