Radial neuropathy due to occupational lead exposure: Phenotypic and electrophysiological characteristics of five patients

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Abstract

Lead is a ubiquitous and versatile metal that has been used by mankind for many years. It is a toxic heavy metal that ranks as one of the most important environmental poisons in the world. Research conducted in recent years has increased public health concern about the toxicity of lead at low doses and has supported a reappraisal of the levels of lead exposure that may be safely tolerated in the workplace. Neuropathy is one complication of lead poisoning. The aim of this study is to describe the phenotypic and electrophysiological profile in five male patients working in a battery factory who developed radial nerve neuropathy due to lead exposure. All patients had elevated blood lead levels that were in the toxic range. The concerned regulatory bodies should make it mandatory for workers to undergo regular health checkups to detect signs of lead poisoning and must ensure that workers are aware about the ill effects of exposure to this metal. Chelation therapy removes lead from the blood and soft tissues and chronic lead exposure often requires repeated courses of treatment.

Key Words

Electrophysiology, lead, neuropathy, radial nerve

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Introduction

The common causes of neuropathy in India include Hansen's disease, diabetes mellitus, Guillain-Barré syndrome, chronic inflammatory demyelinating neuropathy, genetically-determined neuropathy, and various drugs.[1] Exposure to toxins like acrylamide, carbon disulfide, inorganic mercury, methyl n-butyl ketone, polychlorinated biphenyl, thallium, triorthocresyl phosphate, arsenic, lead, styrene, and toluene could result in neuropathy, and correct diagnosis calls for a high index of suspicion.[2]

Patients with lead neuropathy present with weakness that primarily involves the wrist and finger extensors, but which could also spread to involve other muscles.[3] Patients with unusually long exposure to inorganic lead may show mild sensory and autonomic neuropathic features rather than the motor neuropathy classically attributed to lead toxicity.[4] Lead intoxication in humans causes axonal degeneration, but in some other species it causes a primarily demyelinating neuropathy. Diagnosis of lead neuropathy is important because it is potentially reversible and also because its early detection and treatment may prevent other systemic complications. There are only a few reports of lead neuropathy from India.[5]

The aim of this study is to describe the phenotypic and electrophysiological profile of five patients with lead neuropathy.

Materials and Methods

In this retrospective audit, we reviewed the case records of five patients who had been diagnosed with lead neuropathy at the Department of Neurology, National Institute of Mental Health and Neurosciences (NIMHANS), Bangalore, India, during the period from 1992 to 2006. The clinical diagnosis of lead neuropathy was based upon the finding of asymmetric or symmetric distal motor weakness, without sensory symptoms or signs, in the presence of a history suggestive of lead exposure. The diagnosis of lead neuropathy was confirmed by the presence of elevated blood lead levels (considered acceptable up to 9 μg/dl). For measuring blood levels we used the ESA lead analyzer in the Department of Biochemistry, St. John's Medical College and Hospital, Bangalore, India.
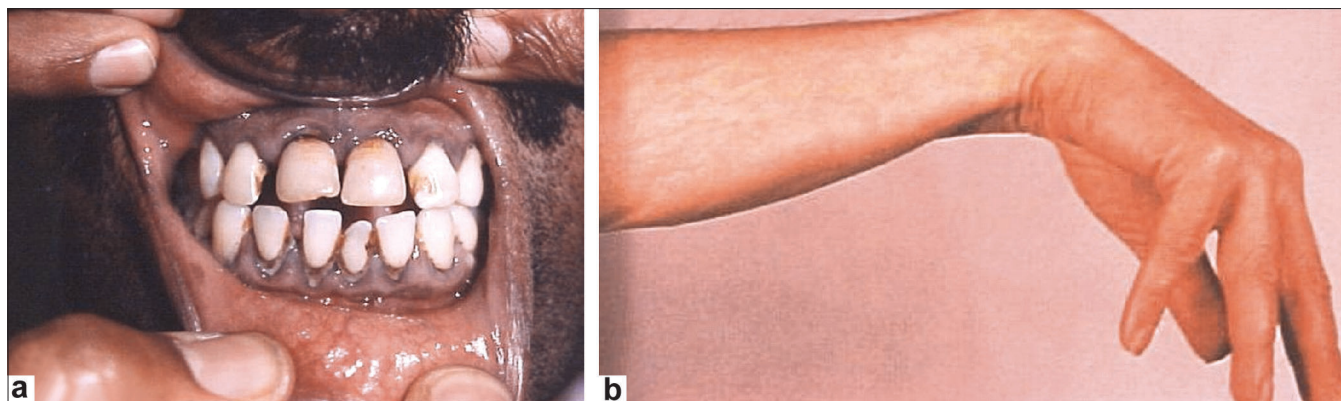
Figure 1: (a) Patient 2 with lead line in the gingiva; (b) wrist-drop in patient 3

