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Alleviation of notalgia paresthetica with duloxetine after several lines of failed treatment: A case report

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ABSTRACT

Chronic pruritus affects up to 20% of the population; about 8% of patients suffer from neurogenic pruritus, including notalgia paresthetica (NP). This is a syndrome of benign, chronic itch of the unilateral medial border of the scapula of unknown etiology and limited treatment efficacy.

Here we report the background on NP, followed by a classic case presentation of a 63-year-old woman. We report on difficulty in her diagnosis and numerous failed lines of treatment, until initiation of treatment with duloxetine, which provided her with long-lasting benefit for the first time.

Delay in diagnosis is common for NP, and though there are many options for treatment, evidence is lacking to support their efficacy. Finding an effective, well-tolerated regimen to alleviate long-term suffering brought on by this syndrome is heavily dependent on early identification. Our case provides anecdotal evidence for both treatment efficacy as well as the etiology of this poorly understood phenomenon.

1. Introduction

Pruritus is a common condition, a symptom rather than a diagnosis, that accompanies or is caused by several different conditions. Most commonly, pruritus is secondary to skin pathologies; however, it can also be caused by ailments of rheumatic, endocrine, renal, hepatic, infectious, malignant, iatrogenic or neurogenic nature. The last are grouped together as neuropathic pruritus, or the "neuropathic itch" group, and include brachioradial pruritus, postherpetic neuralgia, multiple sclerosis, notalgia paresthetica (NP) as well as other, rarer, causes [1].

Notalgia paresthetica is a neurogenic pruritus syndrome of unknown etiology, with studies producing conflicting results regarding its origin and pathogenesis, though it is generally agreed that it is a neuropathy with a thoracic origin. It is usually a unilateral, chronic itch that manifests on the medial border of the inferior scapula, frequently on the non-dominant side. It is a benign condition that predominantly affects older women with no racial preference, unlike brachioradial pruritus, which affects mostly patients with fair skin and lasts typically months to years. While neurogenic pruritus comprises about 8% of all cases of chronic pruritus, it is hard to tell how many of those are attributed to NP [2].

Few studies have explored the etiology of NP. Possible causes for NP include increased dermal innervation, viscerocutaneous reflex mechanism, chemical neurotoxicity and spinal nerve injury – either by trauma or entrapment. Numerous small studies have shown thoracic radiculopathy to be associated with NP. A recent radiographic study evaluated 43 NP patients, and found that 34 had various vertebral pathologies, including degenerative changes and herniated nucleus pulposus [3]. However, opponents of this school of thought cite the regional rather than dermatomal distribution as lessening the likelihood that this is indeed a pathology of spinal nerve roots [2]. It is also important to remember that degenerative changes are common in the population, and most are asymptomatic.

Diagnosis of NP is largely clinical in nature and is based on a thorough history. Physical findings do not include any primary dermatologic lesion, but excoriations, hyperpigmentation and lichenification secondary to scratching. Imaging is not generally required as there are no diagnostic imaging criteria. Treatment for NP is varied; however, success rates are low. Options include oral treatment, such as anti-gapaergic, anti-histaminic and anti-inflammatory drugs. Topical treatment is most often with capsaicin, but other options include steroids, anesthetics, amitriptyline/ketamine, and doxepin. The efficacy of each of these has not been formally evaluated. Injection of botulinum toxin A showed encouraging results at first, but more recent studies show marginal, if any, benefit. More recent trials of transcutaneous electrical nerve stimulation (TENS) showed mixed results. Importantly, NP is a benign condition, but can take months to years to resolve [4–7,2]. A recent review of treatments attempted to create an algorithmic approach

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to the use of the above-mentioned substances to provide an escalating treatment plan for NP [8].

2. Case presentation

Here we report the case of a 63-year-old woman whose medical history included hypertension, hypothyroidism, hyperlipidemia, obesity, anxiety and depression as well as hip osteoarthritis and right sacroiliac joint (SIJ) dysfunction. She was treated with SIJ injections for her chronic pain. The patient first presented with a complaint of itch and a finding of hyperpigmentation over her should blade that were consistent with NP. At first presentation, she complained of a year-long itch that had been chronic and bothersome. She presented to the pain clinic for further investigation, where it was found that she had been scratching her right scapular region several times each hour for about 20 years. She had seen multiple dermatologists with no clear diagnosis and had tried numerous steroidal and antihistamine preparations, as well as capsaicin topical treatments, with no alleviation of her symptoms. A previous thoracic MRI scan had not revealed the etiology of her itch.

