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PAIN MANAGEMENT IN A PATIENT WITH POEMS SYNDROME: A CASE REPORT

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Background: Pain is a usual symptom in patients with POEMS syndrome. The pain occurs in the superior and inferior limbs and it is featured as numbness, weakness, and tingling that worsens with movement of the affected limb.

Case Report: A 58 year-old-woman began to feel numbness, tingling, and burning in the lower members with progression to her upper extremities, hyperpigmentation, and cutaneous sclerosis. She was in treatment for chronic inflammatory demyelinating polyneuropathy (CIDP) but the symptoms worsened and she was admitted to the hospital. Her laboratory exams showed increases in pro-BNP (N-terminal prohormone of brain natriuretic peptide), platelets, B-2-microglobulin, monoclonal IgG lambda, thyroid stimulating hourmone (TSH), and decreases in T4 and cortisol levels. Computed tomography angiography showed moderate bilateral pleural effusion, pericardial effusion, hepatomegaly, and severe pulmonary hypertension. Thus, she was diagnosed with POEMS syndrome. She reported constant burning, paresthesia, and tingling in both hands with a Visual Analog Scale (VAS) score of 8 of 10, while taking daily doses of 1800 mg of gabapentin, 400 mg of carbamazepine, 4 g of dipyrone, and 100 mg of amantadine. Topical lidocaine 2% + amitriptyline 4% cream was prescribed twice a day. After 2 days of using the cream, the patient reported significant pain improvement, and after 7 days her VAS pain score was 1 of 10. Afterwards, the patient was discharged for ambulatory follow-up.

Conclusion: POEMS syndrome is a paraneoplasic disease whose diagnosis can be confused with CIDP at the beginning. The treatment is done with radiotherapy, plasmapheresis, intravenous immunoglobulin, interferon alpha, corticosteroids, azathioprine, and autologous stem cell transplantation. The pain management is complex; therefore, following the usual neuropathic pain treatment guidelines with the addition of topical agents can be a good option.

Key words: Neuropathic pain, pain, POEMS syndrome

BACKGROUND

POEMS syndrome (polyneuropathy, organomegaly, endocrinopathy, monoclonal gammopathy, and skin changes) is a rare paraneoplasic disease associated with demyelination neuropathy and multiple organ system involvement. Its features include polyneuropathy, organomegaly, endocrinopathy, monoclonal gammopathy, and skin changes (1,2). POEMS is also known as Crow-Fukase syndrome, peculiar progressive polyneuritis (PEP) syndrome, or Takatsuki syndrome (3). A study conducted in Japan in 2003 evidenced that the prevalence is nearly 0.3 per 100,000 (4). POEMS syndrome is diagnosed by clinical and laboratory features that include 2 mandatory major criteria, at least one other major criterion, and at least one minor criterion. The mandatory major criteria are polyneuropathy and

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monoclonal gammopathy. The other major criteria can be Castleman disease, sclerotic bone lesions, or elevated vascular endothelial growth factor. The minor criteria can be organomegaly, endocrinopathy, extravascular volume overload, skin changes, papilledema, or thrombocytosis/polycythemia (5).

Therefore, neuropathy is present in all POEMS patients, and 50% present early manifestations of polyneuropathy as a sole symptom. It is usually presented as peripheral, ascending, symmetrical neuropathy, leading to sensorial and motor changes (5). Pain caused by neuropathy is common and 76% of patients report worsening of quality of life due to pain in POEMS disease (6). Other common neuropathy symptoms are weakness, numbness, and tingling that may lead to wrong diagnosis, confounding POEMS with chronic inflammatory demyelinating polyneuropathy (CIDP) (7).

There is little evidence on how to treat neuropathic pain in these patients. Hence, we report the case of a patient with POEMS disease with pain refractory to previous treatment who was successfully treated with topical amitriptyline and lidocaine.

Patient Consent

Written consent was obtained from the patient for publication of this report and it was approved by the ethics and research committee of our institution.

CASE

A 58-year-old woman with hypertension began to feel numbness, tingling, and burning in her lower extremities, with progression to her upper limbs associated with hyperpigmentation and cutaneous sclerosis 2 years ago. Treatment for CIDP was initiated with methylprednisolone and cyclophosphamide. Symptoms progressed and after 2 years the patient presented with reduced motor response in her upper and lower limbs associated with dyspnea.

