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Abstract

A 73-year-old Japanese man developed chronic intractable itching due to prurigo nodularis. High-dose glucocorticoid ointment failed, and the treatment resulted in poor glycemic control. Repeated scratching caused hematogenous bacterial dissemination via cutaneous injuries, resulting in the formation of iliopsoas and spinal epidural abscesses that required long-term antibiotic treatment. Pregabalin was administered to treat the pruritus, and a considerable improvement was observed. A reduction in the dose and intensity of the topical corticosteroids improved the patient’s glycemic control, resulting in the complete resolution of the abscesses. Pregabalin significantly improved the patient’s pruritus and decreased the risk of infection.

Key words: pregabalin, pruritus, itching, prurigo nodularis, iliopsoas abscess, spinal epidural abscess


Introduction

Diabetic peripheral neuropathy (DPN) is common in patients with diabetes mellitus, particularly after a long disease duration. Painful DPN continues to adversely affect the quality of life (QOL), irrespective of treatment with various medications. Since pregabalin has been shown to be effective in cases of painful DPN, the therapeutic strategy for treating this condition has changed (1). The developmental pathways of pain and pruritus are similar (2). Furthermore, the efficacy of pregabalin for treating pruritus has been previously reported (2-5). We herein present a case in which we prescribed pregabalin for the treatment of chronic intractable itching that led to repeated cutaneous infections.

Case Report

A 73-year-old Japanese man had an 8-year history of diabetes. Systemic pruritic nodules had appeared three years earlier, for which glucocorticoid ointments did not have any effect. A skin biopsy revealed a pruritic rash, identified as prurigo nodularis (PN). Despite the application of 0.5 g/day of clobetasol propionate ointment and the administration of oral antihistamines, the patient’s sleep was disturbed and he scratched his entire body to the point of bleeding. The use of large quantities of glucocorticoid ointment caused worsening of his HbA1c level up to 7.5-8.5%, despite the administration of intensive insulin therapy. Six months prior to the current admission, he was admitted to the Department of Dermatology at our institution for the treatment of left leg cellulitis and osteomyelitis caused by repeated scratching.

Four months after he was discharged from the Department...
The etiology of the infection was intractable itching. Therefore, the administration of pregabalin was attempted. The severity of the pruritus was measured using a visual analogue scale [VAS (6)], the Dermatology Life Quality Index [DLQI (7)] and a 5-D itch scale (8). The pretreatment VAS rating was 10. Treatment with 150 mg/day of pregabalin improved the VAS score to 0 on the first night. The next day, the VAS score rose to 2 and continued at this level for two weeks. At the time of discharge, the dose of pregabalin was increased to 225 mg/day. The VAS score decreased to 1 after two weeks, and this score was maintained for 50 weeks. Other findings are presented in Fig. 2. The pretreatment DLQI score was 15, which decreased to 3, 2
and 1 after two, four and 50 weeks of treatment, respectively. The 5-D score was 22, 10, 8 and 7 at pretreatment and after two, four and 50 weeks, respectively.

Pregabalin was remarkably effective in relieving the patient’s unbearable pruritus. The decreased frequency of scratching reduced the number, size and redness of the PN, as shown in Fig. 3. The patient did not experience any dizziness, vision disorders or drowsiness that interfered with his daily activities. The clobetasol propionate ointment was changed to mometasone furoate, allowing the insulin dose to be reduced from 25 units/day to only 10 units/day and improving the patient’s glycemic control. The changes in the levels of an inflammatory marker, C reactive protein (CRP), are shown in Fig. 4. The CRP level decreased soon after the intravenous antibiotic treatment was started and was maintained at a low level even after the antibiotic therapy was switched to oral administration at discharge. During the follow-up period as an outpatient, the patient’s CRP level became elevated to 0.79 mg/dL (at approximately 50 weeks; Fig. 4). However, the value was not remarkably different from the CRP level (0.31 mg/dL) observed at discharge. Moreover, the elevation in the CRP level at approximately 50 weeks was not likely to be a premonitory symptom of the recurrence of inflammation considering the patient’s good clinical condition. The patient’s glycemic control, represented by the average blood glucose values over four time points (before every meal and at bedtime), also improved during the admission period, and the HbA1c level as a follow-up examination marker was maintained at a reasonable level in the outpatient clinic. A follow-up MRI scan performed six months after discharge revealed the complete resolution of the abscesses.

