Hepatic and portal vein thrombosis

Closely associated with chronic myeloproliferative disorders

Until recently most cases of hepatic vein thrombosis were considered to be idiopathic—although occasional cases were linked to underlying diseases such as myeloproliferative disorders, systemic lupus erythematosus, paroxysmal nocturnal haemoglobinuria, and antithrombin III deficiency. As a result of advances in the early diagnosis of chronic myeloproliferative disorders, recent evidence now suggests that most patients who develop hepatic vein thrombosis have an associated, occult chronic myeloproliferative disorder.1

The chronic myeloproliferative disorders are distinguishable clinical entities that have a common origin from a single malignant haemopoietic stem cell. These disorders have long been known to be associated with thrombosis, particularly in untreated polycythaemia vera and myelofibrosis, in which the incidence of postoperative thrombosis can rise to 75%.2 The risk is less in essential thrombocythaemia and chronic granulocytic leukaemia.3,4 Thromboses commonly affect the cerebral and coronary arteries, but there is also a high incidence of intra-abdominal thrombosis in the inferior vena cava or in the splenic, hepatic, portal, mesenteric, and renal vessels.7

The diagnosis in polycythaemia vera is confirmed by an increased red cell mass, the presence of splenomegaly, a normal arterial oxygen saturation, and high white cell and platelet counts, leucocyte alkaline phosphatase activities, and serum concentrations of vitamin B-12. Treatment with phlebotomy and myelosuppressive drugs is effective and symptom free survival for 10-20 years common. In myelofibrosis there is leucoerythroblastosis and the bone marrow shows typical collagen-rettinulin fibrosis. In some patients with myelofibrosis the disease does not progress and they may survive many years, but most need chemotherapy to control splenomegaly and blood transfusions for anaemia.

There are several different causes of polycythaemia, and in some cases the aetiology is initially unclear. Over a period of years, however, two thirds of patients develop recognisable polycythaemia vera.2 More recently cytogenetic analysis and in vitro haemopoietic stem cell cultures have identified clonal bone marrow characteristics and cell culture growth patterns that have made it possible to identify chronic myeloproliferative disorders at an even earlier stage.13 In these occult cases the usual clinical or haematological features of chronic myeloproliferative disorders may develop later.

Recent reports showing that up to three quarters of patients with hepatic vein thrombosis have associated occult forms of myeloproliferative disorder3 may also explain why hepatic vein thrombosis can recur after successful liver transplantation.7 Patients with thromboses associated with myeloproliferative disorders should be treated with anticoagulant drugs, initially heparin and in the longer term warfarin or low dose aspirin.8 If thrombosis recurs—and there are no contraindications such as oesophageal varices, thrombocytopaenia, or severe liver dysfunction—lifelong treatment with anticoagulants should be considered.

The cause of thrombosis in chronic myeloproliferative disorders has been the subject of a longstanding debate. Infiltration of the hepatic portal tracts with extramedullary haemopoietic tissue might predispose to thrombosis in the hepatic or portal vein. In polycythaemia vera there is a prethrombotic state in which the raised packed cell volume and increased blood viscosity lead to a low grade disseminated intravascular coagulation and activated fibrinolysis.13,14 These
Second malignant tumours in head and neck cancer

Commoner than elsewhere

Although advances in surgical repair, radiotherapy, and chemotherapy have improved control of cancer of the head and neck, these improvements have hardly influenced survival. One of the main reasons for this failure is the development of second malignant tumours, which occur more commonly in the head and neck than in any other site. Among patients with head and neck cancer more are alleged to die from second tumours than from their original disease. Despite recent interest in second tumours little is known about risk factors and in particular about the influence of treatment of the first primary tumour on development of a second.

Several workers have tried to assess the influence of TNM stage, sex, site, and behavioural characteristics on the development of second malignant tumours. The risk of a second primary tumour is thought to be independent of the stage of the first and seems to be no greater in men than in women, but whether it is influenced by the site of the primary tumour remains controversial. The greatest risk, however, seems to be continued use of alcohol and tobacco, though opinion varies about which is more influential. Wynder et al found tobacco but not alcohol to be associated with an increased risk. They also found, however, that stopping both smoking and drinking did not prevent further tumours from developing, although Moore showed a decreased incidence when smoking ceased. Moore also noted a greater risk of second malignant tumours with continued smoking, although Castigliano did not. Others have found that smoking and drinking together seem to increase the risk of second malignant tumours. Thus, although smoking and drinking may increase the risk, stopping smoking and drinking do not seem to remove it.

The increased interest in second malignant tumours has not been matched by an equally critical appraisal of the effect of treatment on the primary lesion. Most squamous carcinomas of the head and neck region are managed with surgery, radiotherapy, or a combination of both. Most studies have not clearly distinguished between the numbers of second tumours arising after surgical treatment of the primary tumour and after radiotherapy. Those that have recorded them separately have made little or no attempt to correlate this with the extent of disease at the time of initial treatment, although one study found that the risk of second malignant tumours was independent of the stage of the disease.