

# Hepatic Vein Thrombosis Treated with Streptokinase

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## SUMMARY

A case of hepatic vein thrombosis in a patient suffering from polycythaemia vera is described. The patient was successfully treated with thrombolytic therapy. The use of streptokinase therapy in clinical medicine is reviewed.

*S. Afr. Med. J.*, **48**, 2319 (1974).

Budd-Chiari syndrome, or occlusion of the hepatic veins, as described by Budd in 1845 and Chiari in 1899, is a rare condition, the aetiology of which is unknown in two-thirds of cases.<sup>1</sup> Of the known predisposing factors to the syndrome, polycythaemia vera is the commonest.<sup>2,3</sup> The prognosis of the acute form is uniformly poor, usually resulting in hepatic coma and early death.<sup>4</sup> Until recently the treatment of this syndrome has been largely symptomatic, with the role of surgery being controversial and of no value in the majority of cases.

In view of the poor prognosis of acute occlusion of the hepatic veins there appears to be a place for thrombolytic therapy. Streptokinase acts by activating the fibrinolytic system of the body, resulting in the degradation of fibrin in newly-formed clots throughout the entire body. Thus theoretically there is no reason why streptokinase should not act on recent clot formation in the liver as it acts elsewhere in the body.

We found 3 cases reported in the literature in which acute Budd-Chiari syndrome responded well to thrombolytic therapy.<sup>5-7</sup> We report a further case occurring in a patient with polycythaemia vera who was successfully treated with streptokinase.

## CASE REPORT

A 46-year-old female presented with a 3-month history of headache, lethargy and dizziness, associated with abdominal pain and distension, pruritus and night sweats. On examination she was plethoric with no icterus or evidence of bleeding. Abdominal examination revealed an 8-cm hepatomegaly, 6-cm splenomegaly and minimal ascites. The rest of the examination was within normal limits.

Special investigations showed a haemoglobin of 20,6 g/100 ml and a packed cell volume of 68%. Red cell mass

was 64,9 ml/kg (normal value 26 - 34 ml/kg), and plasma volume was 36,5 ml/kg (normal value 39 - 48 ml/kg). White cell count was 18 200/mm<sup>3</sup> and platelet count 215 000/mm<sup>3</sup>. The neutrophil alkaline phosphatase was 294 units (normal value less than 100), and the uric acid was 8,6 mg/100 ml. Bone marrow trephine revealed a very hypercellular marrow in which all elements were increased. These features are compatible with a diagnosis of polycythaemia vera. Radioactive scanning of the liver, using technetium-99m sulphur colloid (<sup>99m</sup>Tc) showed gross enlargement of the liver with uptake of isotope only in the caudate lobe. Massive splenomegaly was noted (Fig. 1, left). Percutaneous closed liver biopsy showed prominent central venous congestion, with anoxic damage to hepatocytes in areas surrounding central veins and replacement fibrosis in some of these zones. In addition, marked extramedullary haemopoiesis was present.

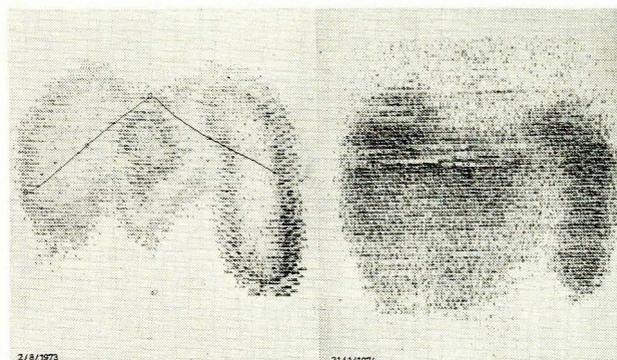


Fig. 1. Liver scan at time of clinical presentation (left) and 6 months later (right).

At this time the patient deteriorated rapidly. The most striking feature was clinical jaundice with the bilirubin rising from 1,3 to a total of 4,9 mg/100 ml. This was associated with further enlargement of the liver and rapid accumulation of gross quantities of ascitic fluid. She also developed evidence of portal encephalopathy as manifested by drowsiness and a flapping tremor. This clinical picture was compatible with acute venous occlusion on an underlying hepatic venous congestion.

