ACUTE HAEMOLYTIC ANAEMIA AS A COMPLICATION OF TYPHOID FEVER

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Haemolytic anaemia as a rare complication of typhoid fever was first recognized by Osler in 1895. Since then, however, less than 40 authentic cases have been described in the medical literature.\textsuperscript{1–16} We wish to report a patient who had typhoid fever and presented with acute intravascular haemolysis.

CASE REPORT

A 36-year-old Bantu labourer was admitted to the Karl Bremer Hospital on 11 March 1963. He had been in good health until 3 days previously when he fainted on arriving home from work. He subsequently passed much red blood per rectum and felt weak and feverish. The next day he remained in bed with progressive malaise and headache and noticed that his urine had become ‘like black coffee’. At no time did he experience rigors, vomiting, diarrhoea or significant abdominal pain. On the third day of his illness he again passed blood per rectum and was admitted to hospital.

The patient had come from the Transkei a year previously. His past history and further clinical interrogation revealed nothing else of note, except ‘kidney trouble’ in 1954. No typhoid contacts could be traced.

Clinical Examination

An ill, well orientated man of normal build presented with a temperature of 102°F and a respiration of 24/min. There was mild scleral jaundice but no significant adenopathy, bleeding tendency, splinter haemorrhages or skin rashes.

Cardiovascular system. BP 150/90, pulse 84/min. (good volume), heart normal.

Abdomen. Mild peri-umbilical tenderness but no masses or peritoneal irritation; liver was just palpable but spleen not clinically enlarged; rectal examination showed melaena but no other abnormality; proctoscopy was normal. The rest of the clinical examination was non-contributory.

Urime. Dark red colour. Microscopy: abundant epithelial cells but no red cells, pus cells or cylinders. Chemical tests: protein ++++, orange sugar reduction with Benedict’s reagent; bile and urobilinogen not demonstrated; porphyrins absent. Spectroscopy: oxyhaemoglobin present. 

Peripertite fluid. Hb. 5·8 G/l00 ml.; PCV 16%; MCHC 36%; leucocyte count 30,000/cu.mm. (lymphocytes 14%, neutrophils 77%, staff cells 4%, metamyelocytes 5%, occasional myelocytes); normoblasts 4/100 leukocytes; reticulocyte count + + ; orange sugar reduction with Benedict’s reagent; bile and urobilinogen not demonstrated; porphyrins absent. Spectroscopy: oxyhaemoglobin present.

Blood urea was 16 mg./l00 ml. (13 March); 64 mg./l00 ml. (15 March); 104 mg./l00 ml. (16 March). However the urine output remained satisfactory and on 26 March the blood urea had fallen to 48 mg./l00 ml.

The haemoglobinuria decreased rapidly and disappeared on the third day after admission. All clinical signs of haemolysis were absent. The rest of the haematology was normal. No malaria parasites were found. The blood Wasserman and Kahn tests were negative. The direct and indirect Coombs’ tests were negative. Schumm’s test was positive. No red cells, pus cells or cylinders were found and no serum haemolysins could be demonstrated. The occurrence of severe renal haemorrhage recurred, necessitating a blood transfusion of 8 pints. On the same day the Microbiology Department reported isolation of Salmonella typhi from blood cultures taken on admission.

Immediate treatment with chloromycetin (500 mg. 4-hourly for 3 days followed by 500 mg. 6-hourly) was instituted and 5 days later the patient was afebrile.

The glycosuria and raised blood sugar values suggested diabetes mellitus. On a 1,200-calorie diabetic diet the glycosuria disappeared and the blood sugar fell to 74 mg./l00 ml. (26 March).

No further complications were noted and on 27 March he was transferred to the City Hospital for Infectious Diseases, where he made an uninterrupted recovery.

Subsequent follow-up was not possible as the patient returned to the Transkei after discharge from hospital.

DISCUSSION

The occurrence of haemolytic disease in the course of typhoid fever might not be as rare as is generally thought. Osler\textsuperscript{1} found 1 case among 1,500 typhoid patients, but Huckstep\textsuperscript{2} in 1962 recorded an incidence of 2%, while Berman et al.\textsuperscript{12} found an incidence of 5·9% in 1945. McFadzean and Choa\textsuperscript{14} reported the rather similar figure of 4·6% among the Chinese of Hong Kong in 1953; they remarked on the absence of haemolysis in paratyphoid A, B and C. Nevertheless Ruggieri\textsuperscript{16} as recently as 1961 reviewed the world literature and could find no more than 32 reported cases of haemolytic anaemia from salmonella infections, and at least 5 of these are doubtful instances.\textsuperscript{4,7}

