

Transient, selective factor X deficiency and acute liver failure following chest infection treated with erythromycin BP

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Summary

A 57-year-old man developed symptoms of a respiratory tract infection which was treated with erythromycin BP. He subsequently went into acute liver failure. Investigation of a very prolonged prothrombin time revealed a marked, selective factor X deficiency (1% of normal activity). He later recovered virtually normal liver function and completely normal factor X activity.

KEY WORDS: erythromycin, chest infection, acute liver failure, factor X deficiency.

Introduction

Selective factor X deficiency is a very rare condition occurring as the hereditary Stuart Prower disease (Telfer, Denson and Wright, 1956) and as an acquired form in patients with paraproteinaemia (Lackner, 1973) and amyloidosis (Dam *et al.*, 1975). Recently, a case of acquired, transient factor X deficiency has been described following *Mycoplasma pneumoniae* (Peuscher *et al.*, 1979). We report a case arising in a man who developed acute liver failure after a chest infection partially treated with erythromycin BP. Neither the cause of his factor X deficiency nor that of his acute liver failure was immediately obvious.

Case report

A 57-year-old man presented in May 1981 to his general practitioner with a 2-day history of cough and rigors, for which he was treated with erythromycin BP, 250 mg 4 times a day. Twenty-four hours later, he developed a rash and 6 days later he complained of epistaxis and pale stools. He was noted to be jaundiced and pyrexial, and was admitted to hospital.

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The patient had had an episode of infectious hepatitis 10 years previously and drank 2 glasses of sherry daily. Examination revealed a disorientated, jaundiced man with a flapping tremor and a macular, erythematous rash on the buttocks and extensor surfaces of the limbs. His temperature was 37.5°C and his blood pressure was 110/70 mmHg. Crackles were heard at the left lung base posteriorly. There was no hepatosplenomegaly, or ascites.

A chest X-ray showed bilateral diffuse opacities. Haemoglobin was 12.4 g/dl, white cell count 20×10^9 /litre (differential: 86% polymorphs, 10% eosinophils), plasma sodium 127 mmol/litre, potassium 4.3 mmol/litre, bilirubin 28 μ mol/litre (normal 3-17), alkaline phosphatase 866 iu/litre (normal 30-300), aspartate transaminase (AST) 61 iu/litre (normal 5-35), albumin 35 g/litre. Prothrombin time 196 s (control 22 s), platelets 529×10^9 /litre, fibrinogen titres normal, clotting factor activities: II 100%, 72%, VII 24%, X 1%. No organism was isolated from urine, sputum, blood or stool. Extensive serological tests, including those for *Mycoplasma*, *Legionella* and *Leptospira*, were negative. Hepatitis B surface antigen and liver autoantibodies were negative. Ultrasound showed a small liver only.

He was treated with a standard liver failure regimen and intravenous antibiotics. He improved rapidly over the next 5 days but the prothrombin time increased despite the administration of 11 units of fresh frozen plasma and 8 units of factor IX concentrate (which also contains large amounts of factors II and X). By 5 days after admission, the prothrombin time was over 5 min (control 22 s) with no spontaneous bleeding. No more plasma or factor IX concentrate was given and 9 days after admission the prothrombin time had fallen to 129 s (control 24 s) and the factor X activity had risen to 4%. At follow-up 1 month after admission, he was well, prothrombin time was 31 s (control 23) with a factor X activity of 136%, AST 48 iu/litre, alkaline phosphatase 399 iu/litre and albumin 47 g/litre. He declined liver biopsy.

Discussion

This almost total factor X deficiency (1% of normal) is much more marked and selective than the general prothrombin group deficiency (factors II, VII, IX and X) usually seen in liver failure. The much less marked factor VII deficiency (24% of normal) can probably be explained on the basis of liver failure alone. The possible explanations for the factor X deficiency in this case are failure of factor X production or presence of a serum inhibitor or antibody to factor X. Further tests to demonstrate such an antibody or inhibitor were inconclusive.

Erythromycin sensitivity is the likely cause of acute liver failure in this case. Cholestatic jaundice due to erythromycin estolate is well known (Lunzer *et al.*, 1975), but there have been 2 recent reports of cholestatic jaundice following erythromycin ethylsuccinate (Viteri, Greene and Dyck, 1979; Sullivan, Csuka and Blanchard, 1980). This patient had simple erythromycin BP and this suggests that the erythromycin molecule itself, as well as the ester, is hepatotoxic.

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