A CASE OF SKIN ATROPHY, NEUROGENIC MUSCULAR ATROPHY AND ANXIETY REACTION FOLLOWING LONG EXPOSURE TO STYRENE

Shunichi ARAKI[†], Akira ABE[†], Koichi USHIO[†] and Masayuki FUJINO^{††}慢性スチレン中毒と思われる皮膚萎縮, 神経原性筋萎縮, ならびに
不安神経症の1症例

荒記 俊一*, 阿部 彰*, 牛尾 耕一*, 藤野 雅之**

Introduction

Styrene ($C_6H_5-CH=CH_2$) is colourless irritative liquid of strong odour which is being used in the manufacturing of plastics, resins and glues in increasing quantities.

Recently, in addition to the well-known local irritations to the skin, the eyes and the upper respiratory tract (Spencer, 1941¹⁾), various neurological manifestations and psychiatric disability have been reported, which include disturbances of the autonomic nervous system, cranial (I, II, VIII) and peripheral nerves, pyramidal and extrapyramidal tracts and the sensory nervous system as well as neurasthenia or anxiety neurosis (Carpenter, 1944²⁾; Barsotti, 1952³⁾; Klimková-Deutschová, 1962⁴⁾; Pratt-Johnson, 1964⁵⁾; Stewart, 1968⁶⁾; Matsushita, 1968⁷⁾; Hara, 1970⁸⁾). Liver affection has also been reported (Katz, 1962⁹⁾). But further case-reports are necessary for the establishment of the consistent clinical manifestations of styrene poisoning, because the clinical features are not uniform throughout those reported cases.

The purpose of this paper is to present a clinical case showing sensory changes, anxiety reaction, and atrophy of the skin and the muscle. The atrophy of the skin and the muscle has not yet been described up to date.

Case Report

A 55-year-old man (E. K.) was admitted to Tokyo Rosai Hospital on May 1, 1969 because of numbness and myalgia of the upper and lower extremities.

For the past fourteen years he had been working

[†]Department of Internal Medicine, Tokyo Rosai (Labour Accident) Hospital.

^{††}The First Department of Internal Medicine, Faculty of Medicine, University of Tokyo.

Received for publication June 17, 1971.

*東京労災病院内科

**東京大学第1内科

昭和46年6月17日受付

Fig. 1 Thin and atrophic skin in the bilateral palms. The skin is wrinkled in the hypothenar.

Fig. 2 Muscular atrophy in the lower extremities.

Fig. 3 Skin biopsy of the back of the left hand. H. E., $\times 760$. Thinning of the prickly cell layer, flattening of the papillary layer and marked edema with mild perivascular infiltration of round cells throughout the dermis. No increase of the collagen fibers.

Fig. 4 Muscle biopsy (M. gastrocnemius sinistra, H. E., $\times 700$). Degeneration of the muscle fibers with increase of the sarcolemmal nuclei, in some places.

at a factory manufacturing polyester resin tubs for chemicals. Since styrene evaporates during the process, he often experienced lacrimation and nasal irritation. In addition, he handled the material with his bare hands. Eleven years before admission, he noticed the development of numbness, myalgia, headache, insomnia, general malaise and anxiety, which were gradually aggravated. About the same time, he was admitted to another hospital for two months because of jaundice. One of his colleagues also complained of myalgia.

Past history disclosed arrhythmia in adolescence. He smoked twenty cigarettes a day but drank no

alcohol.

His father committed suicide at the age of 51, mother died from diabetes mellitus and a sister from progressive muscular dystrophy.

On admission the skin was generally thin and atrophic, especially on the bilateral hands (Fig. 1). Raynaud's phenomenon was not recognized. Motor examination of the trunk and extremities disclosed slight generalized muscular atrophy (Fig. 2); fasciculations were not observed. The deep tendon reflexes were generally exaggerated. Pathological reflexes were not elicited. Sensory examination revealed paraesthesia of all the extremities and

Tab. 1 Clinical reports of styrene poisoning.

reporters	No. of Cases	Clinical manifestations*																				
		anosomia	constriction of visual field	loss of visual acuity	facial palsy	nystagmus	labyrinthine disturbance	Romberg's sign	exaggerated deep tendon reflexes	peripheral neuropathy	muscular atrophy	EEG abnormality	EMG abnormality	vegetative symptoms	neurotic reactions	skin atrophy	hepatosplenomegaly	hyperbilirubinemia	gammaglobulinemia	leukopenia	reticulocytosis	macrocytosis
Carpenter et al. (1944)	2**						+								+							
Barsotti, et al. (1952)	(41)			+																+		
Klimková-Deutschová (1962)	4 (35)				+	+	+	+	+	+	+	+	+	+	+							
Katz (1962)	57 (526)																					
Pratt-Johnson (1964)	1		+	+													+	+	+	+	+	+
Stewart, et al. (1968)	(5**)	+						+														
Matsushita, et al. (1968)	1 (14)		+	+					+	+		+			+							
Hara, et al. (1970)	1***																					
Ours (1971)	1								+	+	+	+	+	+	+	+						

* : Local irritations in the eyes, upper respiratory tract and skin have been excluded from this table.

