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Pathophysiology 15 (2008) 13–17

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PATHOPHYSIOLOGY

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Schwann cell injuries of radial nerve after lead (Pb) exposure in rats

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Received 25 May 2007; received in revised form 5 November 2007; accepted 8 November 2007

Abstract

Lead toxicity is still a common problem. The aim of the present study was to clarify neurotoxical effects in peripheral nerves using rat's radial nerve as model. Adult male rats were divided in two groups. The experimental group received intraperitoneally 20 mg/kg of lead acetate for 10 days and the controls water only. Blood lead level was measured by atomic spectrophotometer absorption. The morphology of radial nerves was studied with light and electron microscopy. Active macrophages, edema and disarrangement of myelin sheath layers and reduction in myelin sheath diameter and nuclear density of Schwann cells as well as granules in mitochondrial matrix were found.

Keywords: Radial nerve; Schwann cells; Myelin; Mitochondria; Lead (Pb)

1. Introduction

Lead (Pb) is used in containers for corrosive liquids, storage batteries, cable covering, plumbing, paints and still also in gasoline. Lead poisoning has been a recurrent problem for more than 20 centuries. Lead is toxic even in low dose, and it exerts extensive damage to the brain, causing severe learning and memory disability [1–3] as well as hyperactivity, impulsiveness, learning disabilities and aggressive behavior in children [4–7]. Around 0.10 mg/l can cause defects in cognitive maturation in children [7]. At blood lead concentrations as low as 0.30 mg/l a reduction in the nerve conduction velocity and electrocardiographic *R–R* interval variability occurs. Pb causes a reduction of neural density in visual cortex of monkey [6], and a decrease the acetylcholine level in rat hippocampus [1]. The short-latency somatosensory and visual evoked potentials and distribution of nerve conduction velocity start at blood Pb levels as low as 0.4–0.5 mg/l [4]. Thomas [5] found in male rats intoxicated with lead acetate in drinking water segmental demyelization in mixed and cutaneous nerves [8]. Death of astrocytes and endothelial cells in blood brain barrier has also been reported [9,10]. The cellular basis of the observed neurobehavioral deficits is probably complex. Both neurons and neuroglia are potential targets for Pb toxicity [3]. In CNS, destruction of myelin layers and changes in the morphology of oligodendrocytes has been reported [11]. In prolonged toxicity of lead, the protein content and the activity of the myelin-specific enzyme CNPase are lowered in mice CNS [12].

Studies of Schwann cells and myelin sheath in peripheral nerves has received little attention, but demyelination and remyelination and increase of laminated bodies in Schwann cell cytoplasm have been described [13,14]. These cellular alternations are often the earliest evidence of neuropathy. Lead is, perhaps one of the factors contributing to demyelinating disease such as multiple sclerosis, too.

Although much is known about the effects of lead on central nervous system, much less is know about its effects on Schwann cells in peripheral nerves. Therefore, the aim of the present study was to clarify the effect of lead poisoning using rat radial nerve as model. Radial nerve is very important both in these animals as also in humans.

2. Materials and methods

Adult male Sprague–Dawley rats ($n = 30$) (180–220 g) kept at constant temperature (26 °C) and cyclic fluorescent light (12 h light and 12 h dark) were used. The rats were

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doi:10.1016/j.pathophys.2007.11.002

housed in wire cages and they received laboratory rat chow and water ad libitum. The experimental rats ($n = 15$) received for 10 days intraperitoneally 20 mg/kg of lead acetate dissolved in deionized distilled water while the controls received water only. Following pentobarbital anesthesia and the drawing of blood sample for lead analysis, the animals were killed by intracardiac perfusion with glutaraldehyde. Radial nerve was exposed at two sites of tricep's head at the back of the arm and divided into 3 mm segments. For light microscopy, the tissue was fixed in 10% formaldehyde solution, dehydrated in graded alcohols and embedded in paraffin. Cross-sections of radial nerve were stained with Weil's staining for myelin sheath. The specimens were stained with hematoxylin, ferric ammonium sulfate and potassium ferricyanide. In this staining method, myelin is black on a yellow background. For electron microscopy, the specimens were fixed in 2.5% glutaraldehyde at 4 °C. After washing with 0.1 M PBS, they were dehydrated in graded alcohols and embedded in araldehite 502/812 resin. Semithin cross-sections of radial nerve were stained with toluidin blue. Thin sections were stained with uranyl acetate and lead citrate and studied by transmission electron microscopy. The number of myelin layers, myelinated and non-myelinated axons, axonal density and ultrastructure of Schwann cell were analyzed. Three regions of nerve were randomly selected for the measurement of axonal density and the number of axons in each regions in nerve surface (mm^2) were calculated.

