δ-ALA LEVELS IN SERUM AND URINE – A DIAGNOSTIC TOOL FOR POSSIBLE LEAD POISONING

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ABSTRACT

We present 2 cases of lead poisoning, the first of a child playing with painted toys and the second of an adult on local medicine. The former presented with acute abdomen and the latter with peripheral muscle weakness. We propose that raised serum δ-amino laevulinic acid (δ-ALA) levels strongly point towards the possibility of lead poisoning.

KEY WORDS

Acute abdomen, δ-ALA, Lead poisoning, Acute/Chronic.

INTRODUCTION

Lead is a ubiquitous pollutant in the global ecosystem because of its natural occurrence and industrial use. It is one of the most common environmental pollutants known to cause poisoning. Lead does not spare any organ in the body and is not known to have served any necessary biological functions in the body, and its presence in the organism has always been considered a sign of environmental pollution (1). Despite its recognized hazards lead continues to have wide spread commercial application(2). Vehicular emission(3), lead based paints(4,5), industrial waste, milk of lead poisoned cattle(6) and certain traditional medicines and folk remedial procedures(7-10) are some of the common sources of lead in India. Lead poisoning is commonly associated with occupational exposure(5) and intake of local medicines(7-10) in adults, apart from pica in children (10). It commonly presents with peripheral muscle weakness(11), fatigue, confusion, acute abdomen, constipation and sometimes with diarrhoea and vomiting(10). Eliminating the cause in most cases reverses the condition, but in more severe cases of poisoning, chelation therapy has to be given(2). Laboratory investigations and clinical correlation help in making the diagnosis of lead poisoning. Laboratory investigations characteristically show increased

concentrations of blood lead(12). Other indices include elevated levels of Zinc Protoporphyrin (ZPP)(9,12) and anaemia with basophilic stippling (9,10). We have found that such patients have increased serum δ-ALA levels with or without urinary porphyrins.

CASE REPORT 1

A 3 years old male child, resident of Jammu, presented with a two day history of pain in the abdomen, more so in the epigastric region with occasional vomiting. There was no history of any change in bowel habits. On examination, the child had epigastric tenderness, but no abdominal distension or organomegaly. Bowel sounds were present. The child was further investigated and managed on the lines of worm infestation, non-ulcer dyspepsia and acute intermittent porphyria (A.I.P.), however, without relief of symptoms. The child was anaemic with a haemoglobin of 9.2g%. Endoscopy of G.I.T. was normal. Urine porphyrins and porphobilinogen were negative. The child was further investigated for serum δ-ALA levels which were found to be high at admission (1500µg/dl) and strongly pointed towards lead poisoning (Table 1). Careful history later revealed that the child had been playing with painted toys for the past one year, which was the probable source of lead although other sources of lead like contaminated water(13), lead based paint present on many surfaces at home(4), air containing lead dust, canned food(14) and repeated ingestion of non food substances like food and candy packages, paper wrappings etc.(4) are not ruled out. The child was managed on the lines of lead toxicity. The δ-ALA levels dropped to

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780µg/dl twenty days post admission indicating, the child was responding well to the treatment of lead toxicity (Table 1).

CASE REPORT 2

A 35 years old male, resident of Amritsar was referred to our hospital from a local hospital at Amritsar with complaints of pain in both lower limbs for the past two months. On examination the patient was found to have muscle weakness and sensory derangement in both lower limbs. There was no history of Diabetes Mellitus, Hypertension or spinal injury. X-ray of spine revealed no spinal column defect. The patient then gave the history of the coincidental existence of his complaints with simultaneous ingestion of a local medicine for the past two months for his problem of haemorrhoids. This aroused the suspicion of some heavy metal poisoning. Urine was sent for screening for porphyrins and porphobilinogen which were found to be absent and serum for δ -ALA levels which were found to be high (Table 2). So a diagnosis of possible lead toxicity was made. As facilities for measuring blood lead levels were not available, the patient was further investigated clinically for complications of lead toxicity. Renal biopsy revealed crescentic glomerulonephritis which explained his proteinuria (Table 2) and also accounted for his transient hypertension. The local medicine was withdrawn and the patient became asymptomatic within two weeks.

