Vascular Diseases of the Liver

Alastair D. Burt
Professor of Pathology
School of Clinical & Laboratory Sciences
Medical School
University of Newcastle upon Tyne

a.d.burt@ncl.ac.uk

In this lecture I intend to "go with the flow"! By this I mean that we will consider the many disorders that can affect the intrahepatic vasculature from the incoming vessels through the sinusoids to the hepatic vein outflow.

Portal Vein

There are a number of well documented and sometimes quite complex developmental abnormalities within the portal venous system and these can be associated with portal hypertension. A more common problem is that of acquired disorders of the portal veins and there are two main categories. First there is thrombosis, either of the large veins including the extrahepatic portal vein branches or the small intrahepatic radicles, and secondly local portal disease which is generally characterised by a phlebitis and often the consequence of inflammation within one or both of the other major components of the portal tracts. The major causes of portal vein thrombosis can be categorised according to Virchow's triad. There are those associated with hypercoagulable states (eg. polycythaemia, anti-phospholipid antibodies), the effects of impairment of flow (cirrhosis, hepatocellular carcinoma) and endothelial/vascular injury (umbilical sepsis, pyelophlebitis, schistosomiasis). Many cases of non-cirrhotic portal hypertension are a result of thrombosis of portal venous branches. It is likely that the majority are due to thrombosis of large portal vein branches but these may become recanalised and some imaging studies can be confusing. This is probably the basis for most cases previously described as hepatoportal sclerosis and histologically this is manifest by a paucity of intrahepatic portal vein branches and by herniation of dilated residual vessels into the parenchyma.

Hepatic Arteries

As with portal venous branches, hepatic arteries are also associated with some complex and unusual developmental abnormalities. Some involve both venous and arterial structures such as the hereditary haemorrhagic telangiectasia. Common disorders such as hyaline arteriosclerosis can also be observed as acquired lesions although atherosclerosis is relatively uncommon. Inflammatory disorders of the hepatic arteries however are well described and the liver can be involved in polyarteritis nodosa, Takayasu's disease, rheumatoid arthritis and unusual giant cell arteritides. Furthermore intraheptic hepatic arterial branches can be affected as part of chronic allograft rejection where there is generally occlusion by a foam cell infiltrate similar to that seen within the kidney in chronic rejection.

Sinusoidal Lesions

The sinusoids are almost unique in their structure being lined by fenestrated endothelial cells without any underlying basement membrane. They are ensheathed by processes from hepatic stellate cells and these cells may act as pericytes controlling intrasinusoidal blood flow. One of the commonest abnormalities of the sinusoids which can impair blood flow is the pericellular fibrosis associated with steatohepatitis. This leads to accumulation of collagens and other matrix proteins within the space of Disse and a related phenomenon is so-called capillarisation where there is a laying down of a basement membrane in the space of Disse in the context of chronic liver disease (in particular when there is cirrhosis). There are a number of conditions associated with sinusoidal dilatation. This includes Hodgkin's disease and the effects of some drugs such as anabolic steroids and the oral contraceptive pill. By and large the sinusoidal dilatation in this setting is of no clinical importance but when there is greater disruption to the framework of the sinusoids and large blood filled spaces emerge (so-called peliosis hepatis) then there may be impairment of liver function and a risk of haemorrhage. The sinusoids are a site at which there may be intravascular fibrin deposits in disseminated intravascular coagulation and this is then associated with necrosis of adjacent and surrounding hepatocytes. Impairment of sinusoidal blood flow can also be seen in restrictive diseases such as amyloidosis and light chain disease and in profound extramedullary haemopoiesis and some metastatic intrasinusoidal malignancies.

