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Long Term Management of SAPHO Syndrome: A Case Report

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ABSTRACT

Synovitis, acne, pustulosis, hyperostosis, and osteitis syndrome (SAPHO syndrome) is a rare cause of non-cancer persistent pain and disability. There are no randomized controlled trials or guidelines for the management of this disorder, A 61 years old woman diagnosed with SAPHO syndrome presented to the Pain Therapy and Palliative Care Unit of University Hospital of Cagliari complaining of severe pain and functional limitations despite a complex pharmacotherapy, including major opioids, immunosuppressants, corticosteroids, biologic disease-modifying antirheumatic drugs. Our management addressed both pain intensity and overall quality of life. We focused on shifting from chronic opioid therapy to safer drugs, introducing a pulse therapy with a nonsteroidal antinflammatory drug (indomethacin), and improving physical and mental fitness with complementary therapies. This case report provides useful hints for the long term management of chronic non-cancer pain.

Keywords: Opioid tapering; Biologic Treatments; Chronic Pain; Tapentadol; Multimodal Analgesia; Indomethacin

CASE PRESENTATION

A 61 years old woman presented to our Pain Therapy and Palliative Care Unit with severe axial pain and gait impairment. Her history was notable for synovitis, acne, pustulosis, hyperostosis, and osteitis syndrome (SAPHO syndrome), diagnosed at age 36. Her medications included transdermal fentanyl (75 µg q. 72 hours), oxycodone (20 mg b.i.d.), pregabalin (150 mg b.i.d), delayed-release prednisone (5 mg t.i.d), tizanidine (4 mg q.d.), methotrexate (7.5 mg b.i.d), sulfasalazine (1000 mg q.d.), anakinra (100 mg q.d), alendronate, colecalciferol, lansoprazole and ibuprofen (800 mg b.i.d.) as rescue medication for pain flares. Past medications included adalimumab, etanercept, infliximab, golimumab.

The patient presented on first examination on a wheelchair, because of severe impairment of standing and gait. She revealed palmoplantar erythematous-maculopapular eruptions with grey scales. She complained of tenderness of manubrium sterni, dorsal and lumbar spine and hips with a reduced range of motion. She rated her usual pain as severe on a 11 points Numeric Rating Scale (NRS 9-10) despite her current therapy.

Electrocardiogram and laboratory results were unremarkable, with an erythrocyte sedimentation rate of 17 mm/h and a C-reactive Protein of 0.29 ng/ml. Skeletal scintigram showed area of hypermetabolism in the iliac bones, sacroiliac joints, manubrium sterni, sternoclavicular joints, and jaw.

She referred a short-lived relief of pain during biologic treatments (adalimumab, etanercept, infliximab, golimumab), followed by severe flares after a few months. Each flare determined also a progressive reduction of overall functionality and quality of life.

We decided to de-escalate and finally withdraw major opioid analgesics fentanyl and oxycodone. We also progressively reduced pregabalin to 25 mgb.i.d.

We added tapentadol up to 200 mg b.i.d., amitriptyline 28 mg q.d. (14 oral drops), and a monthly cycle of intravenous indomethacin 50 mg q.d. for three days. We also addressed her symptomatology through a holistic approach, introducing music therapy and relaxation techniques.

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After six months of therapy, her pain intensity reduced to NRS 6 and she started to stand and walk using a walker.

After a year of therapy, her usual pain was mild (NRS 3). In accordance with the rheumatologists, we continued the same pain therapy, added methotrexate, and withdrew anakinra.

During three years of follow up, we successfully tapered off and withdrew prednisone and pregabalin. We also reduced methotrexate (5 mg q.d. for three days a week), tapentadol (100 mg b.i.d.), amitriptyline (14 mg q.d.), indomethacin (five cycles per year).

We introduced postural gymnastics and psychotherapy as part of our therapeutic plan. At the last follow up visit after five years of treatment, our patient had a complete pain relief (NRS 0) with occasional (2-3 days per month) pain flares managed with diclofenac sustained release 150 mg q.d. Our patient has also experienced a remission of cutaneous lesions.

