Clinical report

The red face: Erysipelas versus, Parvovirus B19, SLE, and Rosacea

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Background: Several conditions can lead to the red face, including Erysipelas, Erythema infectiosum, Systemic Lupus Erythematosus, and Rosacea.

Objective: To describe a case of facial Erysipelas in a patient and discuss the differential comparison with parvovirus B19, Systemic Lupus Erythematosus, and Rosacea based mainly on the visual appearance of the rash and associated signs and symptoms.

Patient and method: A 50 years old female with a history of breast cancer in remission after lumpectomy and radiation therapy completed three years ago, developed fever to 102 F and painful warm red cheeks and periorbital edema.

Results: The patient improved after two days of intravenous penicillin G two million units four times a day; both redness and fever resolved.

Conclusion: Although erysipelas of the ipsilateral upper limb following breast cancer has been described, no reports have been found of facial erysipelas following breast cancer.

Keywords: Butterfly rash, erythema infectiosum, facial erysipelas, rosacea, SLE

Several conditions can lead to the red face, including Erysipelas, Erythema infectiosum, Systemic Lupus Erythematosus and Rosacea. Here, we describe a case of facial erysipelas in a patient with a past history of breast cancer, followed by a brief discussion of erysipelas and a differential comparison with the three other named conditions based mainly on the visual appearance of the rash and associated signs and symptoms. Although erysipelas of the ipsilateral upper limb following breast cancer has been described in the literature [1-3], an attempt to search for reports of facial erysipelas following breast cancer specifically was entirely unsuccessful.

Case report

A 50 years old female with a history of breast cancer in remission after lumpectomy and radiation therapy completed three years ago, developed fever to 102 F and painful warm red cheeks and periorbital edema (Fig. 1, 2). She was admitted and diagnosed with erysipelas. After two days of intravenous penicillin G 2 million units four times daily, the redness and fever resolved. She was discharged on oral Penicillin VK 500mg four times daily for two weeks. The erysipelas has not recurred after five years of follow up.
Discussion

Erysipelas

Erysipelas is a superficial form of cellulitis involving the upper dermis and characterized by diffuse spread via the cutaneous lymphatics. Group A beta hemolytic streptococcus (GABHS) is the most common causative pathogen, though other groups of beta-hemolytic streptococci (C and G), Staphylococcus aureus, Streptococcus pneumonia, Haemophilus influenza, and Yersinia enterolitica have also been isolated [4]. Although traditionally erysipelas is known to affect the elderly, immunocompromised, neonates and small children [5], Erysipelas was a major cause of mortality in prisoner-of-war and German concentrations camps during world war II and later in the Korean conflict. Recent studies, including one described by Edourd M. Gosshan [4, 6], indicates erysipelas to favor adults and predominantly females. Among predisposing factors are described a breach in the epithelial barrier resulting from local trauma, infection, inflammation, or lymphedema following surgical procedures (e.g. mastectomy or saphenous vein harvesting). In addition immuno-suppression secondary to HIV, cancer chemotherapy or radiotherapy, prolonged use of corticosteroids, diabetes, and alcohol abuse have all also been noted [5].

The rash in erysipelas presents as a rapidly spreading painful, shiny, bright red, well defined raised lesion, with a palpable border that is sharply demarcated from the surrounding uninvolved skin. Lymphedema surrounding the hair follicles gives it the characteristic “peau d’ orange” appearance [7]. With severe infection, vesicles, bullae, and areas of hemorrhagic necrosis are found. Although the most common areas affected are the lower extremities, when presenting on the face, erysipelas may be unilateral involving one cheek [8]. However, it classically spreads over the nasal bridge to the contralateral hemiface. Facial erysipelas may be asymmetric; it does not spare the nasolabial folds, can extend to the peri-orbital areas [9] and the pinna of the ear (Milian’s sign). However, the rash spares the scalp and areas below the collar line [10]. The onset is usually acute with associated fever, chills, and regional lymphadenopathy.

