Case Studies involving Bilateral Lower Limb Lymphoedema following Pentazocine Abuse in Sickle Cell Disease Patients

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Abstract

Background: *Lymphoedema which results from lymphatic obstruction can cause significant morbidity in affected individuals. Pentazocine injection has several complications including skin ulceration, scaring and fibrous myopathy and these may predispose to lymphoedema. Sickle cell disease (SCD) being a condition characterized by chronic pain tends to provide a background for frequent pentazocine injection or abuse, and this could in turn be accompanied by other complications. Reports of lymphoedema as a remote complication of repeated pentazocine injection are scarce and efforts must be made to prevent this vicious sequel. This case series highlights Nigerian SCD patients who developed bilateral lower limb lymphoedema following prolonged self administration of pentazocine injection.*

Setting: *University of Benin Teaching Hospital, Benin City, Edo state.*

Subjects: *Three cases of bilateral lower limb lymphoedema following pentazocine abuse in SCD patients.*

Clinical Findings: *The patients all had prolonged self injection of pentazocine. Examination revealed bilateral lower limb lymphoedema. The diagnoses were made largely from clinical evidence and multidisciplinary management instituted for the cases.*

Conclusion: *Preventive and proactive measures must be taken to forestall this apparently increasing complication of pentazocine injection. Such intervention will include minimizing the use of parenteral pentazocine. A high index of suspicion for intramuscular pentazocine abuse is required when dealing with young SCD patients who develop lymphoedema of the extremities.*

Keywords: Lymphoedema, pentazocine, prolonged self injection, sickle cell disease

Introduction

The hallmark of Sickle cell disease (SCD) is the vaso-occlusive pain crises in which the patient may experience excruciating periods of unremitting pains in addition to marked psychosocial and physical co-morbidities.[1,2]

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No conflicts of interest have been declared by the authors

Pain management involves the use of various analgesics including pentazocine, a narcotic analgesic used chiefly for moderate-to-severe pain.[3] For adequate pain management, it is important to assess and reassess pain frequently until pain relief is achieved so as to prevent behaviour that appear as signs of addiction to analgesics.

Adverse effects of pentazocine include hallucinations and other psychotomimetic effects as well as respiratory depressant effect. There have also been reports of skin fibrosis, skin ulceration, abnormal skin pigmentation and symmetrical myopathy cum fibrous myopathy (a rare complication following prolonged pentazocine injection).[3-5] Abuse of pentazocine is reported across the globe[6,7] and it has also been used illicitly in combination with antihistamine drugs (e.g. promethazine) because of the euphoric effect. An important but sometimes overlooked sequela of repeated use of pentazocine injection is the secondary lymphoedema that develops after the resultant disruption or obstruction of the lymphatic pathway; probably from scaring and fibrosis. Here we present three cases of SCD with pentazocine-induced lymphoedema, an under-reported complication. The aim is to create reasonable awareness on secondary lymphoedema from pentazocine abuse, and accentuate the magnitude of the health cum socioeconomic burden of this complication on SCD patients. There is a paucity of data in our environment, thus making these cases worth reporting.

CASE 1

JP was a 31-year old male graduate of school of health technology. He was a known SCD patient (diagnosed at 10 years of age) who presented with bilateral lower limb ulcers and lymphoedema of two years duration. He had a preceding eleven year history of pentazocine addiction and consequent self-injection of pentazocine, intramuscularly. His addiction was consequent upon frequent use of pentazocine injection by healthcare givers to treat him during pain crises. Subsequently he forged doctor's prescription to ensure pentazocine supplies when there was no pain crisis and was able to inject himself. He developed chronic ulcers at injection sites (in the lower limbs) and subsequently lymphoedema which progressed to cause gross difficulty in walking; this ultimately led to loss of his job. He is single, not an alcoholic, has no past history of substance abuse but abuses promethazine together with pentazocine.

Physical examination revealed an ill-looking young man (height 1.6m and weight 60kg) with extensive ulcers in the lateral aspects of the right and left thighs, ulcers extending from the level of the tibial tuberosity to the ankle in the right and left legs, hyperpigmentation and hyperkeratosis of the affected skin, non-pitting edema in both legs and square toes. He had significant movement limitations in both ankles and knees; with gait abnormality. (Image 1).