Table 2: Electrophysiological parameters in patients with lead neuropathy

Nerves	Parameters	Controls	Patient 1		Patient 2		Patient 3		Patient 4		Patient 5	
			Right	Left	Right	Left	Right	Left	Right	Left	Right	Left
Motor												
Median	DL (ms)	2.6 ± 0.5	4.0	-	4.3	4.0	3.5	4.7	4.2	3.9	3.3	5.5
	CMAP (mV)	14.5 ± 3.4	9.9	-	6.5	9.1	5.6	11.7	10.5	12.1	6.5	9.5
	CV (m/s)	58.7 ± 3.8	46.9	-	54.9	53.8	51.3	40.4	51.2	50.0	57.1	59.0
	F Persistence	-	16/16	-	4/16	9/16	12/16	16/16	16/16	15/16	-	-
	F Lat (ms)	25.0 ± 1.8	31.1	-	28.1	28.0	27.7	31.2	26.5	28.1	-	-
Ulnar	DL (ms)	2.0 ± 0.5	3.4	-	3.0	2.7	3.5	3.3	3.2	3.2	2.7	2.2
	CMAP (mV)	10.9 ± 2.6	7.9	-	7.5	6.9	9.4	11.4	10.7	6.9	5.1	4.9
	CV (m/s)	59.9 ± 4.8	41.2	-	52.2	57.5	51.4	40.7	56.1	45.0	55.8	67.6
	F Persistence	-	16	-	9/16	11/16	14/16	16/16	13/16	16/16	12/16	-
	F Lat (ms)	25.7 ± 1.9	31.3	-	28.0	26.8	28.8	28.3	25.3	28.3	28.6	-
Radial	DL (ms)	-	3.0	-	Absent	3.9	3.0	6.6	4.0	4.3	3.3	3.0
	CMAP (mV)	-	1.09	-	response	0.16	3.1	2.5	2.3	2.4	1.9	3.6
	CV (m/s)	-	42.9	-		50.0	40.0	52.9	42.5	48.3	67.8	66.7
	F Persistence	-	Absent	-		Absent	Absent	Absent	Absent	16/16	Absent	-
	F Lat (ms)	-		-						31.3		-
CP	DL (ms)	3.6 ± 0.5	6.4	-	5.5	-	4.5	5.2	5.1	5.4	3.8	6.0
	CMAP (mV)	8.0 ± 2.9	3.2	-	10.4	-	8.8	5.3	7.6	6.6	10.7	11.9
	CV (m/s)	51.1 ± 5.5	37.3	-	47.5	-	54.5	51.0	57.4	57.4	51.6	50.0
	F Persistence	-	6/16	-	4/16	-	16/16	14/16	3/16	5/16	-	-
	F Lat (ms)	42.8 ± 3.1	54.3	-	48.3	-	37.6	45.1	34.3	32.3	-	-
Sensory												
Median	DL (ms)	-	2.5	-	2.6	2.1	2.4	3.1	3.3	3.08	2.9	2.4
	SNAP (µV)	29.9 ± 8.1	30	-	13.7	10.3	23.0	14.0	9.0	14.1	18.2	23.4
	CV (m/s)	59.5 ± 4.2	54.7	-	56.8	57.9	58.3	41.7	48.2	51.9	58.2	62.5
Ulnar	DL (ms)		2.7	-	2.08	2.5	3.0	2.6	3.7	2.7	2.5	2.8
	SNAP (µV)	22.5 ± 6.7	18.3	-	10.6	12.9	10.7	18.6	7.4	16.3	16.1	8.8
	CV (m/s)	56.2 ± 4.1	43.5	-	57.8	63.5	40.0	43.6	37.6	44.2	55.6	59.0
Radial	DL (ms)	-	2.6	-	2.0	18.8	2.4	2.7	2.1	2.4	1.9	2.08
	SNAP (µV)	-	17.2	-	29.1	23.0	6.8	25.8	24.6	21.9	49.4	22.0
	CV (m/s)	-	53.8	-	67.5	69.1	57.4	51.5	66.0	59.3	71.4	67.3
Sural	DL (ms)	-	3.2	-	2.2	-	3.1	5.6	2.7	2.7	2.6	3.04
	SNAP (µV)	21.5 ± 8.5	13.0	-	21.1	-	14.0	24.4	11.1	11.6	13.5	15.4
	CV (m/s)	48.4 ± 4.7	43.8	-	57.9	-	44.3	25.2	51.5	51.3	53.0	46.1

