

(RESEARCH ARTICLE)



## Papulopustular dermatoses of the face, clinicopathological spectrum and response to treatment

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### Abstract

The papulopustular rash on face may be a feature of several inflammatory skin disorders. Clinical features may provide clue to the etiology whereas microbiological testing and histopathologic examination confirm the diagnosis. In adults, facial papulopustular dermatoses include rosacea, perioral dermatitis, eosinophilic folliculitis, infections and medication induced. Our aim was to study variable causes of papulopustular lesions of the face. We conducted a prospective study which included 60 dermatology outpatient clinic patients of variable age groups whom presented with papulopustular lesions involving the face and review their clinicopathological findings as well as their response to therapy.

Several diseases were reported including rosacea (47%), demodicosis (20%), bacterial folliculitis (13%), drug induced (7%) and periorificial dermatitis (3%). One case of tinea barbae, pityriosisporum folliculitis, eosinophilic folliculitis, lupus miliaris disseminatus faciei, Behcet's disease and perforating folliculitis were reported.

In conclusions; Papulopustular dermatoses involving the face are an important problem among dermatology patients with an overlapping in signs and symptoms. Awareness of various causes and their clinicopathological features is important for accurate diagnosis and proper management.

**Keywords:** folliculitis; acneiform; rosacea; demodicosis; drug-induced; face

### 1. Introduction

Papulopustular dermatosis is defined as a disorder characterized by presence of erythematous, follicle-based papules and pustules that may coalesce, with an absence of comedones. The differential diagnosis of papulopustular dermatosis is broad. In most cases, the diagnosis is clinical, based on morphology, distribution and duration of the lesions. Age of the patient and the associated complaints and comorbidity may give additional clue. If there is suspicion about the diagnosis, specific pathological features can confirm the diagnosis (1,2). In adults, a diversity of disorders may cause facial papulopustular lesions, these include rosacea, periorificial dermatitis, drug induced, eosinophilic folliculitis and lupus miliaris disseminatus faciei. Bacterial, parasitic and fungal folliculitis represent the main causes of infectious folliculitis (2,3).

#### Objectives

Our aim was to identify variable causes of papulopustular facial rash among patients attending dermatology outpatient clinic in jumhoria hospital-Benghazi/ Libya, and to review their clinicopathological findings as well as their response to therapy.

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## 2. Materials and methods

This prospective study was done in dermatology department outpatient clinic at Jumhoria hospital. Over 3 years, 60 patients with follicle-based papulopustular lesions over the face of variable age groups were included in this study. Acne vulgaris patients with comedons were excluded. A history was elicited including the onset, symptoms, progression, medication history, environmental factor and associated systemic illness. Detailed examination of the face as well as general examination of the skin, hair and nails was done. Gram stain, KOH preparation were done in selected cases. Skin biopsy was done to all cases whom clinicopathologic review were needed to confirm the diagnosis. Description of appropriate treatment was done with response recording over 3 months.

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## 3. Results

Sixty patients with papulopustular facial lesions were included in this study, age ranged from 14-76 year. Majority was adults (82%), elderly constitute 16% and one case was child of 14 years old. Females' predominance was seen (83%).

Skin biopsy was needed to confirm the diagnosis in 40%, Gram stain and culture in 13%, KOH in 2% whereas clinical diagnosis was definite in 45%.

Several diseases were reported including rosacea (47%), demodicosis (20%), bacterial folliculitis (13%), drug induced (7%) and periorificial dermatitis (3%). One case of tinea barbae, pityriusporum folliculitis, eosinophilic folliculitis, lupus miliaris disseminatus faciei, Behcet's disease and perforating folliculitis were reported. (Figure 1)

Majority of rosacea patients were adult females (80%). Rosacea is mostly diagnosed clinically (71%) and only in 29% diagnosis was confirmed by histopathology (figure 2a-b). Complete clearance of papulopustular lesions was seen in 89% after a course of tetracycline and topical metronidazole for 3 months.

