Parenteral Pentazocine and Diabetes Mellitus: A Double Whammy for Cutaneous Complication

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Abstract
Pentazocine, a non-narcotic analgesic, though has no addictive potential but abused frequently via parenteral route for its psychological dependence. It causes local sclerosis resulting in non-healing ulcer at injection sites. Diabetes mellitus suppress host immunity, making them vulnerable to various bacterial skin and soft tissue infection among which methicillin resistant staphylococcus aureus (MRSA) infection are predominant. We report a case, a 50-year-old shopkeeper who used to inject pentazocine primarily as analgesic, later became addicted to it. Blindly injecting the drug in any approachable soft tissue resulted in woody induration of local skin with multiple ulcers in his both arms. He later developed type 2 Diabetes mellitus which made the scenario even worser.

Introduction
Parenteral drug abuse is quite prevalent all over the world; among these substances over-the-counter medicines are often abused. Opioid group of drugs are notorious for abuse due their potent physical and psychological dependence. Pentazocine, a non-narcotic analgesic produces no physical dependence and got wide popularity immediately after its introduction in 1967 because of its wide therapeutic window and safety profile as compared to morphine. But few years later few case reports demonstrated its abuse potential due to profound psychological dependence, mostly in paramedical staffs. Cutaneous complication following regular use of parenteral pentazocine has been reported, leading to diffuse soft tissue sclerosis, local muscle contracture and often myopathy also. We hereby report a similar case where soft tissue related complication of pentazocine was worsened by diabetes.

Case Report
A 50-year-old married man, shop-keeper by occupation presented in OPD for regular diabetic check up and complained of development of two rounded non-healing ulcer with superficial discharge on his left buttock for last 2 weeks. He was incidentally found with multiple healed ulcers over both of his arms. On enquiry, he admitted that these ulcers resulted from repeated intramuscular injections. Fifteen years ago, following an injury during playing football, he got a compound Colles fracture in his left forearm. Though it united well, but due to excruciating pain he started taking parenteral pentazocine according to his physician’s advice. Besides pain relief, it also gave subjective pleasure; so he later started taking pentazocine intravenously regularly, by himself as an over-the-counter medication and gradually increased the dose. He disobeyed his family members, and became quite obstinate about taking that injection, as discontinuation resulted in marked subjective deterioration in health. He was not a known diabetic at the time of starting this substance abuse. Due to repeated injections, all approachable superficial venepuncture sites got thrombosed after two years. So he started injecting the drug blindly in muscles of both arms. Just following injection, papular lesions erupted at the site which later turned to nodules, sometimes vesicles...
Figs. 1, 2: Multiple healed ulcers with ill-defined margins over right and left upper limbs respectively; skin over these regions were grossly hyperpigmented and ultimately ruptured and formed deep ulcers. During the process of primary healing, extensive fibrosis occurred resulting in multiple deep scars with ill-defined margins at all over the injection sites. Later he was unable to fully extend the elbow due to contracture with associated muscle weakness. His glycaemic status was checked at regular intervals but was within normal limit. Over the last 12 years he was continuing this habit and was quite satisfied. But for the last few years, he was taking the injections in the gluteal region, as it was becoming very difficult day by day to pierce the hard skin in arms. But the healing of ulcers took longer than usual time which used to get healed by 4-6 weeks on an average previously. His fasting and post prandial blood glucose were 187 mg/dl and 285 mg/dl respectively. He was prescribed oral metformin (2 g daily) and glimepiride (2 mg daily) with dietary modification. But due to irregular medication glycaemic status was poorly controlled. He was also addicted to cannabis and alcohol but no other injectable drugs. His family history was otherwise noncontributory.

