

Exchange transfusion of a patient with fulminant Lassa fever

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Summary: We report a patient with fulminant Lassa fever who responded dramatically to a 2.5-litre exchange transfusion of whole blood. On admission he was semicomatose with facial oedema and oral haemorrhage; his platelets showed markedly depressed aggregation to ADP; and his plasma inhibited the aggregation responses of normal platelets *in vitro*. Exchange transfusion resulted in rapid clinical improvement, recovery of platelet function, and disappearance of platelet-inhibitory activity in plasma. The patient died 2 weeks later from an acute encephalopathy. His initial response was sufficiently impressive to suggest that further evaluation of this therapeutic approach is justified in selected patients with overwhelming Lassa virus infection.

Introduction

Lassa fever is an acute arenavirus infection endemic in West Africa.¹ Ribavirin is effective treatment for the disease if commenced within 6 days of the onset of fever.² The prognosis for patients who present late in their illness is poor: despite antiviral therapy they may develop facial oedema, haemorrhage and shock, and the fatality rate in such cases exceeds 90%.^{1,2}

The pathogenesis of severe Lassa fever is believed to involve disturbed cellular function rather than direct virus-induced cellular damage.³ Recent studies have shown that plasma from patients with severe Lassa virus infection exerts potent inhibitory effects on the function of normal platelets⁴ and normal neutrophils⁵ *in vitro*. These findings suggested a possible role for some form of plasma exchange therapy. We report a patient with Lassa fever who received a 2.5-litre exchange transfusion of whole blood.

Case report

A 20 year old African man (54 kg) was admitted to a hospital in eastern Sierra Leone with a 2-week history of fever, dry cough and headache, and a 3-day history of gingival haemorrhage. On examination he was semicomatose and had marked facial oedema. His oral temperature was 38.5°C, pulse

124/min and blood pressure 120/80 mmHg. Apart from mild pharyngitis there were no other abnormal signs.

The packed cell volume was 32%, white cell count $27.5 \times 10^9/l$ (90% neutrophils), platelet count $110 \times 10^9/l$ and serum aspartate aminotransferase (AST) 8032 IU/l (normal <45 IU/l). His serum contained IgG and IgM antibodies to Lassa virus at titres of ≥ 1024 and ≥ 16 , respectively. Platelet aggregation studies showed markedly depressed responses to ADP, with rapid and complete disaggregation evident at final ADP concentrations up to 10 $\mu\text{mol/l}$. His plasma inhibited⁴ the ADP-induced responses of normal platelets *in vitro*.

He was commenced on intravenous ribavirin (100 mg/kg loading dose and 25 mg/kg daily in three divided doses for 3 days, then 12.5 mg/kg for the next 7 days²) but over the next few hours he became increasingly drowsy and had two grand-mal fits. This deterioration, and the presence of several poor-prognosis indicators,^{1,2} prompted consideration of plasma exchange therapy. As no facilities for whole-blood centrifugation were available, a simple exchange transfusion was undertaken.

The patient was placed in a small isolation cubicle and his attendant medical staff were provided with disposable gloves, paper masks and gowns. Chloroquine was given subcutaneously for malarial prophylaxis. Five pints of fresh, ABO-compatible blood were obtained, one from his father and four from unrelated local people (none had Lassa virus antibodies detectable in serum). Over a 24-hour period, a 5-unit exchange transfusion was performed.

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During the exchange the patient remained semi-conscious and unresponsive to verbal commands. Twenty-four hours after the procedure, however, his conscious level had improved, there was no fresh haemorrhage occurring from his mouth, and his facial oedema was less marked. His serum AST level had fallen to 2375 IU/l, his platelets showed improved aggregation responses to ADP, and his plasma showed no platelet-inhibitory activity. Over the next few days he became conversant with his attendants and began to eat and drink. Six days after admission he was afebrile and his platelets showed normal ADP-induced aggregation responses. Thirteen days after admission he was eating well and walking unaided, his white cell count was $6 \times 10^9/l$ and his serum AST 100 IU/l.

However, on the day of his intended discharge from hospital he was found in a state of stupor. He was drowsy but responded to painful stimuli. A diffuse, fine tremor was evident, most marked in the upper limbs, and he had mild left-sided weakness. Reflexes were generally depressed, the plantar responses extensor. His blood sugar was normal and malarial parasites were absent from blood smears. Acute post-viral encephalopathy was diagnosed. Over the next 48 hours his conscious level deteriorated and he developed a chest infection. Despite intensive nursing care, intravenous fluids and antibiotics, he died. An autopsy was refused.

Discussion

This patient had life-threatening Lassa fever and deteriorated despite antiviral treatment. Although transfusion of blood in West Africa poses several major hazards, it was felt that his prognosis was sufficiently grave to justify some form of plasma exchange therapy. The exchange procedure was followed by a dramatic clinical improvement, cessation of haemorrhage, recovery of platelet function, and disappearance of platelet-inhibitory act-

ivity in plasma. Such a rapid recovery from Lassa fever of this severity is exceptional, and it may therefore have been directly related to the exchange transfusion; however, the mode of therapeutic benefit is not clear. Unfortunately, the patient died 2 weeks later from an acute encephalopathy, a complication of Lassa fever which is currently ill-understood.¹

The rationale for performing the exchange was based on the findings of our recent studies which showed that plasma from patients with severe Lassa fever profoundly inhibits the function of normal platelets and normal neutrophils *in vitro*.^{4,5} The nature of the inhibitory factor has not yet been defined, but it appears to be neither virus nor virus antibody since the inhibitory phenomenon cannot be reproduced by supernatants from Lassa-virus-infected tissue cultures, nor by concentrated IgG fraction from convalescent serum.⁴

To our knowledge, no form of plasma exchange therapy has previously been attempted in a patient with Lassa fever. However, infusions of convalescent, immune plasma have been employed, with variable success.^{2,6,7} Since it is now clear that plasma from convalescent Lassa fever patients does not contain significant amounts of neutralizing antibody,² any apparent benefit from its use is unlikely to have been due to direct antiviral activity. An infusion of non-Lassa-immune plasma has also been reported, in a single case, to have been associated with a favourable outcome.⁸ However, there has been too little experience with plasma infusions, both immune and non-immune, to assess the possible efficacy of such therapy in patients with fulminant Lassa fever. The dramatic response shown initially by our patient suggests that further evaluation of this therapeutic approach is justified.

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