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# Histopathologic Evaluation of Acneiform Eruptions: Practical Algorithmic Proposal for Acne Lesions

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Murat Alper and Fatma Aksoy Khurami

Additional information is available at the end of the chapter

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## Abstract

Acneiform lesions are encountered in different chapters in various dermatology and dermatopathology textbooks. The most common titles used for these disorders are diseases of the hair, diseases of cutaneous appendages, folliculitis, acne, and inflammatory lesions of dermis and epidermis. In this chapter, first of all we will discuss folliculitis, and then acne vulgaris that is a kind of folliculitis will be described. After acne vulgaris, other acneiform eruptions and demodicosis will be studied. At the end, simple algorithmic schemes by assembling clinical, pathological, and microbiological data will be shared.

**Keywords:** acneiform lesions, algorithm, histopathologic evaluation

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## 1. Introduction

### 1.1. Histology of pilar unit

Pilar unit is a structure generally made up of three subunits which are hair follicle, sebaceous gland, and arrector pili muscle. Hair follicle is divided into three parts: infundibulum, isthmus, and inferior part. Infundibulum extends between entrance of sebaceous gland duct to the follicular orifice in epidermis. Isthmus: extends between entrance of sebaceous duct to hair follicle and insertion of arrector pili muscle. The basal part of hair follicle is called the inferior segment or inferior part. Histologic structure and function of hair follicle is very intriguing. *Demodex folliculorum* mites, *Staphylococcus epidermis*, and yeast of *pityrosporum* can be seen and can be a normal component of pilosebaceous unit.

The life cycle of hair follicle is divided into three phases: anagen (growth phase), catagen (regressing phase), and telogen (resting phase). The sebaceous gland attached to hair follicle produces holocrine-type secretions. They excrete the sebum through excretory ducts into hair

follicle [1]. Sebum that inhibits the reproduction of bacteria and fungi is rich in triglyceride. When the increased number of *Propionibacterium acnes* is present, triglyceride is hydrolyzed and the biochemical conditions are altered [2].

## 1.2. Routine clinical and pathological conditions

There are bazillion hair and pilosebaceous units on the body surface. As a matter of course, hair follicle-related pathologies (especially inflammatory diseases) comprise one of the most popular topics in dermatology clinics.

In a big pathology center where daily around 40 cases of skin materials and annually a total of 35,000–40,000 different biopsy materials are examined, we rarely do histopathologic examination of disorders in inflammatory pilosebaceous units. It is mainly because the clinicians diagnose clinically and do not need much tissue correlation with their differential diagnosis in these disorders.

We retrospectively searched the information system of our hospital for the last 3 years and found 154 reports in which the term “acne” was aforementioned (132 cases were categorized as acne rosacea). For the last 3 years, approximately 23,000 skin samples have been sent by dermatology or plastic and reconstructive surgery departments (punch biopsies, shave biopsies, incisional biopsies, excisional biopsies included). Although general approach do not persuade for biopsy, sometimes in our clinic there is a little tendency to biopsying central face lesions for differential diagnosis.

## 2. Histopathology of acneiform lesions

### 2.1. Folliculitis, subtypes, differential diagnosis

In follicular eruptions adnexocentric inflammation, microabscesses and pustules on epidermis can be seen [3]. Peri- and intrafollicular inflammatory cells consist: lymphocytes, plasmocytes, histiocytes, polymorphonuclear, leukocytes, and multinuclear giant cells. Most folliculitis emerges as a result of follicular orifice occlusion by normal flora of the skin.

Although different categorization can be found in various textbooks, folliculitis can be divided into two groups: infectious and noninfectious (sterile). Furthermore noninfectious folliculitis can be grouped as neutrophilic, eosinophilic, etc. according to the predominant cell component present in the lesion. Infectious folliculitis can be grouped as bacterial (Gram-negative, Gram-positive), fungal, viral, and symbiotic (demodex) folliculitis [4].

The most common cause of Gram-positive folliculitis is *Staphylococcus aureus*. Similarly, *Enterobacter*, *Klebsiella*, *Escherichia*, *Serratia*, *Proteus*, etc., can cause Gram-negative folliculitis. Gram-negative folliculitis is generally caused in consequence of long-term antibiotic treatment. Hot tub folliculitis is a special form of bacterial folliculitis, which arises 24–48 hours after hot water contact and is caused by *Pseudomonas aeruginosa*. The most common cause of viral folliculitis is herpes simplex virus, varicella zoster virus, and the most common cause of fungal folliculitis is pityrosporum.