** : Human exposure study.

*** : This showed ataxia of gait, exaggerated deep tendon reflexes and mental change following long exposure to vinyltoluene, acrylonitrile and styrene.

() : Numbers of mass examination are shown in the parenthesis.

decrease of cold sensation bilaterally on the legs and feet. The visual field and acuity were intact. The liver and spleen were not enlarged.

Skin biopsy from the back of the left hand revealed moderate atrophy of the epidermis with thinning of the prickle cell layer and flattening of the papillary layer, and marked oedema with mild perivascular infiltration of round cells throughout the dermis (Fig. 3). Electromyogram showed reduced number of motor units at maximal voluntary effort and polyphasic larger action potentials of long duration suggesting neurogenic origin in all four extremities. Muscle biopsy (M. biceps humeri sin. and gastrocnemius sin.) disclosed degeneration of the muscle fibers with increase of the sarcolemmal nuclei in some places (Fig. 4). No remarkable change was found on biopsy of a peripheral nerve (N. suralis sin.). Electroencephalogram was normal.

Chest roentgenogram showed pulmonary emphysema; as to electrocardiogram, low voltage of standard and limb leads; Fishberg concentration test showed 674 mOsm/L; PSP, 25% (15 min.). Creatinuria was noted (0.187 g/day). Urinary hippuric acid was within normal range (0.28 to 0.32 g/day). Otherwise, ESR, CPK, LDH, liver function tests, electrophoresis, hematological findings and urinalyses were all negative.

After admission, myalgia persisted and spontaneous generalized pricking pain attacked him frequently. Furthermore he often fell into a severe anxiety state with palpitation, dyspnoea, headache, insomnia and anorexia.

Differential Diagnosis

Skin atrophy might suggest a diagnosis of scleroderma. In scleroderma, atrophy of the epidermis

and edema of the dermis are among the major cutaneous manifestations, as well as increase of the collagen fibers (Ishizaki, 1966¹⁰), the latter not recognized in the present case. Muscular atrophy and sensory disturbances have been also described (D'Angelo, 1969¹¹; Tuffanelli, 1961¹²). Furthermore a case with the complication of neurogenic muscular atrophy is seen in a Japanese literature (Tashiro, 1956¹³). But in the present case, ESR and serum proteins were normal, CRP negative, and findings of electromyogram incompatible with those of scleroderma, which are usually myogenic (Hausmanowa-Petrusewicz, 1965¹⁴; Araki, 1969¹⁵). Also the Raynaud's phenomenon was absent as well as gastrointestinal, pulmonary, cardiac, and renal manifestations, which are common features of scleroderma. Therefore the present case could not be considered as scleroderma.

Comment

Polymerization to polyester occurs under certain conditions, in which styrene is added to unsaturated polyester composed of unsaturated fatty acids and glycols, and the mixture becomes gelatinous. At this stage this material is laid on the surface of tubs by hands. Styrene evaporates during these processes (Yamasaki, 1970¹⁶).

Tab. 1 sums up a total of eight clinical reports of styrene poisoning from literatures. Peripheral neuropathy, exaggerated deep tendon reflexes and psychic changes are common clinical features through the reports by Klimková-Deutshová and Matsushita and through ours. Although atrophy of the skin and the muscle has not yet been reported, we expect that such skin changes that we have experienced in a case of scleroderma following a long exposure to trichlorethylene (Araki, 1969¹⁵) could similarly occur by styrene as non-specific skin reactions.

The skin and muscular atrophy, and sensory changes might be the result of the direct action of styrene to the peripheral nerves and the skin. Also the disturbances in the autonomic and central nervous systems might be due to the central action to the brain stem through inhalation of the styrene vapour.

At present, it is not certain whether jaundice, noted in the present case eleven years previously, was a manifestation of styrene poisoning or viral hepatitis.

Summary

A case of skin atrophy, neurogenic muscular atrophy and anxiety reaction following a long exposure to styrene was described. Skin biopsy revealed atrophy of the epidermis and edema with perivascular round cell infiltration in the dermis.

Electromyogram and muscle biopsy suggested neurogenic origin. Scleroderma was excluded clinically and histologically. A total of eight clinical reports from literatures was reviewed.

The present case was reported in the 82nd meeting of Kanto Society of Industrial Medicine and the 17th annual meeting of Japan Accident Medical Association.

Histological study was performed by K. Hirokawa, MD, and Y. Esaki, MD, Department of Pathology, Tokyo Medical and Dental University.