DL: Distal latency; CMAP: Compound action muscle potential; CV: Conduction velocity; SNAP: Sensory nerve action potential; '-': Not done/available

decreased SNAP of the right radial nerve in patient 3 and mildly decreased SNAP of the right median and ulnar nerves in patient 4, suggesting mild sensory involvement.

Three of the patients[1,3,5] were treated with oral d-penicillamine (500–750 mg/day), while patients 2 and 4 received meso 2,3 dimercaptosuccinic acid (DMSA). Follow-up data was available only for patient 3.

Discussion

Lead is used in industries such as construction, ceramics, paints, plastics, and metallurgy and hence lead poisoning can be considered a common occupational hazard. Inhalation of inorganic lead in the form of fumes, vapors, and mists is a major form of exposure in the occupational setting. Environmental exposure to toxic lead levels due to soil, food, and

water contamination can also occur. The common sources of lead poisoning are fumes from burnt car batteries, ingestion of flaking paint, inhalation of vehicle fumes, consumption of food cooked in cheap aluminum or brass utensils or in 'kalai,' i.e., vessels that are poorly coated with tin adulterated with lead, and application of 'kajal' (mittal). Tesink *et al*. reported that poisoning is almost always caused by ingestion. Lead is absorbed from the respiratory tract into the circulation and is transported on the surface of the red cell, which carries most of the absorbed lead.[6] There are three compartments in the body where lead can be stored: the RBC pool, the soft tissues, and the skeletal system (stores 95% of the body lead). Though the kidneys excrete lead, only a small proportion of the total body lead is removed, and continued exposure results in accumulation of the metal in the tissues. Some people, perhaps due to genetic factors, are more susceptible to poisoning than others. About 15% of Caucasians have a variant of a gene which encodes for aminolevulinic acid dehydrogenase, a critical enzyme in the production of haem, which may make them more susceptible to toxicity from retained lead. Low levels of calcium, iron, copper, zinc, or phosphorus in the diet or high levels of fat can increase lead absorption.[1]

A classical description of lead poisoning has been provided by Van Gogh in his autobiographical letters. The symptoms include initial debilitation; stomatitis, with loss of teeth; recurring abdominal pains; anemia (with a 'plumbic' skin tone); neuropathy of the radial nerve; and a saturnine encephalopathy, with features such as epileptic crises, progressive changes in character and periods of delirium.[7] Lead poisoning commonly manifests with unexplained abdominal colic, constipation, wrist-drop, footdrop, anemia, hyperuricemia, and hepatosteatosis. Secondary hypertension following excess exposure to lead has been observed due to its effect on the myocardium and the renal circulation.[8] Cognitive decline has been reported following chronic lead exposure.[9] Chronic intoxication with lead and sulfur compounds may rarely cause Parkinson's disease.[10] Neonates may present with encephalopathy and seizures.[11]

