Pentazocine-induced Fibrous Myopathy and Localized Neuropathy

SUWANNA SINSAWAIWONG, M.D.*,
KAMMANT PHANTHUMCHINDA, M.D*

Abstract

A 47 year-old woman who had a 4-year history of intramuscular pentazocine injections in the lower extremities, developed gradual stiffness and weakness of the lower extremities. The thigh and buttock muscles were "wooden-hard" on palpation. The skin was hard, shiny and hairless. Associated clinical and electrophysiological polyradiculopathy and multiple mononeuropathy of the lower extremities were observed. Imaging studies showed calcification and fibrosis of the involved muscles. Muscle biopsy revealed fibrous myopathy. Caution in longterm usage and early recognition of pentazocine toxicity as a neuromuscular complication are important in order to prevent irreversible drug-induced fibrous myopathy and localized neuropathy.

Pentazocine was introduced in 1967 as a non-addictive analgesic[1]. Subsequently, reports of physical dependence from addiction and abuse appeared[2,3]. Recently, there were reports of local and diffuse cutaneous, muscular and neuropathic complications from chronic repeated injection of pentazocine[4-15]. However, such complications are not widely known among physicians. In order to stimulate an awareness of this irreversible complication of the drug, we herein describe a classical case of pentazocine induced fibrous myopathy and localized neuropathy in this communication.

CASE REPORT

A 47-year-old female health-care-worker presented with progressive bilateral foot drop and inability to walk, 3 months before admission. Four years ago, she had a history of leg pain when walking up-hill. She had used intramuscular pentazocine hydrochloride as a pain killer in both thighs. Afterwards she regularly continued the injection of this drug 30-60 mg per day, 2-3 times per week for 4 years. She finally became physically dependent on the drug and even after this hospitalization, self-injection was still observed in the ward. She had not been taking other drugs and there was no history

* Department of Medicine, Faculty of Medicine, Chulalongkorn University, Bangkok 10330, Thailand.

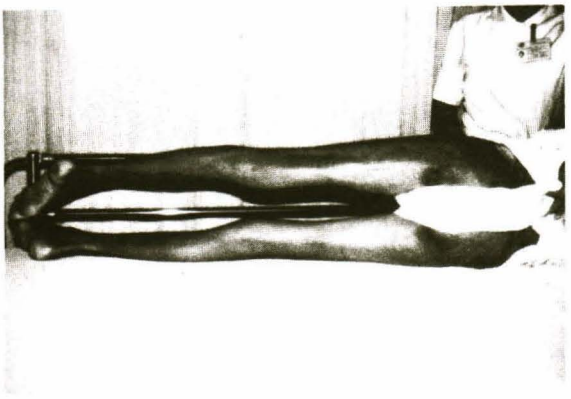

Fig. 1. Severe contracture of the lower extremities.

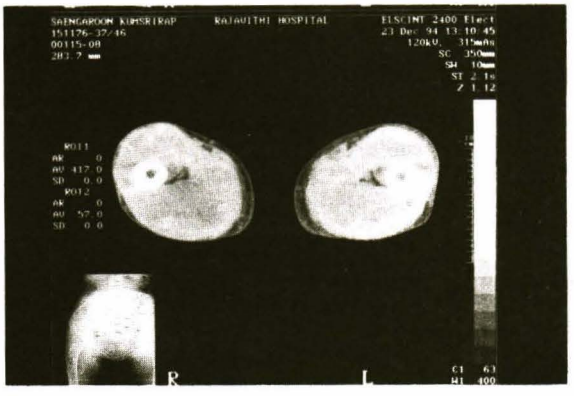

Fig. 2. CT-scan of the thighs showed calcification in the anterior aspect of the thighs and ill-defined muscle bundles due to fibrosis.

of muscle injury or other hereditary or acquired neuromuscular diseases. On examination, she had a full extension contracture of the lower extremities with marked limitation of motion (Fig. 1). Her skin in the lower extremities was shiny, hard and hairless. Both thighs, upper one-third of calves and buttocks were painlessly wooden hard on palpation. The neurological examination revealed atrophy of muscles of lower extremities and marked diminished proximal and distal muscle strength in the lower extremities. The deep tendon reflexes were +2 in the upper extremities and were absent in the lower extremities. There was bilateral decreased