Erysipelas is a clinical diagnosis, and tests are performed only to substantiate an ambiguous case or diagnostic challenge. Blood culture, needle aspiration and punch biopsy are all unreliable yielding true positive results, in less than five to forty percent of all cases [9]. Serological testing includes elevated anti streptolysin (ASO) and anti-DNase titers. Microscopic examination of biopsied tissue shows diffuse dermal edema, occasionally extending into the subcutaneous fat with dilated capillaries and neutrophilic invasion of the lymphatics [5]. Although gram-positive bacteria may be demonstrated in the tissue, serological detection of the streptococcal antigen is a more reliable test.

Penicillin (penicillin G two million units every six hours, or penicillin VK 500 mg orally four times a day

Fig. 1 Patient with facial erysipelas.
for two weeks) has been the standard of care or alternatively, cephalosporins (ceftriaxone one gram intravenously every 24 hours) or erythromycin (erythromycin 250 mg orally every six hours) for documented cases of penicillin allergy.

**Parvovirus B19**

The characteristic “slapped cheek” presents as a distinctive bright red blotchy rash on the face of individuals suffering from Erythema infectiosum caused by Parvovirus B19. The infection which is more common in children between the ages of four to ten years old [11] is also known as “fifth disease”, since it was the fifth childhood exanthematous infection to be reported in the literature at the time. The initial rash appears usually after a short prodrome of low grade fever, headache, and nonspecific upper respiratory symptoms. It presents on the malar area of the face and is followed by circumoral pallor and a maculopapular, reticular, pruritic rash on the trunk and extremities. The rash tends to fade quickly, but can recur with exercise, sun exposure, or bathing. Such a presenting rash is pathognomonic of the illness in children, but is usually less prominent in adults. In the latter, it is more often characterized by acute, symmetrical polyarthritis of the hands and extremities [12-14]. When present in children, the arthropathy tends to involve the knees and ankles rather than the smaller joints. In a clinical study conducted by Anderson MJ et al. [15], healthy volunteers were intranasally inoculated with the virus and the clinical course was delineated by the consequent immunologic response. It was noted that prodromal symptoms corresponded with the initial phase of viremia, followed by the appearance of rash and arthralgias associated with the development of antiviral antibodies. Both the cutaneous rash and the arthropathy, associated with Parvovirus B19, have been assumed to be due to the respective deposition of immune complexes in the skin and joints [13].

Apart from fifth disease and arthropathy, human Parvovirus B19 is also responsible for causing transient aplastic anemia in patients with underlying hemolytic disorders, chronic anemia in immunocompromised patients, hydrops fetalis and congenital anemia in pregnant women, and a painful papular purpuric gloves and stockings syndrome in adults.

Erythema infectiosum is usually diagnosed by its characteristic rash. Elevated IgM antibodies are seen in almost all cases of fifth disease. Viral DNA detection is utilized in the diagnosis of red cell aplasia, and persistent cases where antibody production is minimal. Giant pronormoblasts can be seen on bone marrow biopsy sampling in patients with aplastic anemia caused by Parvo-virus B19.

Fifth disease is a self limiting illness requiring no treatment in the majority of cases. Anti-inflammatory medications can be implemented if arthropathy is prominent, while administration of intravenous immunoglobulin is reserved for persistent B19 infection causing anemia in the immunodeficient patients [16].

**Systemic lupus erythematosus**

Systemic Lupus Erythematosus (SLE) is a relatively common chronic inflammatory auto-immune connective tissue disorder with a higher predilection for young, Afro-American, women and it is infrequent in the elderly male Caucasian population. It is a common disease in southeast Asians. Although lupus can affect virtually any organ system, most patients with SLE have variegated skin abnormalities during their course of illness, the pathognomonic “butterfly” rash being the most commonly found. It is the presenting sign in about 25% of cases, and may not be followed by other signs of SLE for months to years [17, 18].