The mechanism of haemolysis is not clear. As happened in our case, at least 50% of the reported instances of acute typhoid haemolysis with haemoglobinuria occurred during the first week of illness, when bacteraemia is known to be maximal. However, the salmonella is normally an anaemolytic organism. Although early work by Friedberger and Vallen\textsuperscript{17} in 1923 did suggest that bacteriophage interaction may render the salmonella haemolytic under certain experimental conditions, this is unlikely as a spontaneous occurrence. McFadzean and Choa\textsuperscript{14} noticed that haemolysis did not parallel the severity of infection but outlasted the pyrexial illness. A large proportion of their cases also had a positive Coombs’ test and seemed to respond to ACTH rather than to antibiotics. They therefore sug-
gusted an underlying auto-immune aetiology, possibly associated with the lymphoid hyperplasia of typhoid fever. Our patient was Coombs-negative and the haemolytic crisis cleared after a blood transfusion in the presence of undiminished pyrexia. Rapid disappearance of clinical haemolysis as well as repeated large blood transfusions, necessitated by recurrent intestinal haemorrhage, hindered satisfactory appraisal of the haemolytic process. However, the investigations performed showed no cause for haemolysis besides the obvious systemic infection. Heinz bodies suggestive of 'drug-induced' haemolysis were not demonstrated, but the glucose-6P-dehydrogenase content of his erythrocytes was not estimated. McFadzean and Choa considered ACTH of great therapeutic value in their cases, but Ruggieri reported a disappointing response to prednisone. Nevertheless, one feels that steroid therapy should be instituted in this condition, as its value is well established in fulminating typhoid.

The present case illustrates the protean manifestations of atypical typhoid fever. In addition to the haemolytic episode the patient presented with severe intestinal haemorrhage during the first week of illness. The persistent leucocytosis and tachycardia can be partially attributed to the acute blood loss and haemolytic reaction. Diabetes mellitus is not a recognized complication of typhoid, but latent diabetes may be unmasked by the stress of any severe systemic illness.

A general knowledge of first aid measures and their speedy application are among the most important factors for reducing the alarmingly high accident mortality rate in modern industrial society.

It has been estimated that there would be a reduction of 20% in the accident mortality rate if traffic casualties were given proper treatment before arrival in hospital. As far back as 1957, over 100,000 people were killed during the year through road accidents all over the world. Thus at least 20,000 lives yearly could be saved simply by better first aid and care during treatment.

1. Frequency of Severe Injuries in Road Traffic Accidents

In all the categories of road users, head injuries are very frequent in accidents. In the series reviewed, the incidence varies between 50% and 80%, while for thoracic injuries it was between 10% and 40%. In the survey of traffic accidents in Scandinavia, every second casualty had head injuries, and in 69% of fatal accidents, this was the main cause of death. Thoracic injuries represent the second highest percentage of fatal injuries, being the main cause of death in 13%. Injuries to the upper and lower extremities were found in 30% and 38% respectively but they contributed only 2.3% of the deaths. Of the fatal injuries, 31% died at the scene of the accident and 10% during transport to hospital. In these two groups, out of 36 deaths with head injuries, in 16 there was obstruction of air passages with blood, mucus or gastric contents, and in 10 this obstruction was the main cause of death, the cranio-cerebral and other injuries per se being considered compatible with life.

Conclusion. In head and thoracic injuries, interference with the respiration is an important factor contributing to a fatal outcome, and in many cases early elimination of this factor may save the victims. The rescuer must, therefore, have a clear knowledge of the mechanism of the interference with the vital functions in order to give the casualty the best possible chance of survival.

2. Necessity for Immediate Support of Respiration

Whenever there is a disturbance of consciousness, ventilation of the lungs may cease for no other reason than that the air passage is no longer actively held open. The tongue is no longer actively held in such a position that the air can pass freely and protective reflexes such as swallowing and closure of the larynx may not be functioning to prevent foreign matter, e.g. blood, from blocking the pharynx or being inhaled. A cerebral trauma can directly influence and reduce central respiratory activity, and damage to the thoracic cage, pleura or lungs will impair the normal mechanics of lung ventilation. In acute obstruction of the airway (obstructive asphyxia) the resistance of the brain to anoxia is all-important.

Conclusion. The time available for relieving airway obstruction and beginning artificial respiration in an accident with respiratory difficulties is very short, since, owing to anoxia, other vital functions sometimes fail before the complete cessation of respiratory movement. Speed is therefore of the

Abstract

THE ORGANIZATION OF RESUSCITATION AND CASUALTY SERVICES

[Part 2]

ASPECTS OF FIRST AID WITH SPECIAL REFERENCE TO SUPPORT OF VITAL FUNCTIONS IN ROAD TRAFFIC INJURIES

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SUMMARY

A case of typhoid fever is reported, which presented with acute intravascular haemolysis and melaena during the first week of illness. The literature on typhoid haemolysis is briefly reviewed; the association is possibly less uncommon than is generally thought.

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REFERENCES