During her encounter at the pain clinic, the patient was diagnosed with NP and was started on nightly 25 mg doxepin, which she was not able to tolerate due to sedation, and so she was transitioned to nortriptyline, 25 mg nightly, at her next follow-up. This second line, although effective, as before, was also not tolerated due to sedation and dry mouth, and the patient was started on desipramine; a 25 mg dose was not effective, and a 50 mg, though effective, was again not tolerated due to similar side-effects.

After failure of several lines of topical and oral therapy, injection therapy was started in an escalated fashion. Trigger point injections (TPI) of the thoracic paraspinal, subscapularis, rhomboids and latissimus dorsi muscles were attempted with local anesthetics and steroid injectate, which were only mildly helpful; a T4–T5 epidural steroid injection (TESI) was then attempted, which was technically successful but provided no benefit. Repeated TPIs provided partial, very time-limited relief.

Given the limited success of previous treatments, the patient was trialed on gabapentin; however, she did not tolerate it due to its sedative effects. About a year and a half after her initial diagnosis, the patient was started on duloxetine (Cymbalta) 60 mg daily, which was effective for her itch, as well as her depression. For two and a half years, she did not undergo additional TPIs and did well on duloxetine, despite no improvement in her other pain symptoms (hip, SIJ). She continued on duloxetine, which was up titrated to an effective dose of 60 mg twice daily, as 60 mg daily was no longer effective, but this dose was also not effective. She was started on venlafaxine, which was increased up to 75 mg, which was again effective but not tolerated, and so the patient stopped taking it. She was recently seen at follow-up and reported that she returned to taking duloxetine, with renewed efficacy of the 60 mg daily dose.

3. Discussion

We present here a classic case of notalgia paresthetica with compelling history and physical examination findings. Prior to her diagnosis, topical treatments had failed, and her diagnosis was then followed with many lines of treatment, including oral anti-depressants, which were effective but not-well tolerated due to side-effects, as well as interventional techniques that were either ineffective or provided only short-lived benefit.

Importantly, as with many other patients, this patient saw a long delay in diagnosis (20 years)and targeted treatment for her itch, emphasizing the importance of recognition of this not uncommon syndrome, as well as referral to a specialized pain clinic when initial lines of therapy fail. Fewer than 100 cases of NP are described in academic literature [9], making this a difficult diagnosis to make. However, many treatments available [9,2], early diagnosis is crucial in finding an effective, tolerated line of therapy that is appropriate for each patient.

Duloxetine (Cymbalta) proved efficacious in our patient. Duloxetine is a serotonin-norepinephrine reuptake inhibitor (SNRI) that is commonly used to treat anxiety and depression; however, it has also had success in the treatment of neuropathic pain, and is often used as a second line after failure of agents such as gabapentin and pregabalin (Lyrica). It has the added effect of possibly treating these often comorbid underlying conditions. Its efficacy for pain treatment likely stems from neuromodulation of the descending spinal pathway on the dorsal horn. It is a relatively safe drug, but carries the serious side-effects that are often associated with other SSRI and SNRI medications. It specifically requires caution when prescribing in the elderly due to increased risk of hyponatremia secondary to SIADH; dose adjustments, however, are not warranted [10]. It can specifically be used in lieu of gabapentin when the latter is deemed ineffective, or unsafe, such as in elderly patients, co-treatment with opioid medication (though caution is still warranted in both cases) and in patients with respiratory comorbidities [11].

Interestingly, our report may also shed some light on the pathophysiology and etiology of NP. Though there are many proponents to the radiculopathy theory [3], our patient gained significant, though short-lasting, benefit from TPIs while seeing no improvement after TESI. While this is anecdotal, it does support the theory of peripheral nerve entrapment by muscle spasms [2] over that of spinal nerve compression. Another peculiarity of our case is the resumed efficacy of duloxetine after a brief hiatus. It is too early to say if this secondary to symptom unmasking during this hiatus or recovery of alleviation after sensitization to duloxetine, but further research may provide answers to this intriguing question.

In conclusion, NP is a syndrome of chronic pruritus that effects mostly middle-aged women and usually affects the medial aspect of the non-dominant scapula. Diagnosis is often delayed, and year-long, chronic itch persists. Recognition of the syndrome is important to initiate targeted therapy. While therapy is only partially effective, the many lines of treatment offer a plethora of therapy options. Referral to a pain specialist should be considered if first-line treatments fail. Further research is required to elucidate the etiology and provide standardized treatment for NP.

Contributors

Amnon A. Berger collected the data and authored the manuscript.
Ivan Urits assisted in data collection and edited the manuscript.
Jamal Hasoon assisted in data collection and edited the manuscript.
Thomas Simopoulos oversaw clinical care, data collection and manuscript editing.
All named authors meet the International Committee of Medical Journal Editors (ICMJE) criteria for authorship for this article, take responsibility for the integrity of the work as a whole, and have given their approval for this version to be published.

Conflict of interest

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Patient consent

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