Jaundice following warfarin therapy

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Summary
A case of intrahepatic cholestatic jaundice following warfarin therapy is described. The patient made a complete recovery on withdrawal of the drug.

Introduction
Anticoagulant therapy is associated with a number of complications of which haemorrhage is the most common. Although numerous cases of jaundice associated with phenindione have been reported, such a reaction to warfarin is rare.

Case report
A 59-year-old man underwent a right knee arthroplasty in October 1978. For the preceding 4 years he had been taking frusemide, propranolol and methyldopa for mild hypertension. Postoperatively, he developed a deep vein thrombosis and pulmonary infarct and was commenced on warfarin.

He continued on warfarin, frusemide and propranolol until April 1979 when he was admitted to hospital with deepening jaundice, pruritus, pale stools and dark urine. The initial serum bilirubin level was 110 µmol/l with an alkaline phosphatase of 190 i.u./l, an and aspartate transaminase of 50 i.u./l. A full blood count was normal with no peripheral eosinophilia. Percutaneous transhepatic cholangiography revealed normal calibre bile ducts with free flow of bile into the duodenum. Liver biopsy showed mild portal tract inflammatory infiltrate with bile duct proliferation and moderate cholestasis.

Warfarin was stopped on admission, and over the next 4 weeks his serum bilirubin level rose to 330 µmol/l and the alkaline phosphatase to 820 i.u./l, with return of the aspartate transaminase value to normal. Thereafter his jaundice spontaneously regressed, his liver function tests and liver biopsy appearances returning to normal after 15 weeks.

Discussion
Numerous drugs have been implicated in the production of cholestasis, the best known being chlorpromazine (Sherlock, 1975). The mechanism is thought to be a hypersensitivity reaction unrelated to dose, often accompanied by fever, rashes and peripheral blood eosinophilia. The anticoagulant phenindione has been shown to cause such a reaction, either predominantly cholestatic (Portal and Emanuel, 1961) or mixed hepatocellular/cholestatic (Hargreaves and Howell, 1965). The authors are aware of only one previous report of warfarin therapy being followed by jaundice, in which 2 patients developed a cholestatic reaction with complete recovery of both biopsy changes and serum biochemistry after stopping the drug (Rehnqvist, 1978).

Hepatotoxicity has been reported following methyldopa therapy and, although the clinical picture usually resembles acute hepatitis (Cacace and Cohen, 1976), both cholestatic jaundice (Toghill et al., 1974) and a syndrome resembling chronic active hepatitis (Eliastam and Holmes, 1971) have been described. The authors do not think methyldopa can be implicated in this case because the drug was stopped 5 months before the onset of jaundice. They are unaware of reports of jaundice directly associated with frusemide or propranolol therapy.

It is therefore concluded that warfarin should be added to the long list of drugs associated with the development of cholestatic jaundice.

References


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