Unilateral acneiform eruption in a patient with history of contralateral Horner syndrome

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Key words: acne vulgaris; acneiform eruption; acne; Horner syndrome; unilateral acne.

INTRODUCTION

Acne vulgaris is an inflammatory disease of the pilosebaceous unit with a multifactorial pathogenesis. It is characterized by seborrhea, papules, pustules, and comedones with underlying follicular hyperkeratinization, androgen-mediated sebaceous gland hyperactivity, bacterial colonization, and ongoing inflammation.[1] It is hypothesized that cutaneous neurogenic mediators could illicit acne eruption.[2] The facial skin of patients with acne contains substance-P rich nerve fibers surrounding the sebaceous gland and neutral endopeptidase attached to the sebaceous acini.[2]

Toyoda et al[2] have reported that patients with acne have an accentuated expression of neutral endopeptidase in the sebaceous acini compared with normal skin. A neural stimulus from the central or peripheral nervous system, such as stress, could trigger an acne eruption or exacerbate existing acne.[2-4] Seborrhea is an essential mediator of acne breakouts that has a complex mechanism and is regulated by a variety of neuroendocrine processes. One of these regulators is melanocyte-stimulating hormone, which is a melanocortin hormone that regulates pigmentary function and sebogenesis.[4] The sebaceous gland expresses neuroreceptors that regulate sebogenesis, such as β-endorphin, pro-opiomelanocortin, corticotrophin-releasing factor, and neuropeptide Y.[4] This complex interrelationship of neuroendocrine mechanisms of the sebaceous gland reflects the regulation of sebum production.[5] The complex neuroendocrine regulations of the sebaceous gland could explain the manifestation of a unilateral acneiform eruption in a 36-year-old woman with a history of contralateral Horner syndrome.

Abbreviation used:

EGF-RI: epidermal growth factor receptor inhibitor

CASE REPORT

A 36-year-old woman presented at the hospital with metastatic breast cancer to the bones, lungs, liver, peritoneum, ovaries, and leptomeninges. On her second day of hospital admission, she experienced a sudden unilateral eruption of multiple papules, pustules, and postinflammatory hyperpigmented macules on only the right side of her cheek and forehead (Figs 1 and 2). There were no comedones noted on examination. She reported no history of prolonged pressure on the affected side. The left cheek was clear of any acneiform eruption. Bilateral and symmetric mild hirsutism could be appreciated on her upper lip and chin. She reported a positive history of menstrual irregularities.

Her medical history was significant for Horner syndrome on the left side of the face (contralateral to eruption) with opthalmoparesis involving the sixth cranial nerve, which was diagnosed and managed in 2018 at another hospital. The metastatic breast cancer was positive for hormone receptor and human

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Table I. Hormonal workup

Test	Result	Normal
DHEAS	1.3 umol/L	2-11.1 umol/L
Prolactin	56.86 ng/mL	Premenopausal 7.1-47.3 ng/mL; Postmenopausal 4.5-30.5 ng/mL

DHEAS, Dihydroepiandrosterone sulfate.

epidermal growth factor receptor-2 (and was managed by a modified radical mastectomy). The chemotherapeutics prescribed were trastuzumab, pertuzumab, and vinorelbine, along with dexamethasone injections. Six months previous to the eruption, the patient was started on trastuzumab, pertuzumab, and vinorelbine, given every 3 weeks. Her last dose of anticancer treatment was 5 weeks before the eruption. Dexamethasone intravenous 8 mg was initiated one day before the eruption.

Neither any new medications were taken recently previous to the acneiform eruption, nor were there any changes in the doses of the prescribed drugs. Hormonal workup indicated a low level of dihydroepiandrosterone sulfate and a high level of prolactin (see Table I). The acneiform eruption on the right side of the face improved with the administration of topical clindamycin solution and 0.05% tretinoin cream.

DISCUSSION

Numerous medications, such as corticosteroids, epidermal growth factor receptor inhibitors (EGFRIs), and anabolic-androgenic drugs, can cause acneiform eruptions.[6] EGF-RIs typically induce acneiform eruptions 2 to 4 weeks after administration, with an estimated incidence of 60% to 100%.[7] It is characterized by pruritus and absence of comedones.[6] It is hypothesized that EGF-RIs induce acneiform eruption by alterations in cell growth and differentiation leading to follicular hyperkeratinization, follicular plugging with abnormal bacterial overgrowth, and manifestation of acne-like eruption.[6] In addition, monoclonal antibody inhibitors promote inflammation and neutrophil activation through binding to its Fc domain.[6] Nakahara et al[7] have reported that patients who develop EGF-RIs acneiform eruptions tend to show higher sebum levels than those who did not develop any acne-like lesions.

Kerob et al[8] have reported a unilateral cetuximab-induced acneiform eruption in facial palsy. The eruption affected the ipsilateral side of the facial palsy. They hypothesized that facial palsy reduces lymphatic drainage, causing lymphedema, which in turn promotes the deposition of cetuximab in the skin, resulting in more toxicity. In addition, Tagami et al[9] have also reported a steroid-induced unilateral acneiform eruption in the ipsilateral side of Bell's palsy. It was hypothesized that the lack of normal facial movement, which would promote constant outflow of sebum, was the causative factor behind the unilateral acneiform eruption.

Horner syndrome involves a disruption in the sympathetic innervation of the oculusympathetic pathway. It manifests as ptosis (drooping of the upper portion of the eyelid), constricted pupils, and anhidrosis. The diagnosis is based on clinical evaluation.[10] Nexmand[11] reported the first case of unilateral acne eruption with comedones and seborrhea, which manifested after surgical management of severe otitis in the mastoid area. The acneiform eruption appeared on the ipsilateral side of the face of a 13-year-old adolescent boy.

