Autoimmune progesterone dermatitis mimicking facial erythromelalgia successfully treated with hysterectomy and bilateral salpingo-oophorectomy

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INTRODUCTION

Autoimmune progesterone dermatitis (APD) is a rare skin disease thought to be caused by an autoimmune response to endogenous or exogenous progesterone. APD can present with a variety of skin manifestations, including pruritus, urticaria, annular erythema, and eczematous, vesiculobullous, or erythema multiforme-like lesions. It often occurs in women in a cyclical pattern that corresponds to their menstrual cycle, with flares at the height of progesterone levels 3 to 10 days prior to menses. In the case of exogenous progesterone, flares can be a daily occurrence. Here we describe an unusual case of APD presenting as painful erythema on the bilateral malar cheeks that completely resolved after total hysterectomy. This rare case, in terms of location, symptoms, and treatment, adds to our understanding of the variety of potential clinical presentations of APD.

CASE REPORT

A 48-year-old woman presented with a 2-year history of a painful red rash on the bilateral malar cheeks (Fig 1, A). Daily flares of intense burning pain, exacerbated by heat and wind, disrupted her work and sleep. Over the last year, her flares had become associated with gastrointestinal distress, photosensitivity, body aches, depression, and anxiety. Symptoms improved moderately with cooling measures: water spritzes, fans, and ice packs. She previously failed to tolerate and/or respond to pulsed-dye laser, hydrocortisone cream, metronidazole gel, ivermectin cream, propranolol, and oral doxycycline. Dietary alterations, avoidance of cosmetics, and various naturopathic remedies did not ameliorate her symptoms. Medical history was significant for Raynaud phenomenon. Current medications included combined estrogen/progesterone oral contraceptive pills (OCPs), a long-term medication for this patient.

Physical examination found minimal erythema on the bilateral malar cheeks and purple-red plaques on bilateral hands. Patient-supplied photographs of disease flares showed bright red well-circumscribed patches on the bilateral malar cheeks (Fig 1, A) and white fingertips consistent with Raynaud phenomenon. Extensive autoantibody testing was positive only for anticardiolipin IgM. Antinuclear antibodies and antibodies to the following antigens were negative: dsDNA, Ro/SS-A, La/SS-B, RNP, Smith, Scl-70, centromere, Ku, Ej, Oj, KU, EJ, OJ,

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PL-7, SRP (signal recognition particle), and anticardiolipin IgG.

Her symptoms were suspicious for erythromelalgia, a condition thought to involve both small-fiber neuropathy as well as vasculopathy, so she was initiated on pentoxifylline, 400 mg 3 times daily, and gabapentin, 300 mg nightly. Pentoxifylline was discontinued because of worsening symptoms, and she was unable to tolerate increased doses of gabapentin. Around this time, the patient discontinued oral contraceptive pills, and the frequency of her facial flushing decreased from daily to a cluster once monthly, a week prior to menses. During a flare, her progesterone level was 12.9 ng/mL, within the normal range for the luteal phase of the menstrual cycle. Although the burning character of her facial rash was clinically consistent with erythromelalgia, the cyclical flaring of the rash during the luteal phase of menses raised suspicion for autoimmune progesterone dermatitis. Between dermatology visits, under the guidance of her gynecologist, she underwent a total abdominal hysterectomy with bilateral salpingo-oophorectomy (TAH-BSO) for the indication of abnormal uterine bleeding as well as suspected APD. In the 13 months since her hysterectomy, she has had no flares of her painful facial rash and remains symptom free with only residual faint pink patches on the cheeks (Fig 1, B).

**DISCUSSION**

This is a case of burning erythema on the bilateral malar cheeks of a 48-year-old woman. The differential diagnosis of a malar rash is broad, including seborrheic dermatitis, rosacea, and acute cutaneous lupus erythematosus, none of which fit well with her presentation. The debilitating burning and erythema she experienced that was resistant to treatment and partially relieved with cooling was quite reminiscent of erythromelalgia. Although erythromelalgia usually presents on the hands and feet, it has rarely been reported on the face. However, her daily flares while taking progestin-containing OCPs and the subsequent change in frequency to align with monthly progesterone surges after discontinuation of exogenous progesterone raised suspicion for APD. Complete resolution after TAH-BSO confirmed the diagnosis of APD.

This is a unique clinical presentation of APD in terms of symptomatology and location. A recent review showed that most patients with APD present with cutaneous reactions that resemble a type I hypersensitivity reaction, whereas far fewer present with type IV hypersensitivity. Only 3 of 89 patients mentioned a burning and painful sensation associated with their rash, in stark contrast to our patient. Further supporting the rarity of these symptoms in APD, to the best of our knowledge, there have been
no case reports of APD that include erythromelalgia on the differential diagnosis. About 50% of patients with APD have localized lesions, as in our patient, yet only 5 cases report APD occurring on the face. A presentation of APD that mimics erythromelalgia of the face is extremely rare.

A variety of treatment options exist for APD that have met with varying degrees of success, including antihistamines, topical corticosteroids, systemic corticosteroids, conjugated estrogen/ethinyl estradiol, tamoxifen, GnRH, danazol, progesterone desensitization, and TAH-BSO. TAH-BSO, although certainly the most invasive, also appears to be the most effective. In a recent review, all cases in which TAH-BSO was done resulted in complete remission of symptoms. Our patient’s symptoms also completely resolved with TAH-BSO. A consultation with an obstetrician-gynecologist should be made to review treatment options that are in line with the patient’s wishes.

Although APD often presents as a type I hypersensitivity reaction, it has a wide variety of clinical morphologies and symptomatology that rarely includes intense erythema and burning mimicking erythromelalgia. Providers should consider a potential hormonal component to any rash occurring in a monthly cyclical pattern in a female of childbearing age. It is important to recall that OCPs affect progesterone surges and may dramatically alter the typical cyclical nature of APD. Lastly, this case supports that TAH-BSO can result in complete remission of symptoms, even when symptoms are severe and life altering.

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