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A case of recurrent abdominal pain

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تقرير عن حالة ألم البطن الراجع

فيصل التميمي ، براساد جورج ، فيندوكومار انكاراث

المستخلص: نستعرض هنا حالة مريض يبلغ الأربعين سنة من العمر تم إدخاله الى مستشفى نزوى المرجعي وكان يشكو من ألم البطن الراجع . وأثبتت الفحوص المخبرية وجود نسبة مرتفعة من الرصاص في دم المريض وكانت إستجابته للعلاج سريعة .

ABSTRACT. The paper decribes the case of a forty-year-old male patient who was admitted with recurrent abdominal pain. Investigations revealed high levels of blood lead; symptoms responded promptly to treatment. The paper also reviews lead poisoning and its treatment.

Key words: lead poisoning, plumbism, sodium calcium edetate, case report, Nizwa, Oman

HEAVY METAL POISONING, ESPECIALLY LEAD, is one of the rare causes of recurrent abdominal pain. However, lead is still widely used in traditional medicines, cosmetics, and food additives.[1] In any chronic, ill-defined abdominal pain, history of using lead containing traditional medicines or cosmetics is of relevance as illustrated in the case described here.[1,2,3]

THE CASE

A forty-year-old Omani national was admitted with recurrent attacks of abdominal pain and vomiting for six weeks. The onset of the symptoms had been sudden. The pain was severe and generalised with no particular radiation. The peak of the pain was associated with vomiting which was bilious and non-bilious without any blood. During the episodes the patient was constipated. There was no abdominal distension, borborygmi, fever, weight loss, or change in appetite. A typical episode would last 2–4 days with continuous baseline pain and periodic exacerbation, to recur again in 5 to 7 days. There were no other gastrointestinal, cardiovascular, respiratory, or psychiatric symptoms.

He had been admitted with similar complaints twice previously, 4 and 6 weeks earlier. Detailed investigations in both instances had not yielded any diagnosis and his symptoms had settled spontaneously.

He had undergone appendectomy 22 years earlier, which was reported to be uneventful. There was a history of psychiatric treatment from the Sultan Qaboos University Hospital, Muscat, for a brief episode of abnormal behaviour. No details were available. He was diagnosed to have hypertension a few months previously.

The patient had a history of moderate alcohol intake for 15 years, which he stopped 5 years ago. The smoking history was similar. There was no history of any major illness in the family, related, or unrelated to the present problem. He was on Atenolol 50 mg daily for hypertension. He revealed that he was also taking some indigenous Omani drugs for 4 years for behavioural problems.

On examination he appeared well built, alert and oriented. His pulse rate was 82 per minute, regular and blood pressure ranged from 130 to 180 systolic and 70 to 110 diastolic. He had no fever. He looked ill with pallor and mild jaundice. There was no cyanosis, clubbing, lymph node enlargement, skin, eye or oral lesions and no stigmata of chronic liver disease. The chest and cardiovascular systems were normal. The abdomen was soft, not distended and without any mass or visible peristalsis. There was mild epigastric tenderness. The bowel sounds were initially high pitched, but later turned sluggish. The rest of the physical examination, including that of the nervous system, was normal.

INVESTIGATIONS

Total WBC count 8.2×10^9/l (normal 3.8–9.8), neutrophils 6×10^9/l (1.8–6.6), lymphocytes 1.6×10^9/l (1.2–3.3), monocytes 5×10^9/l(0.2–0.7), eosinophils 0.022×10^9/l (0–0.4), basophils 0.06 (0–18.8), RBC 2.88×10^{12}/l (4.5–5.7), haematocrit 22.2% (40.7–50.3%), MCV 77.1 fl (80–97.7f), MCH 26.6 pg/cell (26.7–33.7), MCHC 34.6 g/dl

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(32.7–35.5), platelets 308×10^9/l (140–440) and ESR 7 mm in the first hour (0–15). The haemoglobin was repeatedly around 7 to 8 g/dl; the reticulocyte count, which was 5%, later rose to 18% (0.5–1.5%). RBC sickling and Direct Coombs test were negative and Hb electrophoresis was normal. Peripheral smear study showed aniso-poikilocytosis with hypochromia and target cells. WBC and platelets were normal. Malarial parasites were not seen.