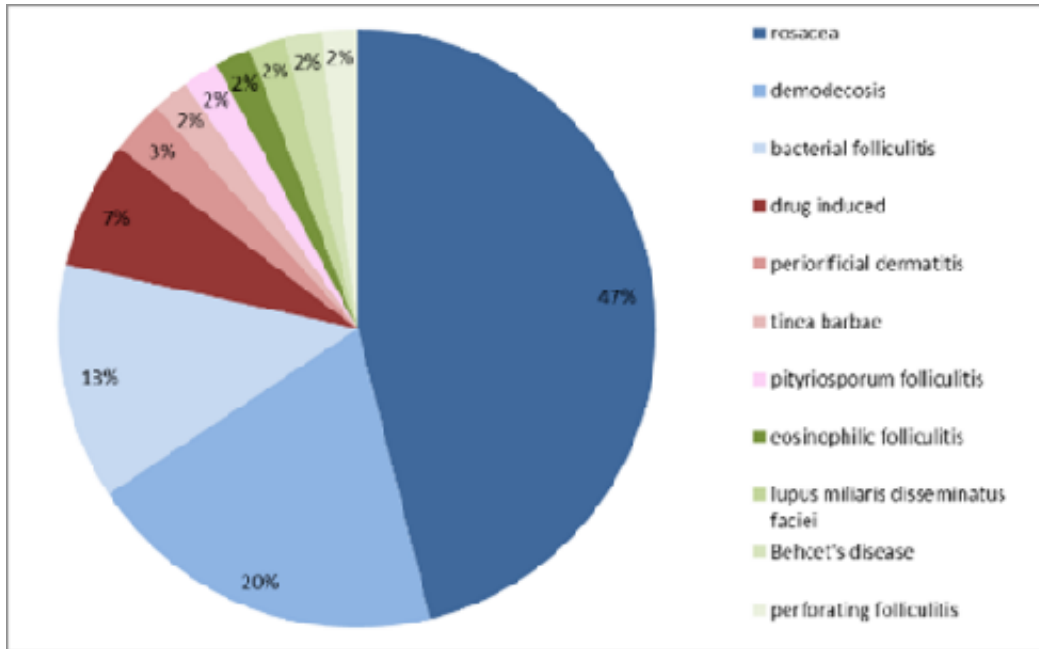
Two third (62%) of primary demodicosis was reported in females. Diagnoses were confirmed by histopathological examination in all patients. (figure 3) Adults constituted 78% and only one patient was child of 14 years old. The response to systemic metronidazole was observed in 69% (figure 4), while the response in 29% was achieved after adding topical ectomethrine cream (figure 5).

Bacterial folliculitis was due to staph aureus in 85% and gram negative bacteria in 2 cases (figure 6), all were responded well to oral antibiotics.

Pityriusporum folliculitis (figure 7) was improved with clotrimazole cream whereas tinea barbae (figure 8) was treated successfully with systemic antifungal.

Three cases of steroid acneiform eruption were reported (figure 9), all were female; one was associated with skin thinning, telangiectasia and secondary demodicosis and all were treated successfully with doxycycline and metronidazole (figure 10a-b). One case of acneiform eruption following erbitux; an EGFR inhibitor was reported (figure 11), the patient showed improvement with topical clindamycin lotion.

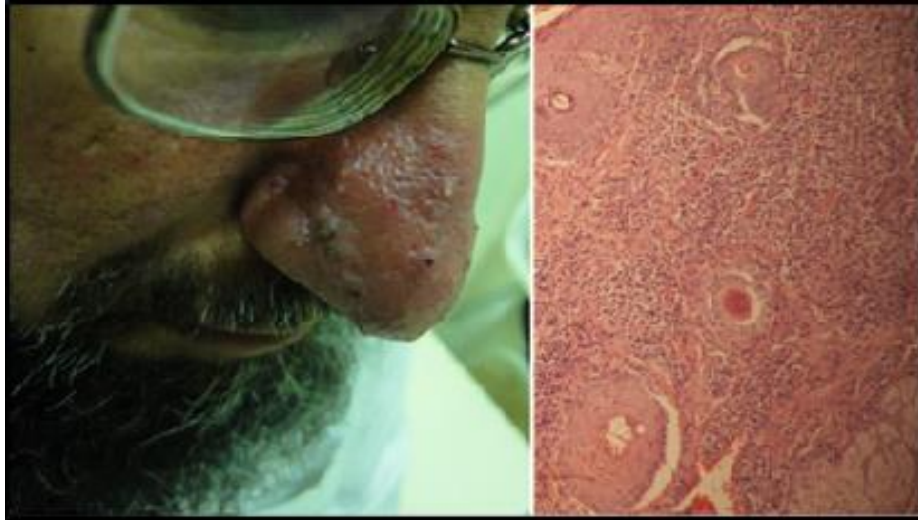
Eosinophilic folliculitis (figure 12) and lupus miliaris disseminatus faciei (figure 13) had dramatic response to systemic steroid. Perforating folliculitis (figure 14a-b) and the associated pruritus had initially responded to gabapentin and the patient with Behcet's disease (figure 15) was started prednisolone, unfortunately both of them had been lost to follow-up.



