

A medical mystery

J M van der Klooster

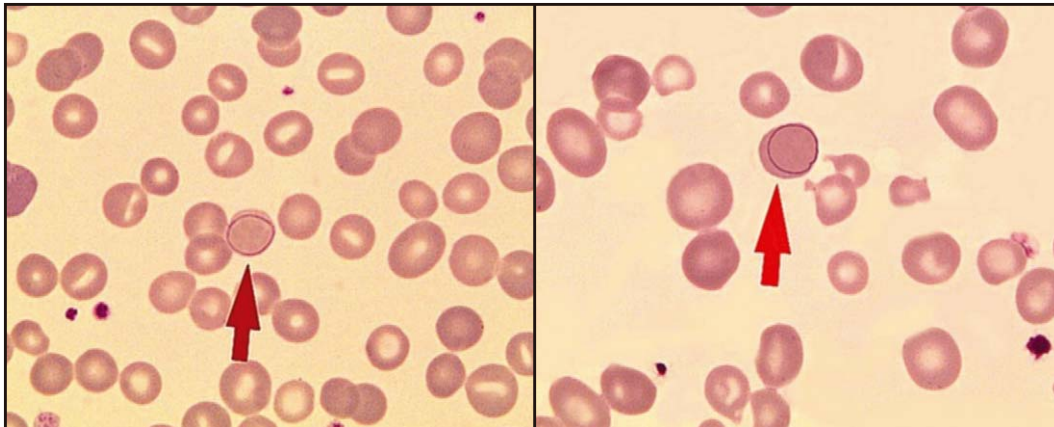


Fig.1 Peripheral blood films (May-Grunwald Giemsa stain, x1000).



Fig.2 Peripheral blood films (May-Grunwald Giemsa stain, x1000).

CASE PRESENTATION

A 25-year-old man was admitted because of abdominal pain, nausea, vomiting, weight loss, and anaemia. His medical history consisted of schizophrenia for which he received outpatient psychiatric treatment. Physical examination showed a pale and jaundiced patient. He was in a malnourished condition with generalised muscular atrophy of the limbs, especially the hands. His blood pressure was 90/60 mmHg with a regular pulse rate of 100/minute. His body temperature was

normal and melaena was not observed. Laboratory examinations showed the following results: Hb 4.7 mmol/L, MCV 80 fl, bilirubin 75 µmol/L (normal <18), LDH 950 U/L (normal <350), haptoglobin 0.1 g/L (normal 0.3-2.0), and reticulocyte count 93% (normal <20). Total and differential leukocyte count and platelet count were normal. Endoscopy of the upper digestive tract showed no abnormalities. What do the peripheral blood films (Figs. 1 & 2) show? What is the diagnosis?

Department of Intensive Care Medicine
Ikazia Ziekenhuis
Montessoriweg 1
3083 AN Rotterdam
The Netherlands

J M van der Klooster,
MD
Intensivist

Correspondence to:
Dr Johan M van der Klooster
Tel: (31) 10 2975000
Fax: (31) 10 2975400
Email: vdklooster@cistron.nl

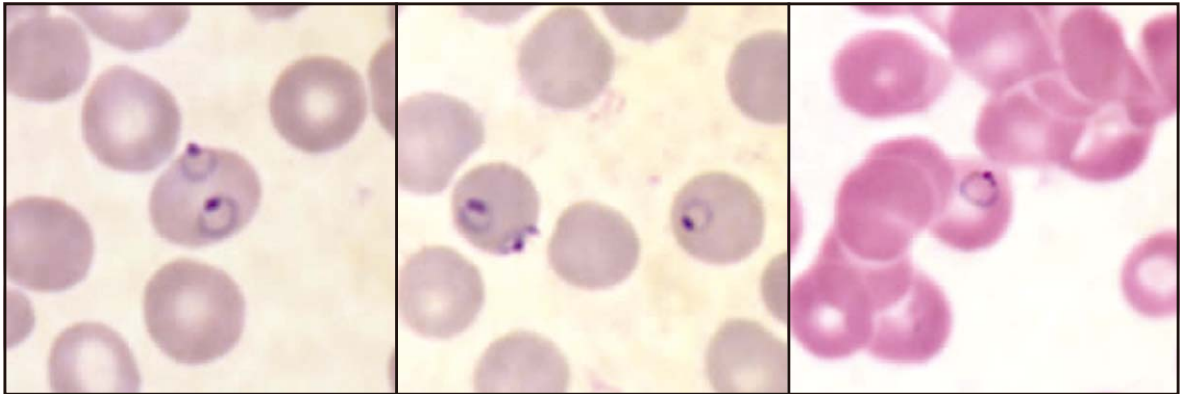


Fig. 3 *Plasmodium falciparum* rings have delicate cytoplasm and 1 or 2 small chromatin dots. Red blood cells that are infected are not enlarged; multiple infection of red blood cells are more common in *P. falciparum* than in other species. Occasionally, appliqué forms (rings appearing on the periphery of the red blood cell) are present.