Urine examination, blood glucose, and renal function tests yielded normal results. Serum bilirubin was 42 µmol/l (normal 0–18.8), indirect bilirubin 10 µmol/l, ALT 58 U/l (0–35), AST 33 U/l (0–35), ALP 321 U/l (39–117), total proteins 7.9 G/dl (6.5–8.5), and albumin 4.3 G/dl (3.5–5.5). Serum amylase ranged from 501 to 660 IU/l (25–115), with pancreatic specific amylase 37 IU/l (normal up to 48) and urine amylase was 156 IU/24 hrs (60–450). Serum cholesterol, triglycerides, calcium and uric acid were at normal levels. The urine was negative for haemoglobin and porphobilinogen. Antinuclear antibodies and hepatitis B and C markers were negative. X ray of chest, plain X ray, ultrasound and CT scan of the abdomen, barium meal follow-through and ERCP yielded normal results.

In view of these results, the possibilities considered were biliary or pancreatic disease, subacute intestinal obstruction in view of the previous appendectomy, metabolic problems like acute intermittent porphyria and haematological problems like acute haemolysis or paroxysmal nocturnal haemoglobinurea. However, the imaging studies including ultrasound and CT scans did not support any biliary or pancreatic pathology. Plain X ray abdomen and barium meal were not in favour of intestinal obstruction. The patient's urine was negative for porphobilinogen. The investigations did support low-grade haemolysis but not paroxysmal nocturnal haemoglobinurea.

On reviewing the history, consumption of traditional medicines was viewed with suspicion. Therefore a blood lead level was asked for, which was reported to be more than 165.7 µg/dl (Blood lead assay conducted by Laboratory Marcel Merieux, France; analytical cutoff of the reference lab: <4 µg/dl). A repeat sample showed the level to be above 200 µg/dl, suggesting ongoing lead exposure. Since the patient was not occupationally exposed to lead, the likely source was his traditional medicines. He was hospitalised for chelation therapy.

He was given a course of sodium calcium edetate 25 mg/kg for 5 days followed by d-penicillamine 250 mg twice daily for 5 months with close monitoring of blood lead levels. This dropped to <40 µg/dl by the end of chelation therapy and the symptoms subsided [Figure 1].

The long time taken for the blood lead to fall to acceptable levels was most likely due to the slow mobilisation of stored lead from different tissues, although ongoing consumption could not be completely ruled out.

The patient's haemoglobin, which had been 8.3 g/dl at the beginning of chelation, steadily rose to 15 g/dl towards the end of treatment [Figure 2].

DISCUSSION

Lead is an element found in the environment, but not naturally in the body. It is also one of the commonest environmental toxins. It is poisonous in all forms and especially hazardous because of its cumulative toxicity. Intoxication occurs either by ingestion, inhalation, or absorption through the skin.[4,8] Rarely it has been reported due to retained bullets.[5] Inhalation mainly occurs from emissions of motor vehicles, lead smelters, mining, plumbing, cable making, and lead glass blowing.[4] However, the commonest source of chronic intoxication

