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Morphological changes of Schwann cells as neurotoxic responses

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신경독성에 의한 Schwann 세포의 형태적 변화

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초록 : 본 실험에서 초산납 투여로 인한 실험초기에 관찰할 수 있는 신경독성은 Schwann 세포의 종창이었다. 종창의 정도를 계측하기 위해 각 실험군 rat의 좌골신경을 횡단 조직표본으로 제작하여 Schwann세포의 두께와 핵의 장경을 측정 비교하였다. 즉 제1실험군은 30일간 0.5% 초산납이 함유된 음료수를 공급하였고 제2실험군은 제1군과 동일한 처리후 일반 실험실 조건에서 30일간 회복되게 하였으며 제3군은 대조군으로 정상 사육하였다. 초산납을 투여한 제1실험에서는 Schwann세포의 두께가 대조군보다 유의한 증가치를 보였는데, 제2실험군은 대조군과 유의한 차이가 없었다. Schwann세포핵의 직경 역시 제1군이 대조군보다 증가되었으나 유의한 차이는 없었다.

Key words : Schwann cell, neuropathy, lead acetate, myelinated fiber

Introduction

Neurotoxic manifestations in animals can be evaluated morphologically, functionally, biochemically, and electrophysiologically. Each method has an important role in evaluating toxic agents and in defining mechamisms by which the agents produce damage to the nervous system. The ideal system for evaluating neurotoxic chemicals would contain a combination of these methods, although this rarely can be achieved in a single laboratory[1]. Howevr, there are no ideal techniques which would always detect the neurotoxic effects of a compound without false negative and positive results.

In order to quantify early morphological manifestations of neurotoxicity, we have explored the validity of size variables of Schwann cells in experimental lead neuropathy as new technique. It was found that measuring mid-sectional thickness of Schwann cell nucleus and cytoplasm produced reliable data for the evaluation of mild peripheral neurotoxicity.

Materials and Methods

Sprague-Dawley rats, 7-8 weeks of age and 140-160g in weight, were obtained from KRICT and used. The animals were randomly divided into three experimental groups. Group 1 animals were exposed to 0.5% lead acetate in the drinking water *ad libitum* for 30

days and then sacrificed for histological examination. Group Ⅱ animals were also exposed to lead for the same period of time, but then allowed to recover on a normal diet for 30 days. Group Ⅲ animals were maintained in standard laboratory conditions as controls.

The examination was carried out on sciatic nerves, processed for histological and morphological analysis as described by Coria and Monton[2]. Measurements were performed on transverse thin or semithin sections of each nerve, stained with hematoxylin-eosin(H-E) or toluidine-bule. Schwann cell nucleus and cytoplasm areas were obtained from Schwann cell profiles displaying a nucleus with a well defined neucleous; it was assumed that this represented section through the midpoint of the cell body[3]. In these way 30-40 Schwann cells were selected for measurement of the cell thickness and major diameter of the nucleus in each nerve. For morphological analysis a homogeneous composition of the nerve fibers was necessary, thus demyelinated and remyelinated fibers were excluded. Differences between experimental groups were an analysed by Duncan test.

Results

Exposure of lead acetate to rats for 30 days induced Schwann cell swelling of Sciatic nerve accompanying increased nuclear size(Fig 1,2).

The mean($\pm$SE) thickness of Shwann cell of group Ⅰ was 2.23 ± 0.08, while those of group Ⅱ and Ⅲ were 2.05 ± 0.10 and 1.81 ± 0.10, respectively. The mean($\pm$SE) major diameter of Schwann cell nucleus of group Ⅰ was 3.34 ± 0.09 compared to 3.22 ± 0.12 and 3.21 ± 0.15, respectively of the two latter groups. The cell thickness and nuclear diameter revealed decreasing tendency in recovery group and no significant differences were found between group Ⅱ and Ⅲ (Table 1). These results suggested that the Schwann cell size was increased significantly in the intoxicated group compared with control group($p<0.01$).

Additonal information was sought by comparing the morphological changes of myelinated fibers of each group: myelinated fibers of these three group showed no apparent difference in the fiber diameters and structures.

Discussion

Lead exposure in animals results in a peripheral neuropathy with prominent segmental demyelination[4] and in humans has demonstrated an axonopathy with a predominantly motor neuropathy[5]. Also exposure to α-chlorohydrin, the earliest neurptoxic changes are severe distension of astrocytes in CNS[6]. In most morphological observation on neuropathy, lesions of the myelin sheath have been focused without any consideration on Schwann cell itself[7]. In terms of cell pathology, however, it is important to recognize that among many pathological conditions myelin destruction is the end-result of a derangement of the metabolic machinery of Schwann cells[8], which can be manifested as morphological changes in the nucleus, cytoplasm, and organelles. These cellular alterations are often the earliest evidence of neuropathy and therefore provide clues about the mechanism of action of the noxious agent. Also these changes may be interpreted either as a predegenerative state or as a compensatory, reversible response of the cell. Thus this study provides quantitative confirmation that Schwann cell swelling is an early, measurable changes of lead intoxicated nerves, and that the cellular profiles returned to normal after withdrawal of the toxin.