Image 1A (Lymphoedema in Case 1)

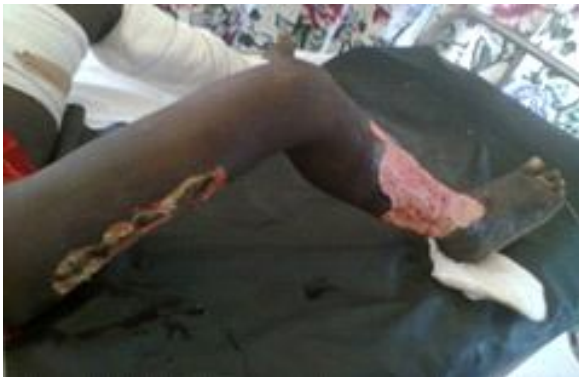

Image 1B (Ulcers and lymphoedema in Case 1)

The available investigation results were as follows: White cell count was 91600/ µl, neutrophils 85%, eosinophils 3%, basophils <1%, lymphocyte 7.9%, haematocrit 17.6% and platelet count 1212000/ µl; Plasma Urea level was 48mg/dl and creatinine 0.8mg/dl. Electrolytes were within reference ranges: sodium 136mMol/L, potassium 3.2mMol/L, bicarbonate 22mMol/L, chloride 100mMol/L; urinalysis was normal and no microfilariae were seen in his blood film. Human Immunodeficiency Virus (HIV) screening was negative.

Due to lack of funds extensive investigations including lymphangiography were not done. However a multidisciplinary management involving the Haematologists, Plastic Surgeons, Nurses, Psychiatrists and Physiotherapists was instituted. Adequate wound dressing was done, elevation of the limbs, antibiotics, chronic blood transfusion and zinc supplement given with significant improvement in his general clinical state. There was a partial regression of the lymphoedema as he was being discharged from the ward.

CASE 2

MO was a 38 year old female SCD patient who was a graduate of psychology. She was referred from a health center on account of multiple chronic ulcers on the right and left forearms, and legs as well as lymphoedema in all four limbs that had lasted for one year and a preceding nine year history of pentazocine abuse. The ulcers which followed repeated self-injection of pentazocine, deteriorated due to poor management and continued self-injection of the drug. She had past medical history of admission into a psychiatric ward were she was managed for pentazocine abuse/addiction but response was short-lived. Social history revealed that she was a state civil servant (a clerical staff) and single mother with a 5-year old daughter.

Physical examination showed a young lady who was pale, febrile and mildly icteric, with non-pitting oedema in all limbs. (weight 58kg, height 1.56m). Pulse rate was 108b/Min. and BP, 90/50mmHg. Musculoskeletal system examination revealed hyperpigmentation with hyperkeratosis and multiple scars from healing ulcers on the forearms and legs. The limbs were oedematous and dirty bandages applied on the ulcers in both forearms and legs. (Image 2). She also had reduced joint movement in the elbows, knees and ankles; with associated abnormal gait.

Image 2A (Scars, ulcers and lymphoedema of the extremities in Case 2)

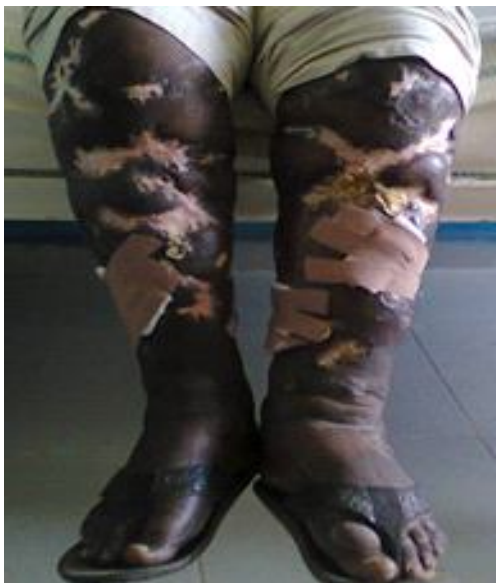

Image 2B (Scars, ulcers and lymphoedema of the lower limbs in Case 2)

The investigation results obtained were:- White Blood Cell count 6500 /µl (neutrophils 80%, eosinophils 2%, basophils 1%, monocytes 7%, lymphocytes 10%), Platelet count 363000 /µl, Haemoglobin concentration 5.4g/dl. Her packed cell volume (PCV) on admission was 18% while her steady state PCV was 22-24%. Electrolytes: Na 136 mMol/L, K 3.8 mMol/L, Cl 108 mMol/L, HCO_3 23 mMol/L. Creatinine: 0.7mg/dl, urea: 16mg/dl. Blood film showed no microfilariae.

Patient was unable to pay for further investigation. Management involved wound dressing, micronutrient replacement with zinc sulphate, hypertransfusion, bed rest with elevation of the limbs, physiotherapy and psychiatric intervention. She requested for discharge after 7 weeks of admission when the lymphoedema had regressed minimally.

