Letters

Pregabalin for Treatment of Docetaxel-Related Hand-Foot Syndrome

To the Editor:

Hand-foot syndrome (HFS), also known as palmar-plantar erythrodysesthesia, is a painful, often debilitating condition related to the use of various chemotherapies. HFS usually presents with erythema, edema, and a burning sensation of the palmoplantar surfaces. The pathophysiology of HFS is not fully understood, and hence treatment options can often be challenging. We describe the case of patient with HFS due to docetaxel use, presenting with extreme hand and feet pain resulting in inability to walk. Use of pregabalin resulted in significant improvement in his symptoms, including his ability to bear weight and walk, with limited side effects.

Case Report

A 50-year-old male with well-treated hypertension and recently diagnosed with Stage IV poorly differentiated gastric adenocarcinoma, HER 2 negative, presented to our institution with three days of burning pain and swelling of both his hands and feet. He was unable to bear weight or ambulate because of his extremity pain. He had been previously treated with six cycles of FOLFOX chemotherapy without remission and was subsequently started on docetaxel as second-line chemotherapy three days before his presentation. He denied any fevers. His outpatient physician had started him on amitriptyline 50 mg once a day with little improvement in his symptoms.

On examination, he was cachectic and had no pallor or jaundice. He had a blood pressure of 120/80 mmHg, pulse rate 100 beats per minutes, and temperature of 36.5°C. He had oral ulcers on his palate and buccal area. His palms and soles were hyperpigmented and swollen with extreme tenderness to light touch. Tightness of the skin over his hands and feet was also noticed. Sensation over his hands and feet was significantly decreased. His handgrip was weak. No blisters or other wounds on his palmoplantar areas were appreciated. His abdomen was distended with ascites. He was unable to bear weight or walk because of the extreme pain. The rest of his examination appeared normal.

His laboratory examination showed a low white blood cell count with a normal hemoglobin level and platelet count. His complete metabolic panel, including liver function test, thyroid hormone, vitamin B12, and folate, was within normal limits.

He was diagnosed with HFS secondary to docetaxel use. He was started on lidocaine cream to be applied to his hands and feet four times a day, with little improvement. Cold pack to his extremities was also recommended but relief was short-lasting. His amitriptyline was increased to 75 mg once a day but stopped on day 2 because of sedation and no improvement in symptoms. We added pregabalin 75 mg twice a day to his regimen on day 2 and increased the dose to 150 mg twice a day on day 4. By day 7, his pain and swelling had significantly subsided with improved sensation of his hands and feet. Tightness of the skin, especially over his hands, still persisted. Most importantly, he was able to get out of bed, bear weight, and ambulate with assistance. He tolerated the pregabalin well with no side effects. He was discharged on pregabalin 150 mg twice a day and returned two weeks after discharge, at which time he continued to show improvement in his symptoms, with decreased pain and improved functionality of his hands and feet. The patient chose to hold further chemotherapy until full resolution of his symptoms.

Comments

HFS, also known as palmar-plantar erythrodysesthesia, is a painful, often debilitating condition usually associated with systemic chemotherapy. It is characterized by erythema, edema, and a burning sensation over the extremities.[1] The highest incidence is usually seen with doxorubicin and capecitabine and is often dose dependent.[2] Symptoms usually start 24–48 hours after therapy and begins to improve within two weeks after cessation of therapy.[3] The exact

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mechanism of how HFS develops remains unclear. However, a high density of sweat glands and thick stratum corneum might be predisposing factors for development of HFS.[4] Other authors have suggested a direct cytotoxic effect on the acral dermis by the inciting chemotherapeutic agent.[3]

The initial symptoms of HFS include dysesthesia with tingling in the extremities, which can progress to burning, pain with dryness, cracking, desquamation, ulceration, and edema.[2] The National Cancer Institute has a helpful grading system for the severity of HFS.

Treatment of HFS remains challenging as the etiology is poorly understood. Suggested therapies include reducing the chemotherapeutic dose, increasing the interval between cycles, or even halting the chemotherapy itself. Analgesics, topical steroids, systemic steroids, and application of cold packs have been used to help improve symptoms. Aloe vera has been shown in some case reports to improve the symptoms and quality of life.[5] There has been much debate on the use of pyridoxine for HFS, but it has not been shown to prevent or delay the onset of HFS.[6]

In our patient, the use of pregabalin improved his symptoms drastically. Pregabalin is an anticonvulsant widely used, specifically for neuropathic pain secondary to various diseases. Pregabalin exerts its therapeutic effects by binding to voltage-gated calcium channels and decreasing synaptic activities and has been shown to be as or more effective than gabapentin with less adverse effects. There is one case report of the efficacy of pregabalin in the treatment of HFS induced by targeted therapies, specifically dabrafenib.[7] As far as we know, there has been no report on the use of pregabalin in docetaxel-induced HFS. However, pregabalin was shown to ameliorate docetaxel-induced neuropathy in rats.[8] Our patient responded well to pregabalin with improvement in his symptoms and the ability to walk within one week of use. Pregabalin is a viable option to help improve the symptoms and quality of life in patients with chemotherapy-related HFS. However, we need to better understand how pregabalin works in improving HFS symptoms.

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Palliative Care Physicians' Practice in the Titration of Parenteral Opioids for Dyspnea in Terminally Ill Cancer Patients: A Nationwide Survey

To the Editor:

Dyspnea is among the most prevalent and distressful symptoms in terminally ill cancer patients.[1,2] Opioids remain the mainstream treatment for dyspnea. In the last phase of life, parenteral routes such as continuous subcutaneous/intravenous administration are frequently used to ensure timely titration and reliable administration in the setting of impaired oral intake and decreased consciousness. Guidelines suggest how to start parenteral opioids,[3] but the evidence is scarce regarding further management. In particular, the following questions remain unanswered. What is the best opioid titration strategy? Does an upper limit of opioids exist for dyspnea? What are the next steps if further opioid titration is considered clinically controversial, if not prohibitory, due to emerging opioid side effects? The lack of evidence can lead to marked treatment variability and inconsistent levels of dyspnea control in the last phase of life.

As the first step toward treatment standardization, it is imperative to understand the current practice of palliative care physicians. The aim of this study was to examine palliative care physicians' overall practice associated with parenteral opioids for dyspnea in