DISCUSSION

This case report describes a typical case of SAPHO syndrome with adult age onset. SAPHO syndrome is a relatively new disease, generally classified among the seronegative arthritides because of the frequent involvement of axial skeleton, the presence of enthesitis and the association with inflammatory bowel disease [1,2].

This disorder is currently considered rare in the general population and might be significantly under diagnosed [3].

The proposed diagnostic criteria are: bone-joint involvement associated with palmoplantar pustulosis and psoriasis vulgaris, bone-joint involvement associated with severe acne, isolated sterile or growth of *Propionibacterium acnes* in hyperostosis/osteitis (adults), chronic recurrent multifocal osteomyelitis (in children), bone-joint involvement associated with chronic bowel diseases [2,4]. Infectious osteitis, tumoral conditions of the bone, non inflammatory condensing lesions of the bone are exclusion criteria [2,4].

The disease prognosis may be variable, presenting as a chronic stable or a relapsing-remitting course.

In our case, each flare determined a progressive decline of quality of life with persistent pain and reduced mobility. Our therapeutic plan focused on treating pain to regain overall functionality and improve quality of life administering the minimal effective dose of drugs. The immobility caused by gait impairment is per se a significant contributor to the painful symptomatology because of muscle wasting, abnormal posture and emotional distress. After the pain management reduced pain intensity, we introduced the patient to physical activity and addressed her emotional suffering with alternative techniques.

Our therapeutic approach started with tapering and withdrawing major opioid analgesics.

Elder patients on chronic opioid therapy carry an increased risk for delirium, cognitive impairment, falls, and traumatic injuries [5]. Tolerance, hyperalgesia, dependence, abuse, misuse, and addiction are common in patients on chronic opioid therapy [6].

We introduced tapentadol, a mu opioid receptor agonist and a norepinephrine reuptake inhibitor, because its opioid sparing effects, its safety profile, its reduced impact on cytochrome based metabolism of xenobiotics, and its effectiveness on different phenotypes of pain make it more suitable to a polypharmacy regimen in comparison to major opioids [7-10].

We also introduced nonsteroidal anti-inflammatory drugs (NSAID) in a “pulse” administration. This regimen is a key factor to prevent the adverse effects of chronic NSAID therapy. This strategy is supported by a large nested case-control analysis by Rodríguez et al., who showed a significant increase in relative risk of myocardial infarction only in patients with >365 days of consecutive NSAID prescription (consecutive in this paper is defined as a less than one month of interval between two cycles of therapy) [11].

The nephrotoxicity of NSAID may lead toacute renal failure due to hemodynamic perturbation in the kidney, tubulointerstitial nephritis, glomerular injury, impairment of natriuresis and aquauresis, hyperkalemia, and hypertension [12]. The risk of NSAID related nephrotoxicity is significant in chronic kidney disease, congestive cardiac failure, the concurrent use of calcium channel blockers or diuretics, high dosage of NSAID.[12]A cumulative high dose of NSAID in the long term period may accelerate the decline in glomerular filtration rate (GFR), with odds ratio 1.26 (1.04-1.53)for a decrease in GFR $\geq$ 15 mL/min/1.73m^2 [13].

Because of the scarcity of data nephrotoxicity in continuous versus on-demand or pulse administration, we recommend an active surveillance of GFR during treatment [14].

Our patient did not suffer any adverse cardiovascular event and her GFR, estimated according to CKD-EPI equation, did not change significantly (baseline GFR 97mL/min/1.73m^2, last follow up GFR 106 mL/min/1.73m^2) [15].

CONCLUSION

Physicians treating cases like the one we described should be aware of simple strategies to minimize the risk of a complex polypharmacy, like tapering drugs to the minimal effective dose, avoiding high-dose opioids, using NSAID in a “pulse” regimen, and integrating physical activity and relaxation techniques in a holistic management of patients’ care.

CONFLICTS OF INTEREST

We have no conflict of interest to declare. Our patient signed a module of informed consentto write, submit, and publish this case report.

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