Image 3 (fixed flexion and lower limb lymphoedema in Case 3)

CASE 3

EU was a 32-year old male SCD patient who presented with chronic bilateral lower limb swelling and inability to walk. There was a history of repeated self administration of intramuscular pentazocine which he was addicted to. He was single, unemployed, not an alcoholic and with no past history of substance abuse. Physical examination showed bilateral lower limb lymphoedema with fixed flexion of the knee joints. There were multiple scars from healed ulcers on the anterolateral aspects of the right and left thighs (injection sites) and hyperpigmentation of the legs. Movements at the knee joints were grossly limited and his toes were square-shaped. (Image 3). Results of investigations done revealed: Haemoglobin concentration of 6.8g/dl, PCV 21% and there was no microfilaria seen in the blood film; kidney and liver function test results were essentially normal. HIV screening was negative. A multidisciplinary approach to his management was instituted. Bed-rest with elevation of the limbs, physiotherapy and psychotherapy were commenced but he was discharged on request (against medical advice) before any significant progress could be made and eventually lost to follow-up.

Discussion

Lymphoedema is swelling of the extremity that arises from interference with lymph transport and with resultant pooling of lymph within the interstitial space. Its prevalence is estimated in the range of 1.3 to 1.4 per 1000 of the population.[8] A review of medical literature revealed the paucity of publications on lymphoedema in SCD.

Lymphoedema is caused by an obstruction or interruption of the lymphatic system. These include lymphatic hypoplasia, functional insufficiency or absence of lymphatic valves, infection, malignancy or scar tissue.[9] It can be primary or secondary and the secondary type is commoner;[10] just as observed in our reported cases. The lymphoedema in this case series may probably be due to inflammation, myopathy, ulceration, scaring and fibrosis associated with repeated parenteral administration of pentazocine (especially with poor technique and subcutaneous deposits).[3-6] The clinical features are limb swelling and feeling of heaviness, tightness and pain.[10] Advanced cases may show hyperkeratosis of the skin and fluid weeps from lymph-filled vesicles. It can take a

psychological toll with patients experiencing symptoms of anxiety, depression and adjustment problems. Consequently lymphoedema can affect the patients' vocational, domestic, social and sexual lives; and adversely affect their quality of life.[11] Virtually all of these clinical features were present in our patients.

In most patients the diagnosis of lymphoedema can be made based on history and physical examination alone,[12] hence our index patients were diagnosed accordingly. Although we did not have the benefit of investigations (for radiological diagnosis) such as lymphangiography, isotope lymphoscintigraphy, computed tomography scan and magnetic resonance imaging, history and examination findings showed typical features of lymphoedema which served as basis for diagnosis. The management strategies for lymphoedema include bedrest and leg elevation, compression garments, sequential external pneumatic compression, lymphatic massage, antibiotic therapy and surgery.[12-14] However our patients could not afford surgical interventions and other advanced treatment as they had great financial constraints.

Parenteral pentazocine abuse by SCD patient is apparently commoner than is imagined. The lymphoedema complication of pentazocine injection is therefore a cause for concern as it evokes significant health and socioeconomic challenges. Each of the patients admitted to repeated self-injection of pentazocine prior to development of the lymphoedema. Filariasis is the commonest cause of lymphoedema world wide.[15] However history and blood film did not suggest filarial aetiology in these cases although lymphoedema of filariasis occurs long after infection and thus microfilaremia may be absent at the time of presentation. There was also no history of malnutrition, malignancy, cardiac, liver or renal disease to suggest probable alternative causes of the lymphoedema.

The three patients abused pentazocine as it was self-administered without doctor's prescription and admitted to using it as a recreational drug. They were SCD patients who got exposed to pentazocine during treatment of their recurrent pain crises. Although these data may be insufficient, the abuse appears to be more in young adults.

Conclusion

Lymphoedema, though uncommon, is an important complication of pentazocine injection particularly if wrongly administered. We therefore emphasize that great caution must be taken while prescribing parenteral pentazocine and concerted effort made in shifting towards the use of oral formulations of pentazocine. Furthermore strict measures should be put in place to forestall over-the-counter sale of this drug in Nigeria. Proactive measures must be instituted with adequate patient education on the possibility of these complications so as to avert a high frequency of lymphoedema in SCD patients. A high index of suspicion for intramuscular pentazocine abuse is required when dealing with young patients who develop lymphoedema of the extremities.

There is also the need to keep surveillance on SCD patients to forestall pentazocine abuse just as their mental health should be assessed frequently. Thus it may be necessary to minimize the duration of exposure to pentazocine and alternative analgesics introduced to achieve adequate pain control.

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