METHODOLOGY

Estimation of δ -ALA in serum and urine

The ALA in a protein free filtrate is heated with acetyl acetone to form a pyrrole derivative. This compound is then reacted with Ehrlich's reagent and measured spectrophotometrically(15).

DISCUSSION

Lead binds to and inhibits the enzyme – δ -ALA dehydratase(16), thereby preventing the breakdown of δ -ALA into porphobilinogen resulting in increased serum δ -ALA levels. The ferrochelatase which causes incorporation of ferrous iron into protoporphyrin IX and the ferrireductase which reduces ferric iron to ferrous iron and thus makes the latter available to ferrochelatase, are both inhibited(10). This results in anaemia (10,16). Anaemia could also be due to decreased synthesis of porphobilinogen and thus decreased availability of protoporphyrin for haem

synthesis, as a result of dehydratase inhibition.

In India various types of local medicines like Ayurvedic, Homeopathic, Oriental and other potions are taken for various causes like impotence(10), haemorrhoids, diabetes(17), hypertension, skin diseases, asthma (18) and other chronic illnesses. In addition nutritional deficiencies are prevalent in Indian children leading to pica which may frequently result in lead poisoning. These factors help while examining a patient with acute abdomen in addition to constipation or diarrhoea and/or peripheral muscle weakness.

In the 1st case, keeping in mind, the age of the child and his presentation of pain in the abdomen, a differential diagnosis of worm infestation, non-ulcer dyspepsia and acute Intermittent Porphyria was made. Worm infestation was ruled out with the failure of deworming treatment to relieve abdominal pain. Normal endoscopic findings ruled out non-ulcer dyspepsia and negative urinary porphyrin levels ruled out the possibility of acute intermittent porphyria. The raised serum δ -ALA levels directed the clinician towards the possibility of lead poisoning which was then confirmed by a positive history of pica and playing with lead painted toys.

In the 2nd case, the patient himself gave the history of intake of a local medicine. Keeping in mind the fact that it could contain some heavy metal especially lead and correlating his peripheral muscle weakness to lead poisoning, the clinician proceeded to investigate him on the lines of lead poisoning. High serum δ -ALA levels confirmed the diagnosis and eliminating the source of lead completely relieved the patient of symptoms.

Although not widely appreciated, definite derangement in liver function tests has also been reported in many cases (8). The cause is either direct toxicity with the lead or because of the presence of other heavy metals in local medicine (19). In addition as in case 2, other organs like kidneys could also be involved (20). Anaemia was a common feature in both the cases due to defective haem synthesis.

In summary, we propose that lead poisoning should be considered in the differential diagnosis of acute abdomen and peripheral muscle weakness. In laboratories where facilities for measuring blood lead levels are not available, raised serum δ -ALA levels with or without raised urinary porphyrins may be relied upon for the diagnosis of lead poisoning.