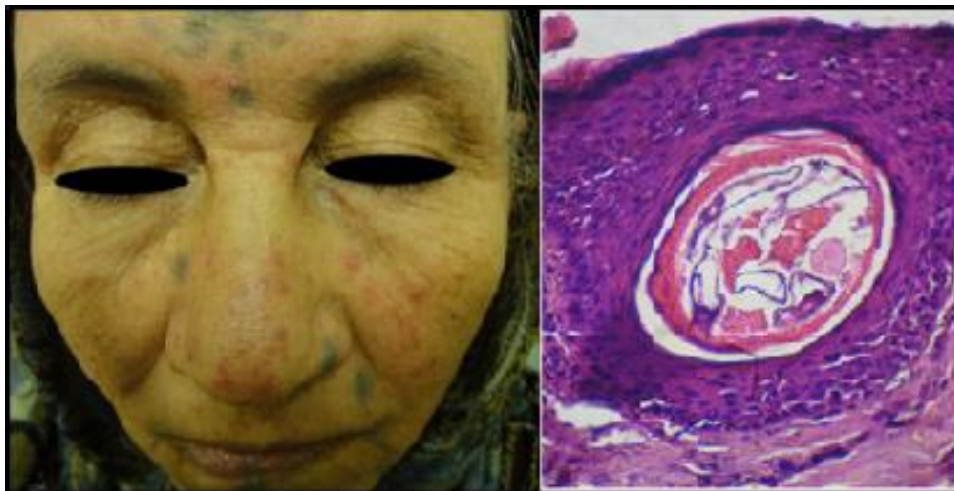
**Figure 1** Frequency of reported papulopustular dermatoses affecting the face



**Figure 2a** Clinically diagnosed papulopustular rosacea with rhinophyma



**Figure 2b** Rosacea histopathology shows perivascular and perifollicular lymphohistiocytic infiltration



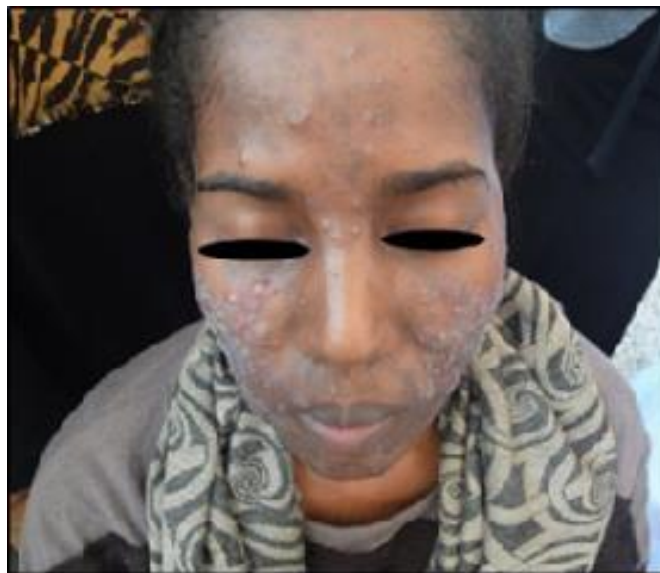
**Figure 3** Demodecosis in elderly female with mite density > 5 mites/follicle