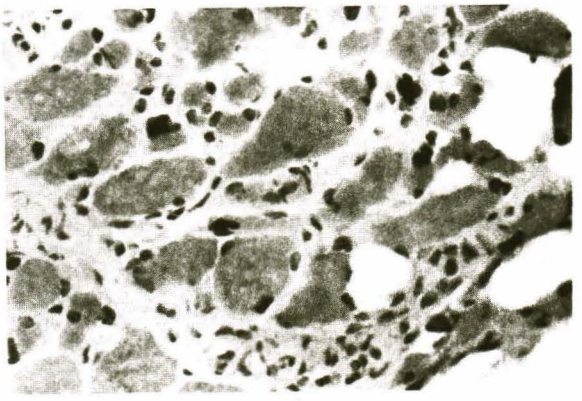

Fig. 3. Muscle biopsy showed degenerated muscle fibers, fat cell deposition, increased fibrous tissue and minimal inflammatory response.

sensation to pinprick in the distribution of L_4 to S_5 dermatomes and the joint position sensation in the lower extremities were impaired. The neurological examination of the upper extremities was normal.

Laboratory studies showed a hematocrit of 32 per cent, a white blood cell count of 18,300/mm^3 with 91 per cent neutrophils, 9 per cent lymphocytes and platelet-count of 467,000/mm^3. The erythrocyte sedimentation rate was 70 mm/h. Urinalysis, plasma glucose, blood urea nitogen, liver function tests, serum creatinine, calcium, phosphate and magnesium were normal. Thyroid function tests, antinuclear antibody, LE preparation, rheumatoid factor and complement level were also normal. Muscle enzymes including creatinine phosphokinase (CPK), lactic dehydrogenase (LDH), serum glutamic oxaloacetic transaminase (SGOT) were normal.

A plain film of the thighs and pelvis showed numerous tiny linear calcifications in soft tissue in the pelvic and thigh muscles. A CT-scan of the pelvis and both thighs revealed numerous muscular calcifications. The muscular plain was not identified due to the severe fibrotic reaction (Fig. 2). The electromyography (EMG) demonstrated bilateral incomplete denervation of gastrocnemius, peroneous, and paraspinal muscles. Focal myopathic patterns of gastrocnemius, deltoid and paraspinal muscles were also observed. The nerve conduction velocity (NCV) showed bilateral slow NCV and

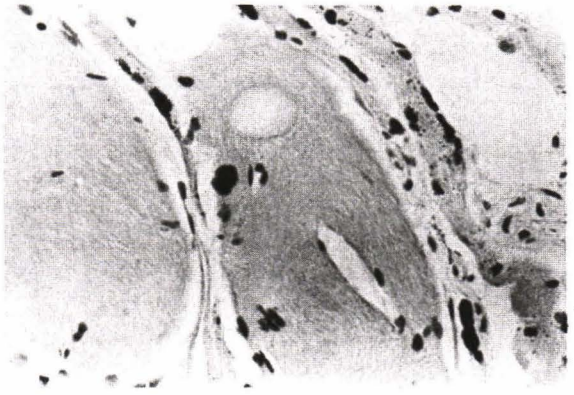

Fig. 4. Degenerated muscle fiber with vacuole and "crystal-like" cleft in the muscle fiber.

low amplitude of both motor tibial nerves and common peroneal nerves. Muscle biopsy of the left gastrocnemius showed fiber size variation with increased fibrous tissue, a few fat cell deposition and a minimal inflammatory response (Fig. 3). Muscle necrosis with myophagia and vacuoles in muscle fibre were seen. Some "crystal-like" clefts in muscle fibers which may represent foreign body crystals or emptied vacuoles were also observed (Fig. 4). The patient refused surgical correction and physical rehabilitation and symptomatic treatment were given.

DISCUSSION

The cutaneous complication from pentazocine which is usually caused by subcutaneous injection, includes extensive fibrosis, nodular sclerosis, pigmentary changes and irregular- shaped deep painless ulcers[4-6]. Dermatopathologic findings reveal dermal and subcutaneous fibrosis with varying degrees of inflammation, small vessels thrombosis and endarteritis[4,5]. Bifriengent cystals in edematous and fibrous subcutaneous tissue have also been reported[7]. Myopathic complications are characterized grossly by "wooden-hard" and contractive muscles[8-15]. Microscopic examination reveals diffuse muscular fibrosis with variable amount of inflammation and focal area of muscle fiber necrosis and atrophy[8,9,11-14]. Our patient had a long history of pentazocine injections and developed "wooden-hard" muscles of both lower extremities. Her prominent muscular complication with mild skin involvement might be explained by deep intramuscular injections. The muscle biopsy revealed classical fibrous myopathy with mild inflammatory response. Interestingly, the microscopic picture in our case demonstrated clear spaces in muscle fibers in the form of "crystal-clefts" which might represent the precipitation of drug in the muscle fiber.