On clinical examination, he was anaemic though there was no history of spontaneous mucocutaneous bleeding. His both arms showed brawny induration of overlying skin which is studded with multiple healed depressed painless ulcers with ill-defined margins (Figures 1, 2). There was mild weakness in forearm and shoulder girdle musculature without any sensory deficit. Fixed flexion deformity found in both elbows which could not be extended beyond 130 degrees and flexed beyond 90 degrees. Movements in shoulder and distal small joints were normal. Superficial veins were sclerosed but without any venepuncture mark. Skin in both arms was hyperpigmented when compared to general body colour. There were two healing ulcers (4 x 3 cm, and 3 x 3 cm) with purulent discharge, over his left gluteal region. Routine laboratory investigation revealed low haemoglobin (9.7 g/dl) and total leucocyte count of 14,500 per cu.mm; FBS was 223 mg/dl, and PPBS was 320 mg/dl, serum creatinine phosphokinase (CPK) level was 860 IU/L; but others including, renal profile, liver function test, chest X-ray, ECG were within normal limits. Special investigations like HIV (Human immunodeficiency virus) serology, HBsAg, VDRL were negative. X-ray of elbow joints was within normal limit. T2-weighted magnetic resonance imaging (T2-MRI) of both arms showed no abnormality. Muscle biopsy from biceps, deltoid showed extensive fibrosis but from soleus and quadriceps was normal. EMG (electromyography) of biceps, triceps were suggestive of myopathy where as EMG of supraspinati, quadriceps was normal. Culture was done of the serous discharge from buttock ulcers which came out to be positive for Staphylococcus aureus growth resistant to methicillin, but sensitive to linezolid and vancomycin. After starting oral antibiotic according to the culture report and premixed insulin along with oral hypoglycaemic drugs, the ulcers in buttoc started healing with generation of healthy granulation tissue within two weeks. His addiction to pentazocine was treated by regular counselling along with oral naltrexone and chlordiazepoxide. His motivation was maintained at a steady level towards deaddiction without any relapse. Following vigorous active and passive physiotherapy, range of movement also improved gradually though the skin induration persisted. Muscular weakness also subsided. Serum CPK level came down to 109 IU/L. In his second follow-up visit after eight weeks, he was completely free of habit of taking pentazocine injection. His glycaemic status was well controlled; buttock ulcers also healed with minimal scarring.

**Discussion**

Pentazocine given via any route may cause blistering, peeling or loosening of skin, red lesions with purple centre, unusual bleeding or bruising, sore, ulcers in lips or mouth, itching. But when administered in parenteral route, it is notorious to cause skin ulcers. Possible mechanism suggested for such skin ulcers was acute followed by chronic inflammatory process after precipitation of the acidic drug in alkaline extracellular media. In contrast to typical methods for injectable drug abuse like ‘mainlining’ or ‘skin-popping’, our patient used method midways between these two. In order to reach the inaccessible venous route, he used to inject the drug in any approachable soft-tissue. The method popularly known as ‘blind-dating’; a similar case was reported by Bhateja et al. Most common cutaneous complications are extensive fibrosis of soft-tissue with peripheral extension, though hyperpigmentation of ulcers, bilateral deep vein thrombosis, toxic epidermal necrolysis, generalised erythematous desquamative rash were also reported. Myopathy as demonstrated in our case was also reported previously, caused by local intramuscular pentazocine injection involving only selective groups.
and hence easily can be differentiated from other form of congenital or infiltrative myopathy with generalised affection.\(^7\) Extensive soft tissue fibrosis followed by fixed contracture deformity has been reported earlier.\(^8\) It classically described as “arm levitation sign” when involves the deltoid muscle which was absent in present case.\(^9\) Repeated local trauma, micro-haematoma during injection explains the elevation of serum CPK level which came down to normal range after discontinuation of injection. Palestine et al reported a case series of 17 patients having cutaneous complications following pentazocine abuse, 53% cases with medical or paramedical background, 18% with diabetes mellitus, 65% with personal or family history of diabetes.\(^9\) Histologic findings of those patients revealed similar pattern in dermis and panniculus along with vascular thrombosis, granulomatous inflammation, fat necrosis and endarteritis which were suggested due to co-association with diabetes. The case discussed hereby was also diabetic but peculiar site and types of ulcers were due to its mode of injection. Skin and soft tissue infections (SSTIs) and poor healing are quite a common complication of diabetes mellitus. Diabetic neuropathy leads to decreased pain sensation, lack of sweating, cracked skin with easy entry for bacteria. Diabetic angiopathy causes local ischaemia and delays healing. Further immunologic deterioration occurs due to dysfunction of phagocytosis and poor intra-cellular microbiocidal action. Among bacterial SSTIs streptococcus pyogenes and staphylococcus aureus are commonest causative organism in diabetic patients followed by anaerobic and Gram negative bacilli. Methicillin resistance among \textit{Staphylococcus aureus} (MRSA) first emerged in 1961, following which it spread through whole world like an epidemic.\(^11,12\) Commonest skin diseases secondarily infected with MRSA are leg ulcers and chronic eczematous lesions. Diabetics have higher preponderance of MRSA infection due to higher rate of colonisation; others associated risk factor being underlying chronic systemic disease, contact with healthcare person or long term institutional care.\(^13,14\) Local soft tissue sclerosis following chronic pentazocine injection, diabetic angiopathy and superadded infection by MRSA was the main reason of delayed healing of ulcers in our patient. Contrary to existing belief that pentazocine addiction is limited to paramedical staff; our case represents an example of pentazocine abuse by a person not related to medical profession. Physicians should suspect for parenteral pentazocine abuse when dealing with such typical indurated skin ulcers, even in absence of voluntary admission for self-medication as earlier detection of this drug dependence is well amenable to treatment.

**Conflict of Interests**

None declared by the authors.

**References**