**Figure 4** Demodecosis in 14 years old female before and after 2 weeks treatment with systemic metronidazole



**Figure 5** Demodex with blepharitis treated successfully with metronidazole and ectomethrin



**Figure 6** Gram negative bacterial folliculitis



**Figure 7** Pityrosporum folliculitis



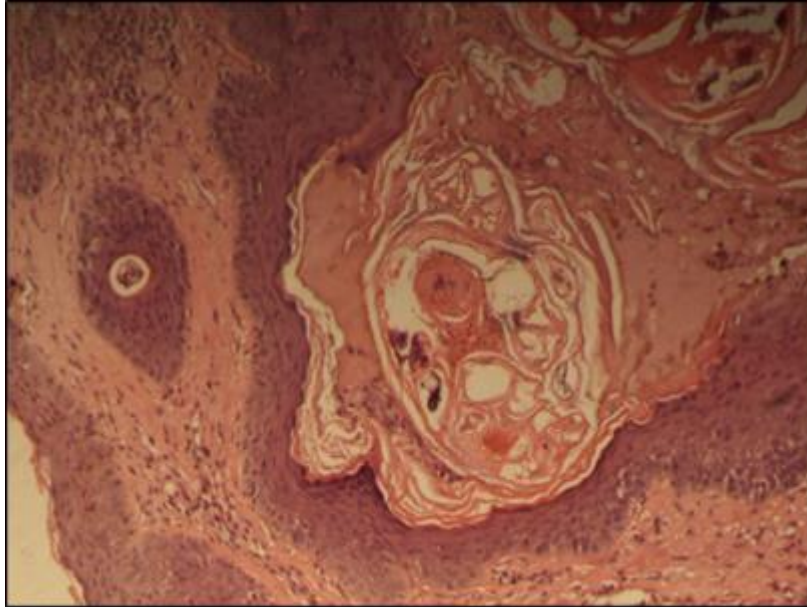
**Figure 8** Tinea barbae



**Figure 9** Steroid induced monomorphic papulopustular lesions without comedones



**Figure 10a** Chronic use of steroid with skin thinning, telangiectasia, papulopustular lesions, periorificial dermatitis and secondary demodexis, successfully treated with metronidazole and doxycycline



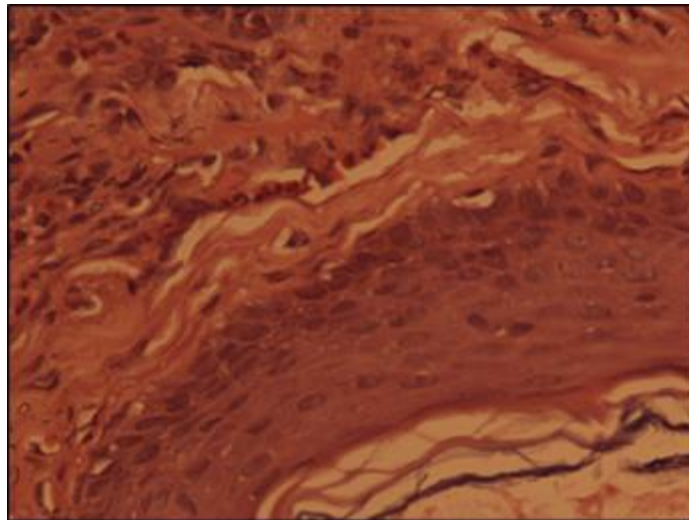
**Figure 10b** Secondary demodexosis after chronic use of topical steroid



**Figure 11** Acneiform eruption following erbitux; an EGFR inhibitor



**Figure 12a** Eosinophilic folliculitis with dramatic response to systemic steroid

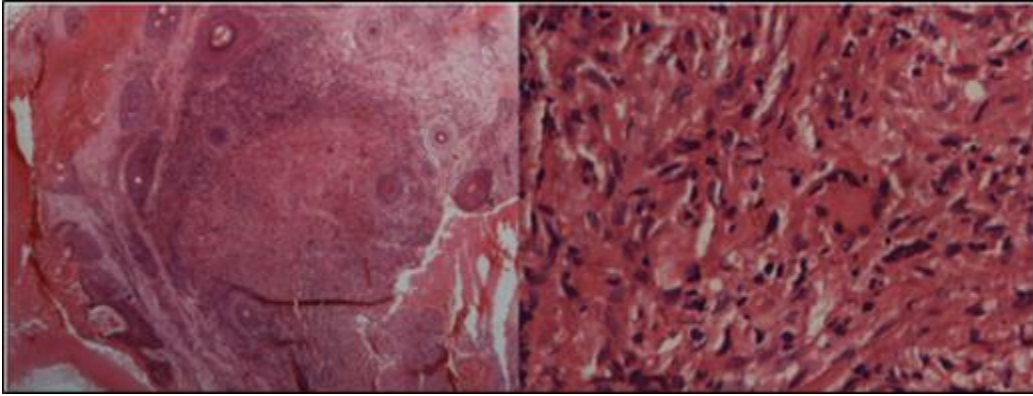


**Figure 12b** Perivascular and perifollicular inflammatory infiltrate composed of eosinophils, lymphocytes and macrophages