Table 1. Morphological changes on sciatic nerves

	Schwann cell thickness(μm)	Major diameter of the nucleus (μm)	Myelinated fiber diameter(μm)
Group Ⅰ	$2.23\pm0.08^{*}$	$3.34\pm0.09^{\triangle}$	$5.34\pm0.19^{\triangle}$
Group Ⅱ	$2.05\pm0.10^{\triangle}$	$3.22\pm0.12^{\triangle}$	
Group Ⅲ	1.81 ± 0.10	3.21 ± 0.15	5.57 ± 0.19

Data expressed as mean$\pm$SE
*Significantly different from control values, $P<0.01$
△Not significantly different from control values
Group Ⅰ : exposed to lead; Group Ⅱ : exposed to lead and recovered; Group Ⅲ : control

Summary

The early change observed in lead-induced neurophathy in the rat was Schwann cell swelling. In order

to quantify this cell swelling, Schwann cell thickness and major diameter of the nucleus were measured using tranverse section with associated myelinated fiber of sciatic nerves. Group I rats were intoxicated with 0.5% lead acetate in the drinking water for 30 days ; group II animals were treated as in group I and then restored to normal laboratory conditions for 30 days; and group III were controls. The results showed that the cell sizes were significantly greater in intoxicated animals, compared with control, and the cell sizes of group II did not differ significantly from control rats.

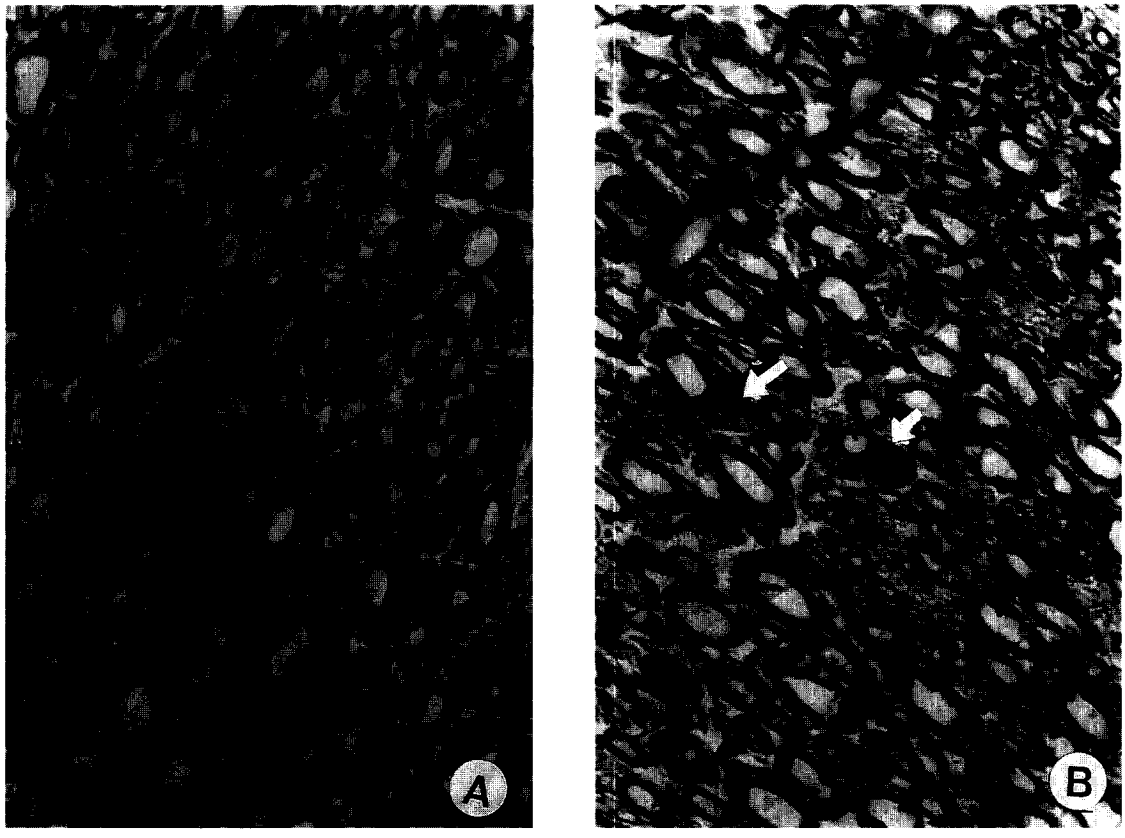

Fig 1. Transverse semithin section of sciatic nerve.
A, Control rat. B, Lead-treated rat : Schwann cells exhibiting an unusually large amount of cytoplasm can be seen(white arrows). Stainded with toluidine blue. X600.

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