

Anaemia and abdominal pain due to occupational lead poisoning

We describe a 47-year-old patient with chronic anaemia with basophilic stippling of erythrocytes, recurrent abdominal colics, discoloration of gums, sensitive polyneuropathy to the four limbs, hyperuricaemia, hepatosteatosi with raised transaminases, and a long ignored history of lead exposure in a battery recycling plant. The diagnosis of poisoning was confirmed by high lead levels in the blood and urine, decreased erythrocyte delta-aminolevulinic acid dehydratase (ALA-D), raised erythrocyte zinc protoporphyrin (ZP), and elevated urinary excretion of porphyrins. Chelation with EDTA resulted in increased urinary lead excretion, gradual improvement of the clinical picture, and progressive normalization of lead biomarkers. The case highlights the importance of occupational anamnesis for the diagnosis of lead poisoning, an uncommon condition which may mimic a variety of internal and surgical diseases. Since antiquity, lead has been extensively mined, produced, and utilized in a variety of industrial settings, such as metallurgy, construction, production of plastics, ceramics, paints and pigments.¹⁻³ Lead and its compounds are systemic toxicants, and a wide range of adverse health effects (including haematological, gastrointestinal, neuropsychiatric, cardiovascular, renal, endocrine, and reproductive disorders) has been observed in exposed workers.^{1,4,5} The general population (particularly children) may also be exposed to toxic lead levels due to air, soil, food and water contamination.^{1,4,6} Thanks to the improvement of workplace hygienic conditions, the pathological picture of occupational lead poisoning (plumbism, saturnism) has gradually become less serious, at least in the most industrialized countries, and has progressively changed into aspecific, subclinical manifestations.^{1,5,7} We describe here an unusual case (nowadays) of anaemia and recurrent abdominal pain due to lead poisoning from battery recycling.

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Report

A 47-year-old male was referred to our Institute for recurrent abdominal colics, after having been hospitalized elsewhere twice. On such occasions, no occupational history had been collected, surgical conditions (acute cholecystitis, intestinal occlusion) suspected, radiodiagnoses and endoscopies performed with negative results. Each time, the patient had denied consent to explorative laparoscopy, had been treated symptomatically, and had resumed working.

On admission, the patient complained of fatigue, diffuse abdominal cramps, alternance of diarrhoea and constipation, and paraesthesiae in the upper and lower limbs. Physical examination revealed grade I obesity, pale skin and mucous membranes, a thin blue-grey line at the upper gum margin (Figure 1), abdominal tenderness, and mild hepatomegaly. Blood tests showed normocytic, normochromic anaemia (RBC: 3.58×10^6 /microL; Hgb: 11.4 g/dL; Hct: 32.2%; MCV: 89.9 fL; MCH: 31.9 pg; MCHC: 35.4 g/dL), reticulocytosis (6.9%), basophilic stippling in 3% of erythrocytes (Figure 2), hypersideraemia (177 microg/dL), mixed hyperbilirubinaemia (total: 2.3 mg/dL; direct: 0.5; indirect: 1.8),

Figure 1. Discoloration of the upper gum margin (*Burton's line*).

raised AST (56 U/L) and ALT (137 U/L), decreased cholinesterase (3693 U/L), and hyperuricaemia (8.0 mg/dL). Abdominal ultrasonography demonstrated hepatosteatosi. Electroneurography revealed slight axonal, sensitive polyneuropathy to the four limbs.

The subject reported to have worked during the previous three years in a lead recycling plant, where used batteries and other scraps were shattered and melted. He reported bad hygienic workplace conditions, and heavy exposure to lead fumes and vapours.

Lead levels were 148 µg/dL in blood (Pb-B) and 120 µg/24 hr in urine (Pb-U). Erythrocyte delta-aminolevulinic acid dehydratase (ALA-D) and zinc protoporphyrin (ZP) were 3 U/L (normal > 25) and 258 microg/dL (normal < 40), respectively. Urinary excretion of porphyrins and their precursors was elevated: delta-aminolevulinic acid (ALA-U), 8 mg/dL (normal < 0.45); porphobilinogen, 0.80 mg/dL (normal < 0.20); uroporphyrin, 167 microg/24 hr (normal < 20); coproporphyrins (CP-U), 1820 microg/24 hr (normal < 100).