**Figure 13a** Lupus miliaris disseminatus facie before and after 1 month of 30 mg prednisolone

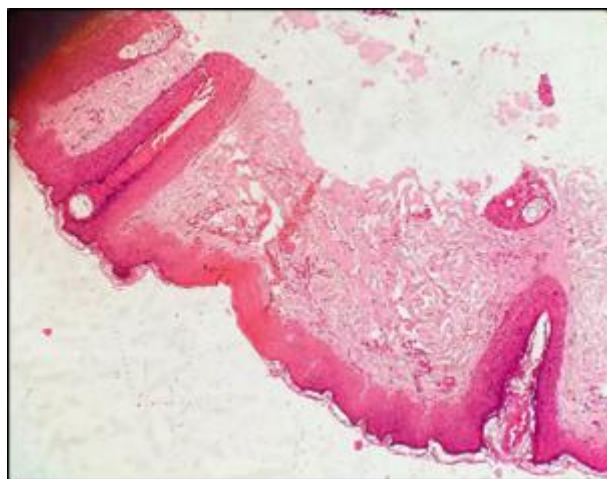




**Figure 13b** Lupus miliaris disseminatus facie pathology; epithelioid cell granulomas with central areas of necrosis and lymphohistiocytic infiltrate with Langhans multinucleate giant cells



**Figure 14a** Perforating folliculitis in uremic patient on haemodialysis



**Figure 14b** Perforating folliculitis histopathology



**Figure 15** Behcet's disease with mouth ulcer and papulopustular lesions on the face

#### 4. Discussions

Facial papulopustular skin disorders are encompassing several differential diagnoses. The site and distribution of the lesions and the associated symptoms and signs like pain, itching and redness as well as the age of the patient may provide strong clues to the etiology. However, due to presence of clinical overlapping, evidence for correct diagnosis may be lacking without infections screening and histopathologic examination (2,3). In this study variable inflammatory skin diseases presented with papulopustular lesions in the face, clinical diagnosis was definite in 45 %, whereas skin biopsy was needed to confirm the diagnosis in 40%, Gram stain and bacterial culture in 13% and KOH in 2%.

Rosacea is a common chronic inflammatory disease with a variety of clinical manifestations, in our study rosacea constituted nearly half of papulopustular dermatoses (47%). It usually develops in middle age and presents with facial flushing, erythema, telangiectasias, papules and pustules over convexities of the face. In addition, there may be rhinophyma and ocular involvement. Majority of our cases were middle age females and all were having papulopustular rosacea. Rosacea is diagnosed clinically, depending on the patient's history, clinical examination and exclusion of other diseases. Perivascular and perifollicular lymphohistiocytic infiltration are common pathological findings with infrequent multinucleated cells, plasma cell, and eosinophils. There may be granuloma and perifollicular abscesses. Rosacea is diagnosed clinically in 71% and only in 29% the diagnosis was confirmed by histopathology (4). Avoidance of precipitating factors as hot temperatures, wind, hot drinks, spicy food and alcohol is important. Topical metronidazole is commonly used as a first-line treatment. Topical ivermectin has been approved for treatment of the inflammatory lesions of rosacea. Oral and topical of 20-50 mg q12h of doxycycline is as effective as the therapy with 100 mg of doxycycline (5,6). Complete clearance of papulopustular rosacea was observed in 89% after treatment with a combined tetracyclines and topical metronidazole.