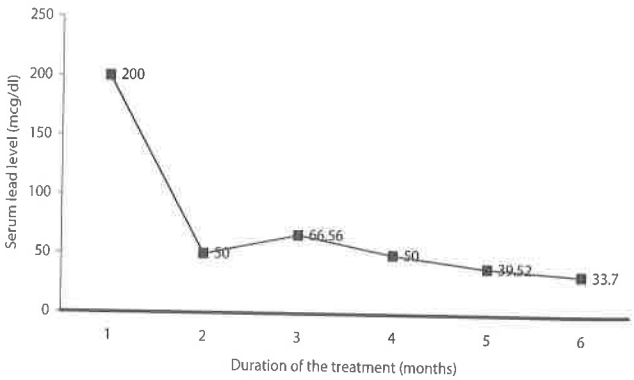

Figure 1. *The drop in blood lead levels after chelation therapy*

is repeated ingestion of small amounts. The common sources are water which dissolves lead in plumbing systems,[6] food,[7] cosmetics,[2] and medicines.[3] Lead containing traditional medicines have been widely used in India, Pakistan, China, the Middle East and African subcontinent for centuries.[1] They range from eye drops to skin ointments[8] and fumes of lead to oral preparations.[3] Traditional hair darkening cosmetics also contain lead, but absorption is thought to be minimal.[7]

Absorption and distribution of lead in humans resemble that of calcium. Once absorbed, the lead is

distributed to three compartments.[9] The first compartment is blood where it has a half-life of about 35 days. The second compartment consists of soft tissues, which accumulates only about half that in the blood and has the same half-life. The third compartment, the skeleton, retains the vast bulk of body lead, where it has a very long half-life extending up to 27 years.

Intoxication from single exposure to lead is rare, but can occur from accidental or intentional ingestion of a soluble salt.[10] The initial signs and symptoms are due to local irritation of the gut. If absorption is sufficient, abdominal pain, leg cramps, muscle weakness, paraesthesias, coma and death may follow in a few days.

Chronic plumbism expresses itself in many ways. Three major syndromes have been recognised.[4]

1. *Alimentary type,* characterised by anorexia, constipation, abdominal cramps (lead colic) and metallic taste. Lead induced abdominal pain may resemble an acute surgical emergency.[11] Slow onset megacolon with return to normal after chelation therapy has been reported.[4]
2. *Neuromuscular type,* characterised by peripheral neuritis, which is painless and restricted to extensor muscles, wrist drop being the commonest. There may be arthralgia or myalgia, but sensation is unaffected. Slowing of motor and sensory nerve conduction velocities has shown a close correlation with blood lead levels.[12]
3. *Cerebral type,* which has also been called lead encephalopathy, is the most common type in children.[4] The characteristic presentation is convulsions or a preconvulsive state. Mild degrees of intoxication are associated with subtle psychological dysfunction including impairment of psychomotor performance and long-term memory, auditory and speech processing and non-adaptive behaviour in the classroom.[13]

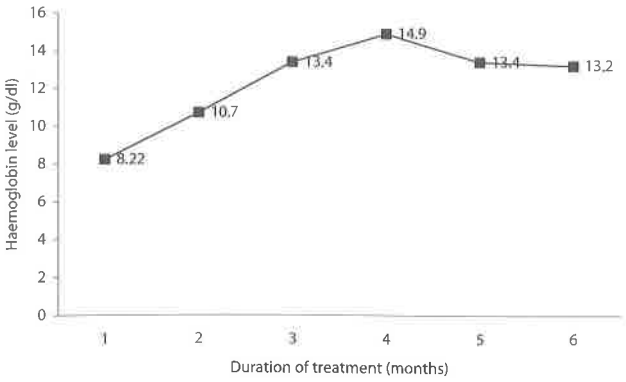

Figure 2. *Change in haemoglobin levels during and after chelation therapy*

Anaemia in lead poisoning is multifactorial. There is a significant association between low-level lead poisoning and iron deficiency anemia.[14] Lead also leads to haemolysis and is a potent inhibitor of delta aminolevulinic acid dehydrase, a compound enzyme in the biosynthesis of haemoproteins. There may be a gingival lead line, which is more likely in chronic prolonged exposure.[4]

Other rarer manifestations include albuminuria in the nephrotic range, porphyrinuria, and the saturine gout where gouty tophi may be seen.[15] There is a weak positive association between blood pressure and blood lead levels, a doubling of the lead level leading to a marginal rise in both systolic and diastolic blood pressure.[16] There have been reports of low birth weight associated with high maternal blood levels.[7] There is no evidence till date that lead is carcinogenic.[17]

DIAGNOSIS OF LEAD POISONING

While treating patients from this region, where lead is a common ingredient in traditional medicines, a high index of suspicion is the first step to diagnosis. Careful analysis of history with particular stress on indigenous medicines is essential.