A typical patient of lead neuropathy presents with symmetric distal upper limb weakness and wasting, especially of the forearm and hand muscles; the extensors of the wrist may be selectively weak. The differential diagnosis includes multifocal motor neuropathy, inclusion-body myositis, specific compressive mononeuropathies, posterior interosseous syndrome, focal forms of motor neuron disease, and hereditary predisposition to pressure palsy. There is axonal type of involvement of the peripheral nerves in the upper limbs. The neurologic manifestations of lead depend on the duration of exposure, in that a shorter duration may predispose them to motor neuropathy, as in our series. Rubens *et al*. (2001) reported 46 patients with neuropathic features who had been exposed to lead for periods ranging from 8 to 47 years (mean 21.7 years). All of them showed mild sensory and autonomic neuropathic features rather than just the motor neuropathy that is classically attributed to lead toxicity. All of them had distal paraesthesiae, pain, impaired pin-prick sensation, diminished or absent ankle jerks, and autonomic vasomotor or sudomotor disturbances. Reduced vibration sensation and postural hypotension were present in all the 20 patients studied. Motor conduction velocity and CMAP amplitudes were normal, with marginally prolonged distal motor latencies. SNAP amplitudes lay at the lower end of the normal range, and the distal sensory latencies were prolonged.[4] The patients in this study had a predominantly axonal type of neuropathy.

Neuropathic features develop only when lead levels are more than 70 μg/dl. However, except in one of our patient (patient 4), blood lead levels were less than 70 μg/dl. Chuang *et al*. observed that measurement of vibration sensory threshold is a relatively effective tool for detecting lead neuropathy in field studies and that lead might cause sensory neuropathy with an effect threshold corresponding to a 5-years' mean blood lead concentration of 31 μg/dl. The motor neuropathy associated with subacute poisoning is more likely to be a form of lead-induced porphyria rather than its direct neurotoxic effect. It is proposed that the development of lead neuropathy may depend on inherent factors (like genetic constitution) which determine how it is metabolized in the body. The normal conduction velocity observed in lead neuropathy is in full agreement with the hypothesis that the axonal degeneration is due to the biochemical damage to the perikarya of the anterior horn cells.

Seppalainen *et al*. reported that even in neurologically symptom-free lead workers, motor and sensory conduction velocities are slow and, in addition, electromyographic abnormalities like denervation activity and loss or changes in the motor unit potentials may appear.[13,14] There are contradictory reports on correlation of lead levels with type of peripheral nerve pathology. In one study on lead neuropathy, blood levels of lead were low with demyelinating type of neuropathy and high with axonal type of neuropathy.[15] In another study there was no correlation between the blood lead level and the neurophysiological measurements.[16] Electromyographic abnormalities consist of fibrillations, diminution of the number of motor units on maximal contraction, and an abnormally long duration of the motor unit potentials. Lead may affect central, peripheral,

and autonomic nervous systems as shown by prolonged evoked potentials, decreased conduction velocities, and reduced R-R interval variability.[17] These tests however were not carried out in our study.

All but one of our patients had anemia; this anemia may have been secondary to the lead toxicity or, on the other hand, it could be that the anemia made them more prone to lead toxicity. Recurrent abdominal pain or constipation is common in lead poisoning. There are instances of patients having undergone surgeries for the abdominal pain.[18] It was earlier believed that pain abdomen was present in all cases and that without this symptom the diagnosis of lead poisoning could not be made. However, only two of our patients had history of chronic abdominal pain, and only one had constipation. The peripheral blood smear may show anisocytosis, basophilic stippling, and Cabot ring bodies in patients with lead poisoning, but none of our patients had these features.