REFERENCES

1. Patterson, C.C. (1965) Contaminated and Natural lead environment of man. *Arch. Environ. Health* 11, 344-360.
2. Kosnett, M.J. (2001) Heavy metal intoxication and chelators. In : *Basic and clinical pharmacology*, Ed. Katzung, B.G. McGraw Hill, London, UK., pp 999-1010.
3. Thomas, V.M. (1995) The elimination of Lead in Gasoline. *Annual Review of Energy and the Environment*. 20, 301-324.
4. Schwartz, J. and Levin, R. (1991) The risk of lead toxicity in homes with lead paint hazard. *Environ. Res.* 54(1), 1-7.
5. Potula, V. and Hu, H. (1996) Occupational and lifestyle determinants of blood lead levels among men in Chennai, India. *International J. Occupational and Environ H.* 2(1), 1-4.
6. Bhatia, I. and Choudhri, G.N. (1996) Lead poisoning in milk- the basic need for the foundation of human civilization. *Ind.J.Public Health* 40, 24-26.
7. McElvaine, M.D., Harder, E.M., Johnson, L., Baer, R.D. and Satsger, R.D. (1990) Lead poisoning from the use of Indian folk medicines. *JAMA*. 264, 17.
8. Dunbabin, D.W., Tallis, G.A., Popplewell, P.Y. and Lee, R.A. (1992) Lead poisoning from Indian herbal medicine (Ayurveda). *Med.J.Aust.* 152, 835-836.
9. Bayly, G.R., Braithwaite, R.A., Sheeban, T.M.T., Dyer, N.H., Crimley, C. and Ferner, R.E. (1995) Lead poisoning from Asian traditional remedies in the West Midlands- report of a series of five cases. *Hum.Exp.Toxicol.* 14, 24-8.
10. Anderson, N.R., Gama, R. and Kapadia, S. (2001) Herbal remedy poisoning presenting with acute abdomen and raised urine porphyrins- report of a case. *Ann. Clin.Biochem.* 38, 408- 410.
11. Mamet, R., Sztern, M., Rachmel, A., Stahl, B., Flusser, D. and Schoenfeld, N. (2001) Lead poisoning : A new biochemical perspective on the differentiation between acquired and hereditary neuroporphyrria. *Clin.Chem.* 47(9), 1710-1713.
12. D'Souza, H.S., Menezes, G. and Venkatesh, T. (2002) Screening for lead poisoning in urban school children of southern India using capillary and venous blood samples. *Ind.J.Clin.Biochem.* 17(1), 1-4.
13. Pocock, S.J. (1980) Factors influencing household water lead: A British national survey. *Arch.Environ.Health* 35, 45-51.
14. Adgate, J.L., Weisel, C., Wang, Y., Rhoads, G.G. and Lioy, P.J. (1995) Lead in house dust. Relationships between exposure metrics. *Environ.Res* 70(2), 134-147.
15. Labbe, R.F. (1976) Estimation of serum δ -ALA. In: *Fundamentals of Clin. Chem.*, Ed. Norbert W. Tietz. W.B. Saunders Company, Philadelphia. pp 470-471.
16. Bergdahl, I.A., Schutz, A., Desnick, R.J., Wetmur, J.G., Sassa, S. and Skerfving, S. (1997) Lead binding to δ -aminolevulinic acid dehydratase (ALAD) in human erythrocytes. *Pharmacol and Toxicol.* 81, 153-158.
17. Keen, R.W., Deacon, A.C., Delves, H.T., Moreton, J.A. and Frost, P.G. (1994) Indian herbal remedies for diabetes as a cause of lead poisoning. *Postgrad.Med.J.* 70, 113-114.
18. But, P. and Chang, C. (1996) Chinese herbal medicine in the treatment of asthma and allergies. *Clin.Rev.Allergy Immunology*, 14, 253-269.
19. Ellenhorn, M.J. (1997) Diagnosis and Treatment of Human Poisoning. In: *Ellenhorn's Medical Toxicology*. 2nd edn. Baltimore Williams & Wilkins. pp. 1532-1614.
20. Solliway, B.M., Schaffer, A., Prate, H. and Yannai, S. (1996) Effect of exposure to lead on selected biochemical and haematological variables. *Pharmacol. Toxicol.* 78, 18-22.

Table 1. Case 1 Investigations

Test	Result	Reference range
Endoscopy (G.I.T.)	Normal	
Urine porphyrins & porphobilinogen	Not found elevated	
Urine sugar	Nil	
Urine Protein	Nil	
Urine pH	Acidic	
Hb	9.2 g%	(10-12 g%)
Total leucocyte count	6200/mm ³	(4000-11000/mm ³)
Serum δ -ALA		
-At admission.	1500 μ g/dl	(150-400 μ g/dl)
-20 days post admission.	780 μ g/dl	(150-400 μ g/dl)
Spot urine δ -ALA at admission	580 μ g/dl	(66-466 μ g/dl)

Table 2. Case 2 Investigations

Test	Result	Reference range
X-ray spine	No obvious abnormality	
Fasting Blood Sugar	72 mg%	(60-100 mg%)
Urine porphyrins & porphobilinogen	Absent	
Hb	9.8 g%	(14-16 g%)
Peripheral Blood Film findings	Anisopoikilocytosis with mild to moderate hypochromia with microcytes, pencil cells and target cells WBCs adequate Platelets adequate	
Serum δ -ALA	750 μ g/dl	(150-400 μ g/dl)
<u>After diagnosis</u>		
24 hr. urine protein	3700 mg/day	(30-150 mg/day)
Renal biopsy	Crescentic Glomerulonephritis	