Blood is the compartment in which lead is most often measured as a marker of exposure although this typically represents only recent exposure. Lead stored in tissues, particularly bone, re-enters the blood during tissue mobilisation. A blood lead level over 25 µg/dl is considered to be significant, which needs close follow up.[18] Treatment may not be beneficial for blood lead levels less than 45 µg/dl.[18] If 24-hour urine shows a value of more than 0.1 mg per litre, it is considered pathognomic of lead poisoning.[19]

Various lead mobilisation tests have been described to diagnose lead poisoning. The AMA Drug Evaluations of 1980[4] recommends administration of calcium disodium ethylenediamine tetraacetic acid ($CaNa_2EDTA$) 500 mg/m^2 (maximum 1 g) in 500 ml 5% Dextrose to be given in 1 hour. Urine is collected for 24 hours before and after infusion. The test is considered positive if the second urine sample has a concentration 3 times the control and a total lead of 50 mcg or more.

Erythrocyte zinc protoporphyrin levels tend to rise once blood lead levels have exceeded 25 µg/dl for several months and may help differentiate between acute and chronic poisoning.

Indications for chelation therapy

IN CHILDREN. The American Academy of Pediatricians[18] recommends chelation therapy for blood lead levels above 45µg/dl. The benefit of treating levels below this is not established. If the levels are between 45 and 70 µg/dl, in the absence of clinical symptoms suggesting encephalopathy, the choice is between Calcium Sodium Edetate and Dimercaprol (BAL). Calcium Sodium Edetate is given at 25mg/kg intravenously daily for 5 days. Alternately, BAL may be given at 30 mg/kg daily for 5 days followed by 20 mg/kg daily for 14 days.

In children with blood lead levels more than 70µg/dl, therapy is recommended with BAL 25 mg/kg/day divided into 6 doses intramuscularly. The first dose of BAL is to be followed by Calcium Sodium Edetate 50 mg/kg daily as intravenous infusion. Both are continued for 5 days. A repeat course can be considered after a 2-day interval if blood lead levels are still high.

Succimer (dimercaptosuccinic acid, DMSA), an oral chelating agent, has been approved by the US Food and Drug administration for use in children with lead poisoning.[20] However, it is considered to be inferior to EDTA in treatment of blood lead levels exceeding 70µg/dl.[21]

IN ADULTS. Chelation based on specific blood levels is controversial in adults.[18] Symptomatic patients should be chelated. Asymptomatic patients with levels between 40 and 79 µg/dl need a provocation test as described above to decide on treatment. In asymptomatic patients with blood lead between 80 to 100 µg/dl, a one to three month course of oral D-penicillamine 250 mg 3 or 4 times a day might suffice. However, if the blood levels are more than 100 µg/dl, calcium sodium edetate is given in a dose of 50mg / kg in two divided doses as intravenous infusion diluted in 250 to 500 ml of isotonic saline or 5% Dextrose for 5 days. This should be followed by a prolonged course of oral D-penicillamine as above. On stopping penicillamine therapy, rebound toxicity can occur and so close follow up is necessary.

Chronic chelation therapy promotes urinary loss of heavy metals like zinc, copper, and iron. Between the courses of chelating agents, dietary supplement of zinc and perhaps other minerals is advisable.[18]

Follow up

When seen last, our patient was asymptomatic except for minor symptoms of depression for which he was under psychiatric care. Attempts to obtain a sample of the traditional drug or its local name failed. The patient had been hesitant to procure any more of it initially and later he claimed that the source could not be located.