References

- 1) Spencer, H. C., Irish, D. D., Adams, E. M. and Rowe, V. K. : The response of laboratory animals to monomeric styrene. *J. Ind. Hyg. Toxicol.*, 24 : 295—301, 1942.
- 2) Carpenter, C. P., Shaffer, C. B., Weil, C. S. and Smyth, H. F. : Studies on the inhalation of 1 : 3-Butadiene; with a comparison of its narcotic effect with benzol, toluol, and styrene, and a note on the elimination of styrene by the human. *J. Ind. Hyg. Toxicol.*, 26 : 69—78, 1944.
- 3) Barsotti, M., Parmeggiani, L. and Sassi, C. : Observations on occupational pathology in a polystyrene resin factory. *Med. Lavoro*, 43 : 418—424, 1952.
- 4) Klimková-Deutshová, E. : Neurologische Befunde in der Plastikindustrie bei Styrol-Arbeitern. *Int. Arch. Gewerbepath. Gewerbehyg.*, 19 : 35—50, 1962.
- 5) Pratt-Johnson, J. A. : Retrobulbar neuritis following exposure to vinyl benzene (styrene). *Canad. Med. Ass. J.*, 90 : 975—977, 1964.
- 6) Stewart, R. D., Dodd, H. C., Baretta, E. D. and Schaffer, A. W. : Human exposure to styrene vapor. *Arch. Environ. Health*, 16 : 656—662, 1968.
- 7) Matsushita, T., Matsumoto, T., Miyagaki, H., Maeda, K., Takeuchi, Y., Takeuchi, S. and Katashima, T. : Involvement of the nervous systems associated with chronic styrol poisoning. *Saigai-igaku*, 11 : 173—179, 1968. (in Japanese)
- 8) Hara, I., Horiguchi, S. and Fuse, T. : A case of neuropathy probably caused by vinyltoluene and styrene. *Proc. Osaka Pref. Inst. Pub. Health, Ed. Ind. Health*, 8 : 54—60, 1970. (in Japanese)
- 9) Katz, B. Y. : Toxicological affection of the liver with styrene under operating conditions. *Gig. Truda*, 10 : 21—24, 1962. (in Russian with English abstract)
- 10) Ishizaki, T. : Pathological study in autopsy cases of systemic sclerosis. *Rheumati*, 7 : 33—47, 1966. (in Japanese)
- 11) D'Angelo, W. A., Fries, J. F., Masi, A. T. and Schulman, L. E. : Pathologic observations in systemic sclerosis (scleroderma). A study of fifty-eight matched controls. *A. J. M.*, 46 : 428—440, 1969.
- 12) Tuffanelli, D. L. and Winkelmann, R. K. : Systemic scleroderma. A clinical study of 727 cases. *Arch. Derm.*, 84 : 359—371, 1961.
- 13) Tashiro, A., Onodera, T., Niisato, S., Ikeda, K.,

- Tsuji, N. and Miyakawa, K.: A case of sclerodermia diffusa with muscular atrophy. J. Tohoku Med. Ass., 54: 83—87, 1956. (in Japanese with English abstract)
- 14) Hausmanowa-Petrusewicz, I. and Koźmińska, A.: Further studies on electromyographic findings in generalized scleroderma. Acta Neuroweg. (Wien), 29: 220—228, 1965.
- 15) Araki, S. and Ushio, K.: A case of scleroderma possibly induced by trichlorethylene. J. Jap. Acc. Med. Ass., 17: 533—539, 1969. (in Japanese with English abstract)
- 16) Yamasaki, Y.: Occupational health measures at the factory manufacturing polyster resin bathtubs. J. Sci. Lab., 46: 431—438, 1970. (in Japanese with English abstract)

和 文 抄 録

55才男子。昭和30年よりスチレンモノマーを架橋用にしたポリエステル樹脂槽の製造に従事した。作業は素手で行ない、流涙、鼻汁を頻回に経験していた。3年後黄疸にて入院治療をうけたが、この頃より頭重感、不眠、全身倦怠感、四肢のしびれ感、筋肉痛が始まり、時には激しい苦痛を訴えた。昭和44年5月当科へ入院した。入院時現症では痩せ、および上下肢、軀幹の表皮が萎縮性を示し、四肢、軀幹に軽度の筋萎縮を認めた。四肢の腱反射の亢進があり、知覚検査で両側上下肢のしびれ感、両側下腿に冷感覚の低下を認めた。

入院時検査成績では、皮膚生検上中等度の表皮の萎縮を認め、筋生検および筋電図は神経原性の変化を示した。尿中クレアチン排泄量は 187 mg/day と増加が認められたが、尿中馬尿酸排泄量は 0.28~0.32 g/day と正常であった。肝機能、血算、血液生化学、血清反応、尿

検査には異常を認めなかった。

入院および経過約1年の観察で、症状はほとんど不変であり、心季亢進、呼吸困難、不眠、頭痛ならびに食思不振を伴う高度の不安神経症状態が出没した。

汎発性強皮症が鑑別の対象になったが臨床ならびに組織学的所見より除外された。

スチレン中毒症と考えられる症例は文献上 Carpenter (1944), Barsotti (1952), Klimková-Deutschová (1962), Pratt-Johnson (1964), Stewart (1968), 松下 (1968), 原 (1970) —以上神経障害例—、および Katz (1962, 肝、脾、血液障害例) らの報告をみる。これらの症例の臨床所見は必ずしも一致していないが、われわれの症例は、末梢性の神経障害、腱反射亢進、ならびに精神症状を示した点が、Klimková-Deutschová, 松下の報告と共通であり、さらに皮膚および筋萎縮の存在が新知見であった。