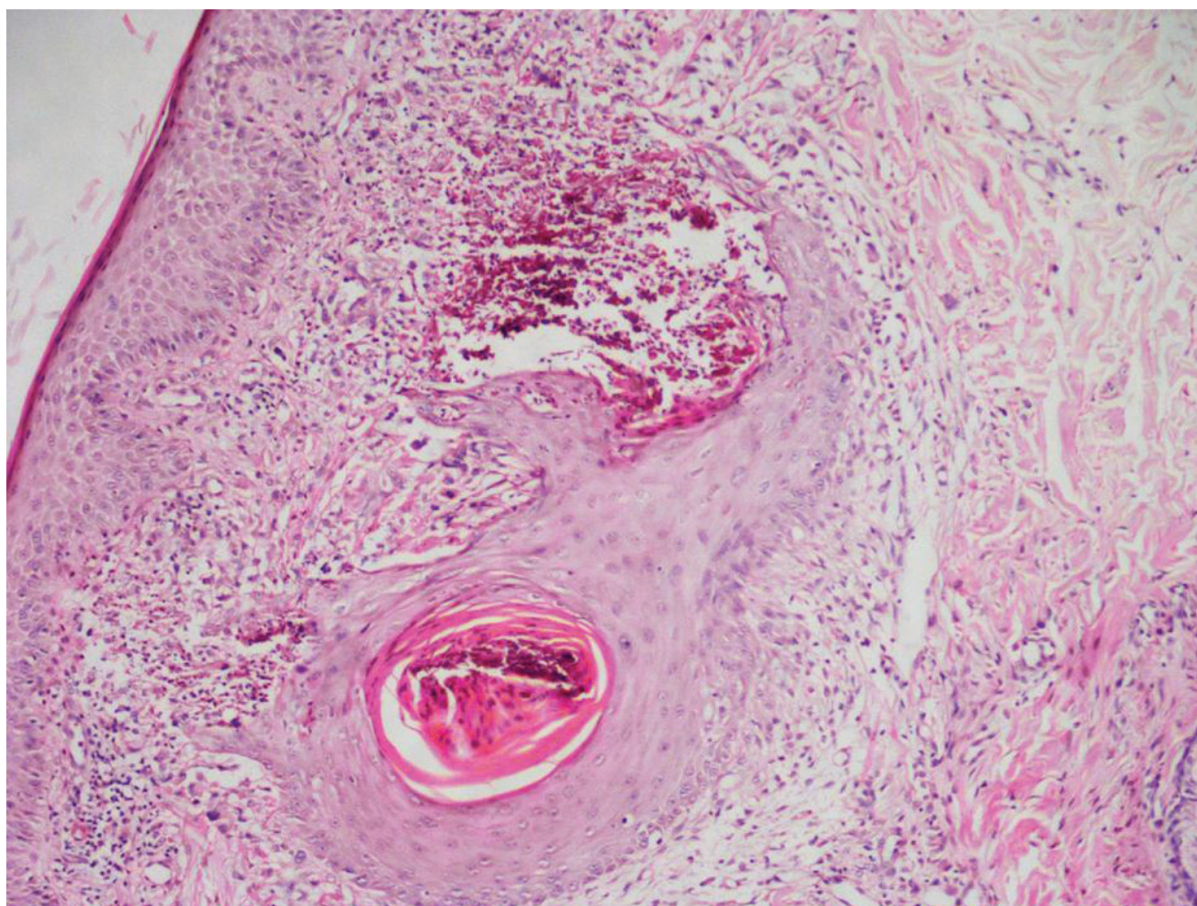
According to some other studies, folliculitis can be classified as superficial and both superficial and deep [5].

Independent of etiology, the primer lesion of folliculitis is generally an erythematous papule or pustule. Histologically in all types of folliculitis, inflammation is seen either in follicular epithelia and/or perifollicular area (**Figure 1**).

Whenever the cause is a bacterium, a neutrophilic infiltrate is dominantly seen in the follicular epithelia and dermis (**Figure 2**). Granuloma formation can be seen in consequence of follicular epithelial rupture and passing of pilosebaceous unit components into the dermis.