Radiographic evidence of muscle fibrosis and/or tissue calcification in the affected area on both plain film and CT-scan are helpful in the diagnosis of pentazocine-induced fibrous myopathy[16]. The imaging features, as described in our case, have been reported previously[16]. Other imaging features which may be detected on CT-scan or MRI are multiple ill-defined enhanced areas or ill-defined hypolucencies caused by a mixture of fibrosis, fatty degeneration, necrosis and variable degrees of inflammation[16].

Only a few reports of neuropathic complications have been described[14,15]. Brachial plexopathy, radial nerve palsy and reflex sympathetic dystrophy are observed in cases with localized myopathy[14,15]. Our patient developed clinical and electrophysiologic evidence of symmetrical polyradiculopathy and multiple mononeuropathy of the lower extremities which have not been previously reported. The etiology may be entrapment of the nerves or direct neurotoxicity from pentazocine[14,15].

The mechanism of pentazocine-induced fibrous myopathy is not clear. Repeated traumatic needle injury and precipitation of pentazocine in the alkaline pH of extracellular tissue with secondary chronic inflammatory response may be responsible for localized fibrous myopathy[7]. In some cases with systemic involvement or local spreading of the complication, the mechanism may be due to the systemic myotoxic[17] or local intramuscular spreading effect of pentazocine[13,14]. Although our case had most of her injections in the thighs and upper parts of the lower extremities, the myopathic changes were also demonstrated in the entire lower extremities and in pelvic muscles. Moreover, electrical evidence of myopathy was also observed in the deltoid muscles. This pattern of manifestation reflected local as well as systemic spreading of the complication. Since damage to the neuromuscular system is usually permanent, medi-

cal treatment with steroids and aluminum hydroxide may give only slight symptomatic relief[18]. Surgical intervention may be helpful in patients with contracture and entrapment neuropathy[14,15].

(Received for publication on January 23, 1997)

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โรคกล้ามเนื้อชนิดเป็นพังผืดและโรคเส้นประสาทเฉพาะที่เหตุจากยาเพนตาโซซีน

สุวรรณา สินไสววงศ์, พ.บ., กัมมันต์ พันธุมจินดา, พ.บ.**

ผู้ป่วยหญิงไทย อายุ 47 ปี มีประวัติฉีดยาเพนตาโซซีนเข้ากล้ามเนื้อบริเวณขาเป็นเวลา 4 ปี และเกิดอาการกล้ามเนื้อขาตึงและอ่อนแรงซึ่งเป็นมากขึ้นเรื่อย ๆ. จากการตรวจกล้ามเนื้อต้นขาและสะโพกมีลักษณะแข็ง "เหมือนไม้" เวลาคลำ. ผิวหนังบริเวณขามีลักษณะแข็งมันและไม่มีขน. นอกจากอาการทางกล้ามเนื้อแล้วยังพบอาการร่วมซึ่งเป็นลักษณะของความผิดปกติของรากประสาทและเส้นประสาทบริเวณขาจากการตรวจทางคลินิกและการตรวจทางไฟฟ้ากล้ามเนื้อ. การตรวจทางเวชนิทัศน์พบหินปูนและพังผืดในกล้ามเนื้อบริเวณที่เกิดอาการ. การตัดกล้ามเนื้อตรวจพบกล้ามเนื้อผิดปกติโดยมีเยื่อพังผืดแทรกแซงอยู่. การใช้ยาเพนตาโซซีนฉีดในระยะเวลานานจำเป็นต้องระวังภาวะแทรกซ้อนทางระบบประสาทและกล้ามเนื้อดังกล่าวและพยายามตรวจวินิจฉัยภาวะแทรกซ้อนจากยาเพนตาโซซีนในระยะเริ่มแรกเพื่อหลีกเลี่ยงภาวะแทรกซ้อนจากยาที่ทำให้เกิดโรคกล้ามเนื้อชนิดเป็นพังผืดและโรคเส้นประสาทเฉพาะที่ซึ่งอาจจะไม่หายเป็นปกติ.

* สาขาวิชาประสาทวิทยา, ภาควิชาอายุรศาสตร์, คณะแพทยศาสตร์ จุฬาลงกรณ์มหาวิทยาลัย, กรุงเทพ ฯ 10330