Hepatic Vein Outflow Disorders

Once again there are some congenital abnormalities which are associated with hepatic venous outflow disturbance and this includes congenital webs within the inferior vena cava. In certain geographic locations such as parts of South Africa it is thought that acquired IVC webs can also occur possibly in relation to environmental toxins. The most common form of hepatic venous outflow obstruction however is that seen in congestive cardiac failure. Hepatic venous thrombosis may be seen in this context but also in a wide range of conditions which, as for portal venous thrombosis, can be considered in categories according to Virchow's triad. Hepatic vein thrombosis can lead to the so-called Budd-Chiari syndrome in which there is massive hepatomegaly, marked ascites formation and in which there may be acute onset hepatic failure. It is important to recognise that the Budd-Chiari syndrome refers to the clinical syndrome rather than a histological abnormality. Distinction needs to be drawn between hepatic vein thrombosis and a true veno-occlusive disease where there is intimal proliferation and in which the basis is not thought to be predominantly a thrombotic occlusion but direct injury to the endothelium and "repair process". This is well described as a consequence of exposure to a number of toxins such as the pyrrolizidine alkaloids and following bone marrow transplantation and hepatic radiation. The effects of veno-occlusive disease are very similar to those of hepatic vein thrombosis and it can be associated with the clinical Budd-Chiari syndrome.

Nodular Lesions associated with Vascular Disorders of the Liver

Many of the above vascular abnormalities of the liver are associated with development of nodules in the liver. Vascular problems are thought to be at the heart of so-called nodular regenerative hyperplasia and it is considered most likely that the mechanism for this disorder, which may be associated with portal hypertension, is:- i) atrophy of liver parenchyma because of impaired blood flow, followed by ii) a compensatory local regenerative response. A localised equivalent of this is the lesion often referred to as focal nodular hyperplasia. Here there is either a congenital abnormality of an intrahepatic vessel or vessels or in some instances an acquired abnormality which leads to a localised regenerative phenomenon. The abnormal vessel can often be seen either histologically or radiologically at the centre of FNH lesions. Multiple FNH-like lesions can be seen in patients with the Budd-Chiari syndrome and when there are numerous FNH-like lesions particularly affecting the hilum, this is described as partial nodular transformation. An extreme example of the effects of vascular impairment with atrophy and compensatory hyperplasia occurs in conditions such as primary sclerosing cholangitis where occlusion of a portal vein branch as a consequence of local inflammatory activity as part of PSC can lead to atrophy of an entire lobe with then compensatory hyperplasia of the other lobe. Finally, mention should be made of the possibility that vascular lesions are at the core of some of the nodular regenerative activity in many (or all) forms of cirrhosis.

Vascular Tumours

Benign vascular tumours in the liver are common. Haemangiomas are frequently an incidental finding at autopsy and can be picked up on imaging in some 5-10% of individuals. Some of these are associated with fibrosis and there is a distinction drawn between sclerosed and sclerosing haemangiomas. Solitary fibrous nodule or necrotic nodules are considered within the spectrum of benign haemangiomas. Rarely haemangiomas may rupture and if large can be associated with thrombocytopenia and consumptive coagulopathy.

There is a spectrum of malignant hepatic vascular tumours. Infantile haemangioendothelioma represents the commonest mesenchymal tumour in the liver in infancy and generally presents within the first 6 months of life. This is not infrequently associated with consumptive coagulopathy and congestive cardiac failure and approximately 60% of children die from the disease. A distinction is drawn between so-called Type 1 and Type 2 infantile haemangioendotheliomas, the latter are often now referred to as low grade angiosarcomas. In adults angiosarcomas represent the commonest form of sarcoma in the liver. This has a marked male predominance and there are well established associations with exposure to Thorotrast, vinyl chloride and arsenic. Some molecular mechanisms have been established for some of this environmental related tumours, for example p53 mutations have been identified in tumours associated with exposure to vinyl chloride. The liver may also be involved in Kaposi's sarcoma where relatively bland looking tumour cells can "invade" the sinusoids compressing the hepatic cords; eosinophilic globules are commonly seen as in Kaposi's at other sites.

Epithelioid haemangioendotheliomas are described in a variety of sites. Within the liver these were previously often misdiagnosed as sclerotic cholangiocarcinomas. The tumour tends to occur more commonly in females and with a mean age of onset at 50 years. This has a propensity to invade the large blood vessels, often leading to obliteration of hepatic vein radicles and producing the Budd-Chiari syndrome.