REFERENCES

1. **Hardy AD, Vaishnav R.** A review of the use of lead compounds in Medicines, Cosmetics, and food additives. *SQU J for Sc Res: Med Sci,* 1999, **1**, 51–54.
2. **Gupta AK, Sehgal SK, Mohan M, Anand NK.** Cosmetic plumbism. *Indian Pediatr,* 1990, **27**, 760–761.
3. **Richard JK.** Adulterants in Asian patent medicine (letter). *New Eng J Med,* 1998, **339**, 827–830.
4. **Goselin RE, Smith RP, Hodge HC.** *Clinical Toxicology of Commercial Products. 5th Ed. Lippincott Williams & Wilkins 1984,* pp: 111–227.
5. **Linden MA, Manton WI, Stewart RM, Thal ER, Fiet H.** Lead poisoning from retained bullets: Pathogenesis, diagnosis and management. *Ann Surgery,* 1982, **195**, 305–313.
6. **World Health Organization.** *Guidelines for drinking water quality. Recommendations. 2nd Ed,* 1993, Geneva, WHO, **1**, 188.
7. **World Health Organization.** *International Programme on Chemical Safety. Environmental Health Criteria: Inorganic Lead. 1995,* **165**, 73–85.
8. **Florence TM, Lilley SG, Stauber JL.** Skin absorption of lead. *Lancet,* 1988, **2**, 157–158.
9. **O'Flaherty EJ.** Physiologically based models for bone-seeking elements. *Kinetics of lead absorption in humans. Toxicol Appl Pharmacol,* 1991, **118**, 16–29.
10. **Chiba M, Toyoda T, Inaba Y, Ogihara K, Kikuchi M.** Acute lead poisoning in an adult from ingestion of paint. *N Engl J Med,* 1980, **303**, 459.
11. **Pagliuca A, Mufti GJ, Baldwin D, Leston AN, Willis RM, Billingham AJ.** Lead Poisoning. *Clinical,* Biochemical, and Hematological aspects of a recent Outbreak. *J Clin Pathol,* 1990, **43**, 277–281.
12. **Treiberg G, Welte D, Walentin H.** Investigation on neurotoxicity of chemical substances at workplace and determination of the motor and sensory nerve conduction velocities in persons occupationally exposed to lead. *Int Arch Environ Health,* 1984, **53**, 189–204.
13. **Strolley BT, Broadbent DE, Banks HA, Lee WR.** Short term prospective study of cognitive functioning in lead workers. *Br J Ind Med,* 1991, **48**, 739–749.
14. **Wright RO, Shannon MW, Wright RJ, Hu H.** Association between iron deficiency and low level lead poisoning in an urban primary care clinic. *Am J Public Health,* 1999, **7**, 1049–1053.
15. **Batuman V, Maesaka JK, Haddad B, Tepper E, Landy E, Wedeen RP.** The role of lead in gout nephropathy. *N Eng J Med,* 1981, **304**, 520–524.
16. **Staessen JA.** Hypertension caused by low level lead exposure – myth or fact? *J Cardiovasc Risk,* 1994, **1**, 87–97.
17. **International Agency for Research on Cancer.** Lead and Lead Compounds. *IARC Monographs on the Evaluation of the Carcinogenic Risk of Chemicals to Humans. 1987,* **7**, 230–232.
18. **Ellenhorn MJ.** Diagnosis and treatment of human poisoning. *In Ellenhorns Medical Toxicology. 2nd Ed. New York,* Lippincott, 1997, pp: 1573–1575.
19. **Moylex MKB.** Use of Single Urine samples for the Assessment

of Lead Absorption. *Br J Ind Med,* 1964, **21**, 203–204.

20. **Staudinger KC, Roth VS.** Occupational lead poisoning. *Am Fam Physician,* 1998, **57**, 719–726.

21. **Committee on Drugs, American Academy of Paediatrics.** Treatment guidelines for lead exposure in children. *Pediatrics,* 1995, **96**, 155–60.