The malar rash is typically bilateral and symmetrical, extending from one malar prominence across the nasal bridge to the other side. The rash appears as minimally discernable subtle faint blush or more strikingly as a prominent red color. It is a clearly demarcated, slightly edematous, macular, lesion characterized by fine scaling, and telangiectasia. It often recurs with exposures to sunlight, Ultraviolet-B light, and stress (including infection, surgery, and pregnancy). The butterfly rash may last from a few hours to a few days; healing can occur without scarring (unlike the discoid rash), although there may be temporary post inflammatory hyper-pigmentation. Although some febrile acute cases of the lupus rashes may be difficult to distinguish from erysipelas, the facial rash of SLE tends to be bilateral and symmetric, and spares the nasolabial folds. In contrast, erysipelas presents as a peau d’ orange texture, involving the nasolabial folds and may be asymmetric.

Despite the fact that SLE is rarely curable, an accurate and timely diagnosis is imperative for the control of symptoms and amelioration of disease
progression. Laboratory testing includes complete blood counts, metabolic panel, and urinalysis as well as serological markers such as antinuclear antibodies, anti-double stranded-DNA, anti-Smith, and anti phospholipid antibodies. Diagnosis is ultimately formulated according to the eleven criteria established by the American College of Rheumatology (see Table 1). The presence of at least four criteria is required for a positive diagnosis. A skin biopsy specimen, demonstrating deposition of immune complexes at the dermal-epidermal junction of the skin (Lupus Band Test), is both sensitive and specific for the diagnosis of Lupus [18, 19]. Definite management depends on organ involvement, stage, and severity of the disease. Most “butterfly” rashes are addressed by avoidance of sun and UV light exposure as well as use of sunblocks. Oral prednisone is usually required to control associated systemic symptoms. Antimalarials (hydroxychloroquine, quinacrine, and chloroquine) may be used in refractory and more diffuse pathology.

Rosacea
Rosacea is a chronic relapsing acneiform disorder of the skin, commonly occurring in the middle aged and older population. It is diagnosed more commonly in females but tends to be more severe in males [20].

Rosacea has been clinically classified into four broad subtypes with further grading [21]: Erythematotelangiectatic (subtype 1), Papulopustular (subtype 2), Phymatous (subtype 3), and ocular (subtype 4). Of these four presentations, the erythematotelangiectatic subtype is the most common one and presents with flushing and persistent erythema of the central face without an inflammatory lesion. Facial flushing can be triggered by various factors including hot and spicy food, alcohol, emotional stress, certain medications, or menopause. There is also prominent telangiectasia of the cheeks and nose, and there may be complaints of associated stinging, itching and burning of the affected areas. The papulopustular subtype is characterized by small inflammatory papules and pustules on a background of persistent erythema, presenting in a Maltese cross distribution over the nose, forehead, cheeks and chin. The circumoral and periorbital areas are typically spared [22]. The phymatous subtype is characterized by thickened, cosmetically disfiguring skin due to the hypertrophy of sebaceous glands and connective tissue with associated lymphedema and prominent follicular pores [23]. Various parts of the face may be affected including the nose (rhinophyma), chin (gnathophyma), forehead (metophyma), ears (otophyma) and eyelids, of which rhinophyma is relatively more common. Ocular involvement occurs in greater than 50% of the patients with rosacea. Although the most common symptoms are dry eyes and chronic blepharoconjunctivitis [24], the spectrum of presentation can range from mild dryness of the eye to severe corneal involvement.

The specific etiology of rosacea is unknown; however, the follicular mite Demodex folliculorum is predominant in rosacea and has been postulated as a causative factor [25].

Table 1. The 1982 revised criteria for classification of Systemic Lupus Erythematosus. To meet the diagnostic criteria of Systemic Lupus Erythematosus, at least, four out of the 11 criteria must be presented simultaneously, or in succession.