Blood lead levels were measured in *n*-butyl acetate extracts by atomic absorption spectrophotometry.

Table 1
The blood lead (Pb) levels in rats treated with lead acetate and their controls[a]

Control group (μg/dl)	0.12 ± 0.004
Lead-treated (μg/dl)	10.5 ± 0.0001[b]

[a] Values represent mean ± S.E.M. ($n = 15$).
[b] $P < 0.01$, significantly different from control group (unpaired Student's *t*-test).

The results have been expressed as means ± S.E.M. Statistical analyses were performed by using unpaired student's test.

3. Results

Intoxicated rats developed no paralysis or any other clinical signs of neurotoxicity during the treatment period. Blood lead levels in treated rats were, however, significantly increased (Table 1).

Light and electron microscopy of radial nerve showed a reduction of myelin diameter of the in lead acetate exposed rats in comparison with controls ($P < 0.001$) (Figs. 1 and 2). The axonal density of intoxicated rats was lower in comparison with controls but the difference was not statistically significant ($P = 0.07$). Endoneuronal edema, as evidenced by expansion of the interstitial space was evident only in the rats receiving Pb. Disarrangement of myelin sheath observed in some myelinated axons in Pb-treated group (Fig. 3). Also low density of nucleous of Schwann cells and many granules in mitochondrial matrix was seen (Fig. 3).

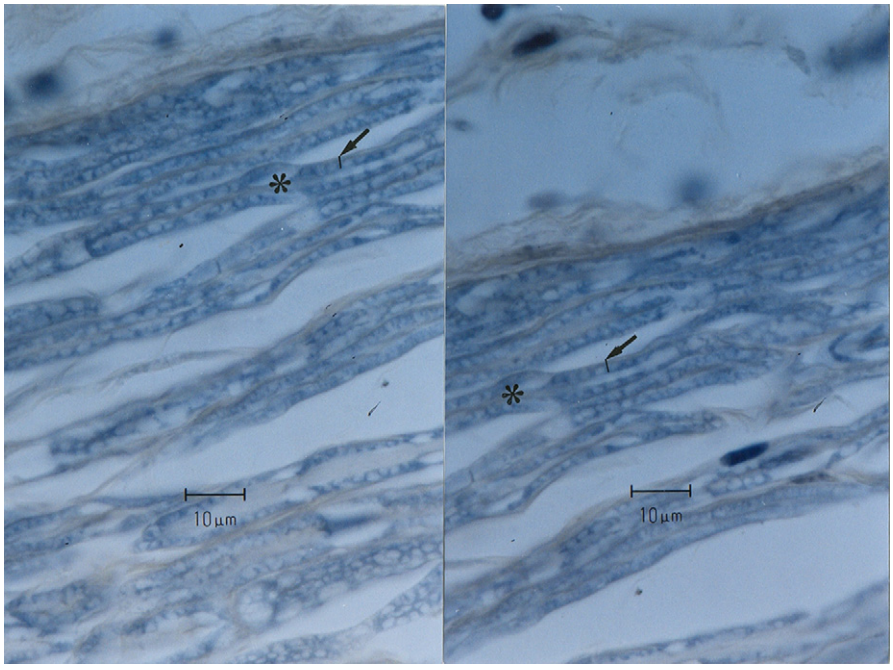

Fig. 1. Transverse section of rat radial nerve with Weil's staining. Arrow shows myelin sheath. Strict shows Ranvier node. (A) Control group and (B) Pb-treated group.