She was admitted to a quaternary university hospital for investigation. Laboratory testing showed increased platelet count (530,000/mm3), N-terminal pro B-type natriuretic peptide (pro-BNP) 2,763 pg/mL, and B-2-microglobulin (3.91 mg/L). Her renal function, electrolytes, and blood count were normal. A serum monoclonal IgG lambda peak was detected with immunofixation electrophoresis. The anti-La antibodies, anti-Ro antibody, antineutrophil cytoplasmic antibody, and rheumatoid factor were nonreactive. The antinuclear factor was reactive (1:80) with a thin dotted nuclear pattern, and C3 and C4 fractions were normal. The evaluation of the endocrine function demonstrated an increase in the thyroid-stimulating hormone (TSH) (6.4 mU/mL) and decreases in T4 (0.83 ng/dL) and cortisol (4.1 ng/dL) levels. Computed tomography angiography showed moderate bilateral pleural effusion, pericardial effusion, hepatomegaly, ascites, subcutaneous tissue densification, and severe pulmonary hypertension (PSAP = 100 mm Hg). She was diagnosed with POEMS syndrome.

She reported constant burning in both hands with a VAS score of 8 of 10 associated with local tingling and paresthesia. We started pain treatment with 900 mg of oral gabapentin per day and 4 g of dipyrone per day. Over the next 5 days, oral medication was titrated to 1800 mg of gabapentin per day and 4g of dipyrone per day, and she was prescribed 400 mg of carbamazepine per day and 100 mg of amantadine per day. Seven days after hospital admission, the patient still complained of burning and tingling in both hands, with a VAS pain score of 6 of 10. Since her main complaint was allodynic neuropathic pain in a wide area in the upper limbs, we prescribed topical lidocaine 2% + amitriptyline 4% cream twice a day. After 2 days using this topical adjuvant, the patient reported significant pain improvement and after 7 days she reported a VAS pain score of 1 of 10. After clinical treatment, the patient was discharged for ambulatory follow-up.

DISCUSSION

We described a case of pain management in a patient with POEMS syndrome with neuropathic pain (NP). NP is originated from somatosensory lesions from a variety of diseases (8,10). Diagnostic criteria for NP include negative or positive sensory signs confined in the innervation territory of the injured nervous structure and diagnostic tests confirming the lesion or disease justifying the pain (9). One of POEMS' diagnostic criteria is polyneuropathy, which can lead to this type of pain. POEMS syndrome is characterized by peripheral ascending neuropathy. In addition, some studies have demonstrated that the painful symptoms in POEMS can occur due to reduction of the inhibitory effect of the myelinated A fibers associated with preservation of the unmyelinated C fibers. Proinflammatory cytokines are increased, mainly IL1-B, IL-6, and tumor necrosis factor (TNF) alpha. Serum vascular endothelial growth factor levels are also elevated and can be correlated with disease progression (6,11,12).

Specific treatment for POEMS syndrome includes radiotherapy, plasmapheresis, intravenous immunoglobulin, interferon alpha, corticosteroids, azathioprine, autologous stem cell transplantation, tamoxifen, and retinoic acid (5,14,15). However, polyneuropathy symptoms may be less responsive to specific treatment than the other POEMS symptoms and systemic analgesics may be required for NP before and after specific treatment (14). Also, there is little evidence available for the treatment of NP associated with POEMS disease.

Most NP treatment guidelines advocate a calcium channel ligand blocker or antidepressant as a first and/or second line of treatment. Second-line treatments often include opioid analgesics and the third line is composed of antiepileptic drugs, N-methyl-D-aspartate receptor antagonists, and other analgesic adjuvants (9,13). In this case, we used systemic adjuvants and analgesics in the initial treatment with limited results. Most guidelines also place lidocaine 5% topical patch as a second-line treatment and other topical agents as possible choices for treating localized or superficial NP. Due to the unavailability of lidocaine patches in our service we used a topical combination of lidocaine with amitriptyline (9,13).

Lidocaine is a widely used local anesthetic that functions by blocking the Na^+ channels. The amitriptyline acts as a peripheral analgesic by blocking Na^+, K^+, and Ca^{++} voltage-gated ion channels and muscarinic, cholinergic, nicotinic, histaminergic, alpha-2-adrenergic, adenosine, and NMDA receptors. The clinical effect of topical amitriptyline has already been demonstrated at concentrations ranging from 5% to 10%. However, its use in high concentrations can be limited by systemic side effects. There is no evidence that combining different topical agents can lead to better analgesia through synergistic mechanisms of action (16,17).

CONCLUSION

In this case report, we described the pain treatment of a patient with POEMS syndrome and NP symptoms. Treatment was initiated with systemic analgesics and later included a topical combination of lidocaine 2% + amitriptyline 4% cream twice a day, after which we observed a significant reduction in VAS pain scores. There is little evidence for treating NP secondary to POEMS syndrome, and we suggest following usual NP treatment guidelines with the addition of topical agents if there is failure with the use of first-line treatment

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