Demodicosis is a skin disease caused by ectoparasitic mites infestation called *demodex folliculorum* and *demodex brevis* which are normal commensals of the human pilosebaceous units especially in adults and elderly. It presents mainly in forehead, cheeks, eyelashes, nasal sides and outside the ear. The presence of the mite is often asymptomatic, it becomes symptomatic when the follicular mite proliferates, its density is greatly increased or when these mites enter the dermis. It causes both dermatological and ophthalmological problems, it may present with itchy papulopustular and nodular lesions and blepharitis (7,8). Demodicosis tends to occur in people with immunodeficiency and chronic renal failure. Although *demodex* infestation is considered much more common in the elderly due to decreased immune status, Vargas-Arzola et al found highest incidence in adults (9), consistent with our finding.

Demodicosis may be primary or secondary. Primary demodicosis occurs in the absence of previous skin disease; however secondary demodicosis occurs in association with other skin disease as rosacea, seborrheic dermatitis, perioral dermatitis and steroid dermatitis. Skin biopsy or skin scraping with potassium hydroxide (KOH) examination confirms demodicosis if mite density > 5 mites/follicle or 5 mites/cm<sup>2</sup> (10). In addition the response to treatment with acaricidal drugs including metronidazole, permethrin, ivermectin or benzyl benzoate can help to establish demodicosis diagnosis. Nearly a quarter (22%) of the papulopustular lesions was due to primary demodicosis. It is believed that children under 16 are relatively rarely infected by *demodex* mite (9), however we report a 14 years old female presented with *demodex* folliculitis.

All patients were diagnosed based on histopathological evidence, the observed dramatic response to acaricidal drugs was helpful in confirming the diagnosis.

Infections are common cause of folliculitis, including bacterial, fungal, and parasitic infections. Other causes include friction, occlusion, and drug induced (2).

Bacterial folliculitis may occur anywhere on the body, including the face.

Superficial folliculitis presents with small papules and pustules whereas in deeper lesions erythematous nodules are seen. Folliculitis occurs usually in nasal carriers of *Staphylococcus aureus* (2,11).

Gram-negative folliculitis occurs due to long-term antibiotic therapy, as in patients treated for acne. The causative gram-negative organisms include *Escherichia*, *Klebsiella*, *Enterobacter*, *Serratia* and *Proteus* species. Nearly 4% of acne patients may develop gram-negative folliculitis after treatment with systemic antibiotics. Isotretinoin is the most effective treatment for gram-negative folliculitis (12).

*Tinea barbae* is a type of folliculitis caused by zoophilic dermatophytes infection, mostly seen in male farmers, typically affects face in the submaxillary skin and chin, it is treated by oral antifungal as terbinafine and itraconazole (2).

*Pseudofolliculitis barbae*, occurs in the bearded area of African American males with coarse, curly hair. It is a perifolliculitis and it occurs due to reentering of the hair in to the skin nearby to its existence site causing inflammation. Chronic foreign body granulomatous may cause scarring. *S aureus* is the most common pathogen and dicloxacillin or cephalosporin is the first choices of treatment (14).

*Pityrosporum folliculitis* is caused by an infection by the lipophilic yeast *Malassezia furfur*, typically it is seen in young adults as intensively pruritic small uniform papules and pustules on the face, back, chest, and shoulders. It occurs usually in hot, humid climates and it is more frequent with long-term antibiotics and in immunocompromised patients. Although many patients improve with topical azole creams, oral antifungals are the most effective agents (15).

The use of medications may cause folliculitis, these include steroids, testosterone, contraceptive pills, lithium, antiepileptics, isoniazid, rifampicin and epidermal growth factor receptor inhibitors (2).

Excessive prolonged use of fluorinated topical steroids may cause papulopustular rash with swollen red skin. In addition this could result from rebound phenomenon after discontinuation of topical corticosteroids. Three females with steroid induced papulopustular lesions were reported, histopathology showed secondary demodicosis in one patient. The management includes pimecrolimus and oral doxycycline as well as slow discontinuation of the topical steroids and (16). It was effective in all the patients.

Papulopustular drug eruption after starting epidermal growth factor receptor (EGFR) inhibitors is a relatively new type presents with follicular eruption on the face, chest, and upper back which appear 2 weeks after initiation of chemotherapy. This acneiform rash is reported as the commonest side effect of EGFR inhibitors, and it occurs in about 50-100% of the patients. It can lead to a stoppage of the EGFR inhibitors therapy. The treatment options includes topical hydrocortisone, clindamycin, pimecrolimus and doxycycline (17). We report one case whom develop papulopustular lesions on the face after starting erbitux, a type of EGFR inhibitor, for metastatic colorectal cancer who showed improvement with topical clindamycin lotion.