Another case report described an 18-year-old woman who developed unilateral acne after developing facial palsy.[12] The lesions manifested in the ipsilateral side of the face with paralysis for 2 weeks after facial palsy.[13] In a series of 42 patients with facial paralysis, 17% of the cases developed acne.[14] It is hypothesized that the cause of acne eruptions is an increase in sebogenesis on the affected side of the face of patients with facial palsy.[6]

In a series of 42 patients who underwent sympathectomy, their acne improved as the sebaceous glands were denervated from the neuroendocrine mechanisms that is responsible for sebogenesis.[3] Similarly, our patient was clear of acneiform eruption on the side affected by Horner syndrome. On clinical grounds, this hypothesis could explain the manifestation of unilateral acneiform eruptions on the right side of the face in this patient with contralateral history of Horner syndrome as the left side is denervated.

The exact etiology of the acneiform eruption in our case is still unclear. It can be a delayed reaction to her EGF-RIs treatment with trastuzumab and pertuzumab. Otsuka et al[13] reported acneiform eruption 24 months after beginning regorafenib treatment. Acneiform eruptions from dexamethasone or hormonal acne are also possible triggers. Horner syndrome appears to be protective against the development of the acneiform eruption in our case, possibly because of denervation in the epithelial melanocyte system and sebogenesis.[3]

The presentation of this patient is rare because unilateral acneiform eruption had previously manifested on the ipsilateral side of the face of patients

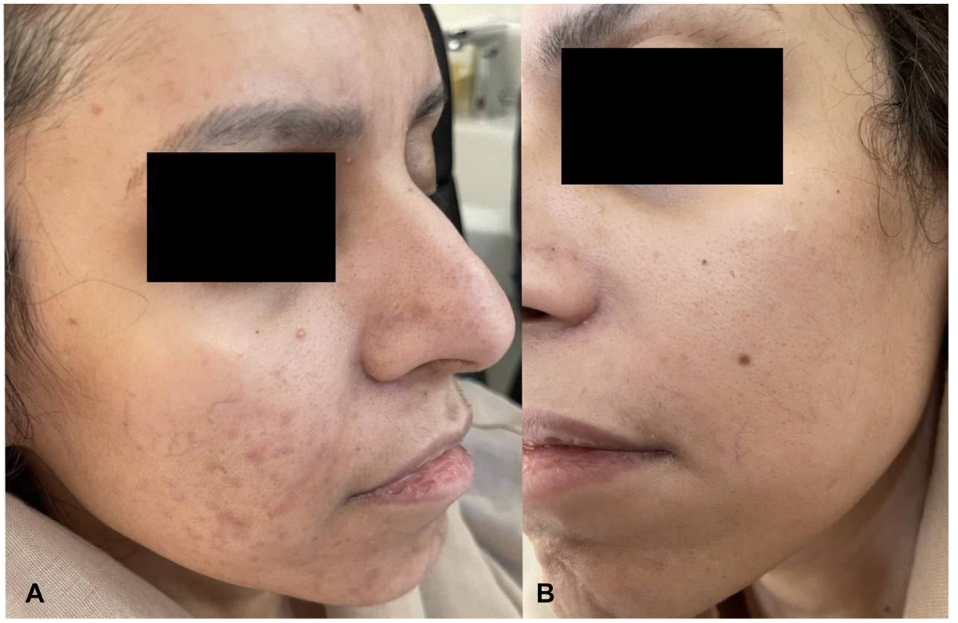

Fig 1. Unilateral acneiform eruption in a patient with history of contralateral Horner syndrome. (**A**) Multiple monomorphic erythmatous papules on right side of the cheek. (**B**) Unilateral acne vulgaris on only the right side of the face.

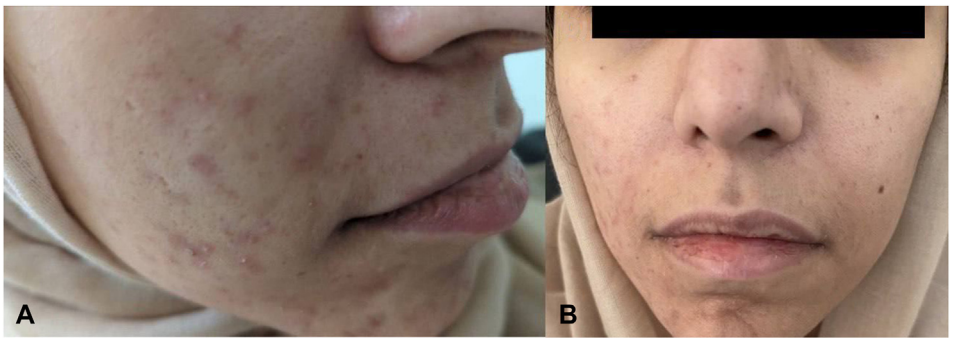

Fig 2. Acneiform eruption on right cheek treated topically with clindamycin solution and 0.05% tretinoin cream. (**A**) Erythematous papules on right side of the cheek and upper portion of the eyebrow. (**B**) Acne eruption sparing the left cheek possibly because of the history of Horner Syndrome.

with a history of facial paralysis,[11,12] whereas the patient in this case developed unilateral acneiform eruption on the contralateral side of the face to the Horner syndrome. Thus, sympathetic denervation could be a possible protective factor against acne.

Conflicts of interest

None disclosed.

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