**Discussion**

We herein presented the case of a diabetic patient with in-
tolerable pruritus caused by PN that induced iliopsoas and cervical epidural abscesses. PN is a chronic condition characterized by pruritic papulonodular eruptions. The classic lesion in PN is a firm hyperkeratotic nodule with a diameter of 0.5-3.0 cm. These lesions are commonly localized symmetrically on the extensor surfaces of the limbs. The trunk, face and palms can also be involved. The etiology of PN remains unknown. Whether PN is a primary dermal disease or a pathological reaction that occurs secondary to pruritus and scratching provoked by a different cause remains uncertain (9). Antipruritic agents, antihistamines, corticosteroids, UV light (10), cryotherapy (11), vitamin D₃ (12), capsaicin (13), cyclosporine (14), thalidomide (15) and naltrexone have been used to treat PN. However, treating PN and interrupting the itch-scratch cycle remain difficult (9). PN has been reported to be associated with metabolic and endocrine disorders; 17% of PN patients have been found to have diabetes (16-18).

Pregabalin is very similar to gabapentin with respect to its structure and mechanism of action. Pregabalin binds to the α₂-δ subunit of the voltage-dependent calcium channel in the central nervous system and reduces calcium reflux into nerve terminals. This reduces the release of neurotransmitters, such as glutamate, noradrenaline and substance P. Therefore, this treatment induces pain relief. Pregabalin is effective for the treatment of neuropathic pain associated with diabetes mellitus (1). The neuronal pathways for pain and pruritus are similar; both involve the transmission by specialized C-fibers in the dorsal horns of the spinal cord that reach the thalamus. This correspondence of pathways suggests that pregabalin might inhibit the sensation of pruritus (2). The efficacy of gabapentin for treating pruritus has been reported (19). Subsequently, the use of pregabalin to treat cetuximab-related itching (5), uremic pruritus (20) and, more recently, pruritus associated with PN (4) has been described.

The VAS is generally used to assess pain severity and has been validated for the assessment of pruritus (6). The VAS consists of a 10-cm long horizontal line scored from 0 (no pruritus) to 10 (worst imaginable pruritus). The DLQI is widely used as a health-related QOL measurement for a variety of dermatological diseases. It consists of 10 questions and covers six domains, including symptoms and feelings, daily activities, leisure, work and school, personal relationships and treatment. The total score is calculated by summing the scores of all items, resulting in a minimum score of 0 (no effect on a patient’s QOL) to a maximum score of 30 (extremely large effect on a patient’s QOL) (7). The 5-D itch score is reportedly sensitive to the multidimensional nature of pruritus and its effect on the QOL (8). The scores in each of the five domains (degree, duration, direction, disability and distribution) are determined separately then summed to obtain a total 5-D score between 5 (no pruritus) and 25 (the most severe pruritus). The VAS, DLQI and 5-D itch scores are complementary to each other, and we used these methods to evaluate the changes in the patient’s QOL that were influenced by itching.

As to the safety of pregabalin, the most common adverse events are dizziness and somnolence. However, these symptoms did not trouble our patient. From the perspective of the severity of pruritus, the alleviation of the intractable itching greatly improved the patient’s QOL and allowed him to participate in daily activities without anxiety.

Diabetes mellitus increases the risk of infection. Several aspects of immunity are altered in patients with poor glycemic control (21). Diabetic patients have a higher risk of contracting IPA (22) and SEA (23). IPA is an uncommon retroperitoneal infection. The triad of IPA includes fever, flank pain and functional impairment that presents only rarely. The most frequent clinical feature is fever. CT scans, ultrasonography and MRI are efficient methods of confirming the diagnosis. IPA is a potentially critical infection. Providing prompt and aggressive treatment is necessary in order to prevent death (24). SEA is also a rare life-threatening infection originating in the spinal epidural space. Making an early diagnosis and initiating the appropriate treatment are the most important determinants of the disease outcome. The advent of CT scans and MRI with gadolinium enhancement has greatly improved the accuracy and rapidity of diagnosis (25). The recommended treatment for both IPA and SEA includes emergent surgical drainage with systemic long-term antibiotic therapy (22-25). Our patient was treated without surgical management due to his renal dysfunction and hyperglycemic status. The coincidental occurrence of IPA and SEA is extremely rare (26). Both of these conditions are caused by the hemogenous dissemination of the pathogenic bacterium *Staphylococcus aureus*. In the present case, the portal of bacterial entry was likely a cutaneous injury arising from scratching due to pruritus.

In conclusion, the present case involved a diabetic patient who developed a severe infection of abscesses caused by refractory itching and scratching arising from PN. Pregabalin remarkably improved the patient’s pruritus, enabling a reduction in the dose of topical corticosteroids required and improving his glycemic control. The treatment did not induce a recurrence of the infection.

The authors state that they have no Conflict of Interest (COI).

References

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