Lead exposure was stopped. The patient was treated with three cycles of EDTA 1 g/die i.v., for 5 days: chelation was well tolerated, and revealed a high lead body burden, as indicated by increased urinary excretion (up to 2851 microg/24 hr on day 3 of the first cycle). Gradually, Pb-B decreased to 16 microg/dL, and the haematological and clinical picture improved, with the exception of the peripheral neuropathy. This was paralleled by progressive normalization of the biomarkers for lead effects (ALA-D, ALA-U, urinary porphyrins), except ZP (109 microg/dL at the end of the third EDTA cycle; 45 microg/dL seven months later).

The Italian Workers' Compensation Authority (INAIL) recognized the occupational origin of the disease.

Discussion

The patient showed the classical features of occupational lead poisoning, characterized by anaemia with basophilic stippling of red cells, discoloration of gums (*Burton's line*) and abdominal pain (*saturnine colic*). This picture is observed exceptionally in current clinical practice, in that Pb-B in exposed workers (the most reliable index of internal dose) nowadays rarely exceeds 60-80 microg/dL, over which overt toxicity occurs.⁸ Few similar cases have been reported during the last years, some of them caused by lead smelting and recycling,⁹⁻¹¹ as

Figure 2. Peripheral blood smear showing erythrocytes with basophilic stippling (May-Grünwald-Giemsa stain).

described here.

The clinical manifestations of chronic lead poisoning appear after a latency period of months to years since the beginning of exposure. The bone marrow is the most sensible target for lead toxicity: the metal interferes with a variety of haeme biosynthetic enzymes, including ALA-D (conjugating levulinic acid to form porphobilinogen) and ferrochelatase, incorporating Fe²⁺ into protoporphyrin IX. Resulting anaemia may be microcytic or, as reported here, normochromic normocytic, with hyper-sideraemia, reticulocytosis and basophilic stippling, due to the persistence of cytoplasmic proteins.⁹⁻¹² Stippled erythrocytes are typical but not specific for lead poisoning, since they also appear in other haematological diseases (e.g., thalassaemia, vitamin B12 deficiency, pyrimidine 5' nucleotidase deficiency), or after exposure to other toxicants such as aniline, arsenic or benzene.^{12, 13}

The reaction of circulating and salivary lead with sulphur ions released by oral microbial activity may cause the deposition of lead sulphide at the interface of the teeth and gums, referred to as Burton's line.^{1, 7, 11} Lead colic (first described by Hippocrates in 370 b.C.) may mimic the acute abdomen.^{2, 7} Neurotoxicity is long-lasting and usually strikes peripheral motor nerves, though sensitive fibres may also be involved, as described here.^{1, 4, 5} Hyperuricaemia and hepatotoxicity (partly due, in the observed case, to dietary factors) are other less common manifestations of lead poisoning.^{1, 2}

Diagnosis usually relies on Pb-B determination: the concentration gradually declines over 2-4 weeks after the patient has been removed from the source. Thus, a subject may be symptomatic with a Pb-B within the acceptable range. In such case, ZP (resulting from the binding of free protoporphyrin IX with zinc) should be additionally measured, in that this biomarker remains in the blood for the life-time of the erythrocyte, reflecting lead exposure over the prior 3-4 months. By contrast, after long exposure, Pb-B may remain elevated for years after cessation, due to redistribution from bone. Urinary lead excretion after chelation is useful to estimate the body burden. ALA-D and ALA-U are both sensitive and specific indicators of lead exposure, though they are not utilized routinely in the clinical setting.^{8, 14}

Management of plumbism requires, first of all, the interruption of exposure. Chelating agents, which form

lead complexes that are eliminated in the urine, are indicated in severe cases: EDTA is currently considered the most reliable and safe drug, the principal risk being nephrotoxicity.¹⁵ As in the patient described, ZP is the last biomarker to normalize after the exposure has ceased, and chelation carried out.^{8, 14, 15}

In conclusion, this case report highlights the importance of occupational history for the diagnosis of lead poisoning, an uncommon condition which may mimic a variety of internal and surgical diseases. In turn, current diagnosis is crucial for prognosis, treatment (preventing unnecessary surgery), and occupational-related medico-legal issues.

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