<table>
<thead>
<tr>
<th>Criterion</th>
<th>Definition</th>
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<tbody>
<tr>
<td>1. Malar rash</td>
<td>Fixed erythema over the malar eminences tending to spare the nasolabial folds</td>
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<tr>
<td>2. Discoid rash</td>
<td>Erythematous raised patches with keratotic scarring, may scar</td>
</tr>
<tr>
<td>3. Photosensitivity</td>
<td>Skin rash as a result of unusual reaction to sunlight</td>
</tr>
<tr>
<td>4. Oral ulcers</td>
<td>Oral or nasopharyngeal ulcers, usually painless</td>
</tr>
<tr>
<td>5. Arthritis</td>
<td>Nonerosive, involving two or more peripheral joints</td>
</tr>
<tr>
<td>6. Serositis</td>
<td>Pleuritis or pericarditis</td>
</tr>
<tr>
<td>7. Renal disorder</td>
<td>Persistent proteinuria (&gt; 3+), or cellular casts</td>
</tr>
<tr>
<td>8. Neurologic disorder</td>
<td>Seizures or psychosis</td>
</tr>
<tr>
<td>9. Hematologic disorder</td>
<td>Hemolytic anemia, or Leukopenia, or Lymphopenia, or Thrombocytopenia</td>
</tr>
<tr>
<td>10. Immunologic disorder</td>
<td>Positive LE cell preparation, or Anti-DNA Ab, or Anti-Sm Ab, or False positive serological test for syphilis</td>
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Adapted from [32].
Rosacea is a clinical diagnosis with no reliable confirmatory laboratory test [20]. Its diagnosis is usually facilitated by the presence of symptoms such as facial flushing, erythema, burning, or stinging sensation, as well as a history of triggering factors. Treatment of rosacea is usually long term and focused on the presenting subtype. Ameliorating strategies involve the use of non-irritating skin cleansers and sun blocks. Individual appropriate trigger identification and avoidance may be beneficial in reducing flares. Interventions to induce remission of inflammatory papules, pustules, and erythema include Benzoyl peroxide 2.5%, topical metronidazole gel and ointments, and oral tetracyclines (tetracycline 250 mg-500 mg twice a day, doxycycline or minocycline 50-100 mg once a day) [26]. In addition, oral metronidazole (500 mg per day) alone has been successfully used by some physicians [23]. Moreover, topical azaleic acid too has been used with results comparable to the topical use of metronidazole [27]. Other agents such as isotretinoin which is more commonly used in the treatment of severe acne has been found to be also beneficial in treating telangietasias and persistent papules, [28] whereas Clonidine and, beta blockers (nadolol and propranolol) have been used to abate flushing associated with rosacea, but with debatable results [29, 30]. Finally, other approaches involve Intense Pulsed Light (IPL) or other lasers for refractory erythema [31] and surgical correction may be limited to rhinophyma involvement.

In conclusion, to summarize the above discussion, the salient features of these four common conditions that may present with a red face rash are outlined in Table 2.