All the patients in our series were ignorant of the ill effects of lead and took no precautions at work to prevent exposure. On exposure at the workplace, management includes removal of the patient from the source of exposure and chelation therapy with EDTA (ethylene diamino tetraacetic acid), BAL (British antilewisite), dimercaptosuccinic acid (DMSA), or D-penicillamine. These compounds attach to lead and are excreted through the renal route. Oral supplementation with calcium, iron, and thiamine has also been tried as part of the treatment. EDTA, penicillamine, and British antilewisite may decrease blood lead levels but may not improve neuropathy. The prognosis depends on the duration and level of exposure. We had follow-up details for one patient and this patient improved by 50% at the end of 4 months. In the series by Ruben *et al.* (2001), examination of 151 individuals working with lead showed that 46 of them were affected.[4] This has important public health implications. People working with lead must undergo periodic health checkups. However, employers may not cooperate for the fear of losing staff and of the possibility of having to pay compensation; employees, on their part may not cooperate for fear of losing their job. Hence, it may be necessary for the government to enact laws and enforce compliance.

References

1. Ghosh B, Sengupta S, Bhattacharjee R, Pal S, Saha SP, Ganguly G, *et al.* Spectrum of peripheral neuropathy in eastern India. J Indian Med Assoc 2006;104 9:168-73.
2. Kimura J. Polyneuropathies. In: Electrodiagnosis in Diseases of Nerve and Muscle: Principles and Practice. 2nd ed. Philadelphia: FA Davis;1989. p. 462-81.
3. Thomson RM, Parry GJ. Neuropathies associated with excessive exposure to lead. Muscle Nerve 2006;33:732-41.
4. Rubens O, Logina I, Kravale I, Eglîte M, Donaghy M. Peripheral neuropathy in chronic occupational inorganic lead exposure: A clinical and electrophysiological study. J Neurol Neurosurg Psychiatry 2001;71:200-4.
5. Herman DS, Geraldine M, Venkatesh T. Evaluation, diagnosis, and treatment of lead poisoning in a patient with occupational lead exposure: A case presentation. J Occup Med Toxicol 2007;2:7.
6. Tesink J. [Lead and health]. Tijdschr Diergeneeskd 1994;119: 197-201.
7. González Luque FJ, Montejo González AL. [Implication of lead poisoning in psychopathology of Vincent van Gogh]. Actas Luso Esp Neurol Psiquiatr Cienc Afines 1997;25:309-26.
8. Zyśko D, Chlebda E, Gajek J. [Effect of lead on the cardiovascular system] Pol Merkur Lekarski 2004;17:512-5.
9. Weisskopf MG, Hu H, Sparrow D, Lenkinski RE, Wright RO. Environ Proton magnetic resonance spectroscopic evidence of glial effects of cumulative lead exposure in the adult human hippocampus. Health Perspect 2007;115:519-23.
10. Winkel R, Kuhn W, Przuntek H. Chronic intoxication with lead- and sulfur compounds may produce Parkinson's disease. J Neural Transm Suppl 1995;46:183-7.
11. Fleece DM, Robinson NB. Encephalopathy in a newborn due to prenatal lead exposure. J Paediatr Child Health 2007;43:409-10.
12. Chuang HY, Schwartz J, Tsai SY, Lee ML, Wang JD, Hu H. Vibration perception thresholds in workers with long term exposure to lead. Occup Environ Med 2000;57:588-94.
13. Seppäläinen AM, Hernberg S. Subclinical lead neuropathy. Am J Ind Med 1980;1:413-20.
14. Seppalainen AM. Lead poisoning: neurophysiological aspects. Acta Neurol Scand Suppl 1982;92:177-84.
15. Windebank AJ. Metal neuropathy. In: Dyck PJ, Thomas PK, Griffin JW, *et al*, eds. Peripheral neuropathy., 3rd ed. Philadelphia:WB Sanders;1993;1549-1570.
16. He FS, Zhang SL, Li G, Zhang SC, Huang JX, Wu YQ. An electroneurographic assessment of subclinical lead neurotoxicity. Int Arch Occup Environ Health 1988;61:141-6.
17. Murata K, Araki S, Yokoyama K, Uchida E, Fujimura Y. Assessment of central, peripheral, and autonomic nervous system functions in lead workers: Neuroelectrophysiological studies. Environ Res 1993;61:323-36.
18. Kirchgatterer A, Rammer M, Knoflach P. Weight loss, abdominal pain and anemia after a holiday abroad-case report of lead poisoning. Dtsch Med Wochenschr 2005;130:2253-6.