Eosinophilic pustular folliculitis presents with follicular papules or pustules due to a noninfectious eosinophilic infiltration of hair follicles. There are 3 variants of eosinophilic folliculitis; the classical type which occurs most commonly in Japan, HIV-associated type, and the infantile type present on the palms and soles. Rarely, it may be related to drugs or neoplasm. Recurrent itchy crops of sterile pustules and papules involving the face in 85% of affected patients. Other locations include the back, chest and the extensor surface of the upper extremities. Histopathological examination is usually necessary for diagnosis; follicular eosinophilic spongiosis and pustulosis with perivascular, and perifollicular inflammatory infiltrate composed of eosinophils, lymphocytes and macrophages. A wide range of medications has been used; topical corticosteroids are the first-line treatment option. Other options include oral corticosteroids, synthetic retinoids, phototherapy with UVB and topical tacrolimus (2,18). In this study, we report eosinophilic folliculitis in one patient who showed dramatic response to systemic steroid.

Lupus miliaris disseminatus facie is uncommon granulomatous disease of unknown etiology. Recently, it is called facial idiopathic granulomas with regressive evolution.

It presents mostly in young adults as asymptomatic small discrete skin-colored, red brown papules and pustules in the face, predominantly on and around the eyelids which healed spontaneously after 1 to 2 years leaving pitted scar. Extra facial involvement is rare (19). Typical histology show dermal epithelioid cell granulomas with central areas of necrosis, and surrounding moderate lymphohistiocytic infiltrate with Langhans multinucleate giant cells. Tetracyclines are the usual first-line treatment, but they are not consistently effective. other effective systemic treatments include corticosteroids, isotretinoin and dapsone (20). we report a young man having lupus miliaris disseminatus facie who showed dramatic response to systemic steroid.

Periorificial dermatitis is papulopustular facial rash which occurs primary in perioral, nasolabial fold and lower eye fold concomitant with a burning sensation. It occurs mainly in females and children. The exact cause of the perioral dermatitis is unknown, it could be caused by chronic application of topical steroids, fluorinated toothpaste or skin care products. Heating, sun as well as hormones may have a role. The diagnosis is made clinically. Histopathologic findings are similar to rosacea. The use of cosmetics, cleansers and moisturizers should be avoided during treatment. Topical and systemic anti-inflammatory treatment like that used for rosacea is required (21).

According to International Study Group Criteria, one of the five diagnostic criteria for Behcet's disease is cutaneous, including pseudofolliculitis, acneiform nodules or papulopustular lesions in adult patients. These are mainly present on the trunk and extremities, but face involvement is rare. Histopathology show perifollicular and perivascular mononuclear, or neutrophilic infiltrations with or without neutrophilic vasculitis (22). IFN- $\alpha$ , etanercept and dapsone may decrease Behcet's pustulosis frequency (23).

Perforating folliculitis may be associated with chronic renal failure and diabetes mellitus.

It presents with multiple keratotic follicular papules on the extremities and buttocks. Histopathology show disruption of the infundibulum, with transfollicular elimination of connective-tissue elements and cellular debris, with degeneration of adjacent dermal connective tissue. Treatment options include topical retinoid, steroid and deoxycycline (24).

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## 5. Conclusion

Papulopustular dermatoses affecting the face are an important problem among dermatology patients. Overlapping in clinical picture and symptoms may cause a difficulty in clinical diagnosis and requiring microbiological and pathological study. They are ranging from common diseases, such as rosacea to rare diseases such as eosinophilic pustular folliculitis. Infections including bacterial, fungal folliculitis as well as demodex were a significant cause and it should be considered in the differential diagnosis of any papulopustular facial dermatosis. As lesions on the face have both psychological and physical impacts, recognition of potential causes and their clinicopathological features is essential for accurate diagnosis and successful management.

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## Compliance with ethical standards

### *Acknowledgments*

I would like to express my sincere gratitude to all the patients and laboratories that have contributed to the research paper.

### *Statement of ethical approval*

Approval from the hospital ethics committee was obtained.

### *Statement of informed consent*

An informed consent was obtained from all patients regarding inclusion in the study and publication.

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