### Table 2: The red face.

<table>
<thead>
<tr>
<th>Facial Erysipelas</th>
<th>Malar rash of SLE</th>
<th>Rosacea</th>
<th>Erythema infectiosum</th>
</tr>
</thead>
<tbody>
<tr>
<td>Acute Bacterial infection involving the upper dermis and superficial lymphatics of the skin.</td>
<td>Chronic inflammatory multi-systemic, immunologic disease.</td>
<td>Chronic acneiform disorder characterized by vascular dilatation of the facial vessels</td>
<td>Common benign childhood exanthematous illness.</td>
</tr>
<tr>
<td>Epidemiology</td>
<td>More commonly affects young children and the elderly with a slight female predominance. Recent trends show increasing incidence in adults</td>
<td>Young and middle aged women are most commonly affected</td>
<td>Middle age and older fair skinned adults. Commoner in females but more severe in males</td>
</tr>
<tr>
<td>Morphology of the rash</td>
<td>Presents as a painful, shiny, bright red, well-defined, indurated, and raised lesion that are sharply demarcated from the surrounding uninvolved skin. Cutaneous edema surrounding the hair follicles may give a ‘Peau’d’ orange’ dimpled appearance. Serious cases may present with bullate formation and severe necrosis.</td>
<td>Presents as an erythematous, slightly edematous semi-confluent, macular rash with telangectasia, and fine scaling. The photo sensitive rash lasts for a few days before healing. It typically leaves no scarring, but often recurs. Unlike rosacea it lacks pustules.</td>
<td>Frequent flushing progressing to persistent erythema with inflammatory acneiform papules and pustules. Comedones are absent. Fixed telangectasia is a constant feature, and there may be some associated stinging and burning of the affected areas.</td>
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</table>
Table 2. The red face (continued).

<table>
<thead>
<tr>
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</tr>
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<tbody>
<tr>
<td><strong>Anatomical distribution</strong></td>
<td>Central face. May be unilateral initially, but rapidly spreads to involve the butterfly area of the face. It may involve the nasolabial folds, and spread to the ears (Milian’s ear sign), and peri-orbital regions.</td>
<td>Classic malar rash that extends over the cheeks bridging the nose in a butterfly configuration. It classically spares the nasolabial folds and peri-orbital areas.</td>
<td>Central face, in a Maltese cross distribution involving the nose, forehead, cheeks, and chin. The circum-oral, and periorbital areas are typically spared.</td>
</tr>
<tr>
<td><strong>Pre-disposing Factors</strong></td>
<td>Breaches in the skin barrier due to local trauma, infection and superficial abrasions, diabetes, prolonged corticosteroid therapy, immunosuppression, radiation, and cancer chemotherapy.</td>
<td>Onset or relapse may be precipitated by exposure to sunlight or UV-B light, stress, surgery, or pregnancy.</td>
<td>The facial flushing may be induced by many things including sunlight, alcohol, hot and spicy foods, emotions, and some medications.</td>
</tr>
<tr>
<td><strong>Associated symptoms</strong></td>
<td>Fever and chills, Regional lymphadenopathy.</td>
<td>Low grade fever, malaise, weight changes, arthritis, and other symptoms due to pulmonary, renal, cardiac, hematological, neurological, or ocular involvement.</td>
<td>Ocular involvement including blepharoconjunctivitis occurs in &gt;50% of the patients</td>
</tr>
<tr>
<td><strong>Microbiology/Etiology</strong></td>
<td>Primarily Beta hemolytic streptococcus-Gr A Occasionally other groups of beta hemolytic streptococi, Staph aureus including MRSA, Strept pneumonia, H Influenzae, and Y enterocolitica.</td>
<td>Exact cause is unknown. Hereditary, environmental, and hormonal factors may play a contributory role.</td>
<td>Exact cause is unknown. An abnormal vascular response to heat and other stimuli has been implicated. The hair follicular mites-Demodex folliculorum is increased in rosacea and has been proposed as a causative theory.</td>
</tr>
<tr>
<td><strong>Diagnosis</strong></td>
<td>Based mainly on clinical manifestations, cultures of blood, needle aspirate and biopsy yield varying results, Rising ASO, and DNase titers. Direct detection of streptococcal antigen, Biopsy showing diffuse dermal edema with dilated capillaries, and neutrophil filled lymphatics with bacteria.</td>
<td>Evaluation of other systemic signs. ANA, anti ds-DNA, anti Smith antibodies, Skin biopsy with immunofluorescence shows immunoglobulin deposits along the dermo-epidermal junction.</td>
<td>Based mainly on clinical findings.</td>
</tr>
</tbody>
</table>
The authors have no conflict of interest to report.

References

20. Wilkin J, Dahl M, Detmar M, Feinstein A, Odom R,