BLOOD FILM INTERPRETATION

The peripheral blood films (Fig. 1) show anisocytosis (variation in size) of the erythrocytes and several stomatocytes. Cabot's rings (arrows) are loop-shaped or "8"-shaped inclusions found in erythrocytes during failure of the erythropoiesis. The inclusions are probably formed from a part of the mitotic spindle. Occurrence in blood is normally not present.

The peripheral blood films (Fig. 2) also show erythrocytes with anisocytosis and basophilic stippling. Basophilic stippling (arrows) is characterised by very fine, pinpoint granules distributed evenly in the cytoplasm. It can be observed in lead poisoning, thalassaemia and other dyserythropoietic anaemias. Occurrence is less than 0.1% of the erythrocytes in normal blood.

The symptoms of abdominal pain, jaundice, haemolytic anaemia, and ring-like structures in the erythrocytes are highly suggestive of tropical malaria. However, the size and shape of the *Plasmodium falciparum* protozoa (Fig. 3) are somewhat different from Cabot's rings, often with a high parasite rate in each red blood cell. More importantly, our patient had no fever, did not travel to malaria endemic areas, and had a rather microcytic blood film. Moreover, basophilic stippling was noted besides Cabot's rings, suggesting failure of the erythropoiesis. The clinical signs and symptoms, and laboratory abnormalities are highly suggestive of lead poisoning.

DIAGNOSIS

Lead poisoning.

CLINICAL COURSE

This patient had classical signs and symptoms of severe lead intoxication (5.7 $\mu\text{mol/L}$, normal range 0.06-0.60). The urinary lead excretion after admission was 1.1 $\mu\text{mol/L}$ (normal <0.28 $\mu\text{mol/L}$). Urinary lead excretion after administration of intravenous edetate

calcium disodium (EDTA) could be increased to levels as high as 38.0 $\mu\text{mol/L}$. Electromyography showed typical motor nerve neuropathy of the arm and hand, due to segmental demyelination and axonal degeneration.

Treatment consisted of administration of lead-chelating agents (intravenous EDTA) and oral 2, 3 dimercapto-succinic acid (DMSA) administered over several weeks. Thereafter, the patient was transferred to a psychiatric hospital because of persisting delusions. All other family members were healthy and had normal lead concentrations in the blood. The source of the lead intoxication could only be elucidated after questioning the mother, who admitted to have seen her son secretly experimenting with lead-containing paint and other chemicals in the garage. The psychiatric symptoms are believed to be the cause, not the consequence, of the lead intoxication.

DISCUSSION

Lead has inhibitory effects on many enzymes of the haem biosynthesis, the major constituent of the erythrocytes (Table I), resulting in the excretion or accumulation of porphyrins. Lead especially inhibits δ -ALA (delta-aminolevulinic acid) dehydratase and limits the intracellular delivery of iron to the site of ferrochelatase, leading to accumulation of zinc protoporphyrins. Typical findings are elevated urinary excretion of coproporphyrins, pentaporphyrins and δ -ALA, with normal urinary excretion of hexa-, hepta-, and uroporphyrins, and significantly elevated zinc protoporphyrins in blood, with decreased δ -ALA dehydratase activity. The accumulation of porphyrins is toxic and may lead to peripheral neuropathy (especially motor nerves), colicky abdominal pain (mimicking the acute abdomen, especially as there may be mild fever and leukocytosis), paralysis, psychosis and rarely, haemolysis.

To establish the diagnosis of lead poisoning, the blood and urine should be checked for porphobilinogens, porphyrins and lead concentrations. The lead concentration measured in the blood of this patient was 5.7 µmol/L (normal range 0.06-0.60). The treatment of choice is urinary elimination of the lead by means of lead- chelating agents. Examples of these agents are intravenous EDTA and oral 2, 3 dimercapto-succinic acid (DMSA), both of which were given to the patient presented.

ABSTRACT

A 25-year-old schizophrenic man presented with abdominal pain, nausea, vomiting, weight loss and anaemia. He was noted to be malnourished with generalised muscle atrophy. Laboratory investigations showed Hb 4.7 mmol/L, MCV 80fl, bilirubin 75 micromol/L and reticulocyte count 93 percent. Peripheral blood films showed anisocytosis, basophilic stippling and Cabot's rings. Electromyography confirmed typical motor nerve neuropathy. The clinical and laboratory findings were that of lead poisoning. The patient was later found to be ingesting lead-containing paint. He was treated with lead-chelating agents.

Keywords: lead-chelating agents, lead poisoning, peripheral neuropathy

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Table I. The effects of lead on porphyrin metabolism.