Streptokinase (Kabikinase) therapy was immediately commenced in an attempt to lyse the acute thrombosis. An intravenous line was established before the onset of therapy and maintained throughout the course of streptokinase. An initial loading dose of 600 000 units was given over a half-hour period. Thereafter, 100 000 units were

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Date received: 7 August 1974.

given every hour for 96 hours by constant intravenous infusion. As prophylaxis against hyperpyrexia, 100 mg hydrocortisone was given intravenously every six hours during this time. A mild pyrexia, which developed during the course of streptokinase therapy, was treated by tepid sponging and fanning the patient rather than by conventional acetylsalicylic acid or indomethacin because of the hazard of gastro-intestinal bleeding. During the course of therapy, coagulation profiles were not measured to minimise the chance of bleeding from venepuncture sites. Four hours after stopping streptokinase therapy a clotting time and prothrombin index were performed and were within normal limits. Intravenous heparin therapy and oral Warfarin Sodium was commenced at this stage to prevent the occurrence of rebound thrombosis and the propagation of any clot which may not have been lysed. An important adjunct to this therapy was the drainage of 3 litres of ascitic fluid after the completion of the course of streptokinase. Furosemide 40 mg/day and subsequently hydrochlorothiazide 50 mg/day were given as supportive therapy to prevent reaccumulation of ascites.

Definitive therapy of the polycythaemia vera in the form of 10 millicuries of radioactive phosphorus ( $^{32}\text{P}$ ) was given. In the interim, the patient was venesected to keep the packed cell volume below 55%.

The patient remains well 12 months after the acute episode, being maintained on anticoagulants and mild diuretics. A repeat liver scan done 6 months after the initial scan showed increased uptake by the liver and marked decrease in size of the spleen (Fig. 1, right).

## DISCUSSION

Budd-Chiari syndrome is a rare complication of polycythaemia vera, only 5 cases being documented in a series of 1 856 cases of polycythaemia vera.<sup>8</sup> Conversely, analysis of 350 cases of Budd-Chiari syndrome before 1971 revealed 36 cases of polycythaemia.<sup>9</sup> Thomas and Caroli<sup>9</sup> studied 21 cases of primary Budd-Chiari syndrome, of which 17 cases of polycythaemia were noted, and only 2 of which were polycythaemia vera.

Treatment of the chronic phase of Budd-Chiari syndrome should be directed towards treating the underlying condition.<sup>9</sup> In the acute phase there is a role for thrombolytic therapy. Streptokinase should be used by constant intravenous infusion, provided therapy is commenced within 96 hours of formation of the clot.

Streptokinase is an enzyme which activates the fibrinolytic system, converting plasminogen to plasmin, which causes the degradation of fibrin in newly-formed clots. Streptokinase is a dangerous drug and should be reserved for life-threatening situations such as massive pulmonary embolism,<sup>10</sup> acute occlusion of major arteries, and hepatic vein thrombosis. A major complication of streptokinase therapy is internal bleeding, of which cerebral haemorrhage is the most serious. Minor complications include hyperpyrexia and bleeding from venepuncture sites. In the event of a life-threatening haemorrhage, treatment should be stopped immediately and epsilon aminocaproic acid, a fibrinolytic inhibitor, administered intravenously. Hyperpyrexia should be treated prophylactically with hydrocortisone. If hyperpyrexia still develops, treatment should be in the form of tepid sponging and fanning, rather than antipyretic agents such as acetylsalicylic acid and indomethacin, since they may cause erosion of the gastro-intestinal mucosa and precipitate haemorrhage.

Review of the literature reveals only 3 cases of acute Budd-Chiari syndrome treated with streptokinase. Warren *et al.*<sup>5</sup> reported the case of a 22-year-old girl on oral contraceptives who developed marked hepatosplenomegaly and radiological evidence of hepatic vein occlusion. She responded well to streptokinase therapy and was asymptomatic 4 months later. Köstering *et al.*<sup>6</sup> and Flörkemeier *et al.*<sup>7</sup> reported cases of primary Budd-Chiari syndrome which responded to streptokinase therapy.

Hepatic vein thrombosis is a serious disease with a poor prognosis. A therapeutic trial with streptokinase is thus indicated if acute occlusion of the hepatic veins is diagnosed early. Our case demonstrates that there is a role for fibrinolytic therapy, even where the acute occlusion occurs against a background of chronic hepatic vein thrombosis.

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