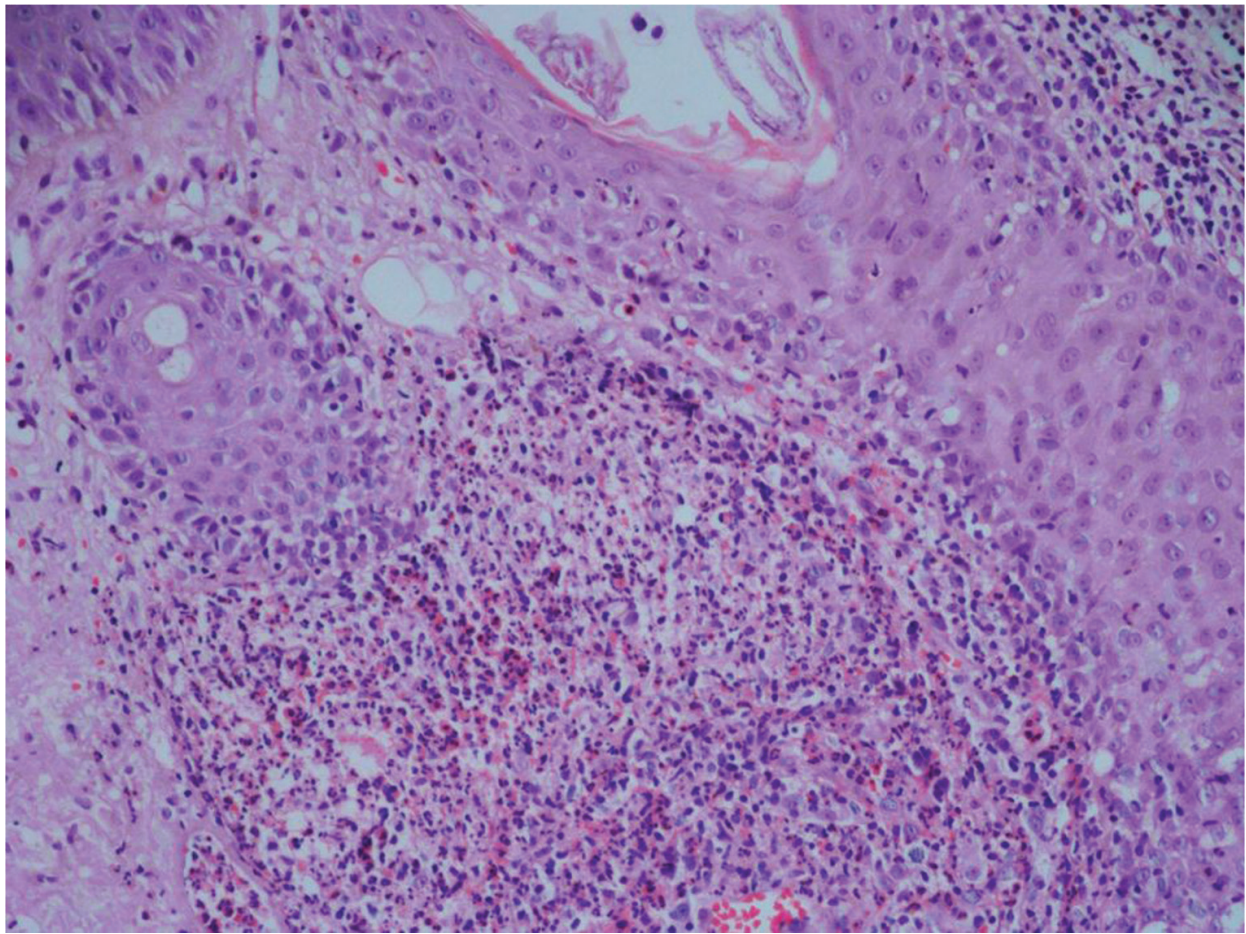
In viral folliculitis, cytopathic effects such as acantolysis, dyskeratosis, multinucleation, inclusions, chromatin marginalization, nuclear molding, etc., can be seen in infundibulum. In early lesions, cytopathic effects cannot be seen [5]. In a viral folliculitis, a lower concentration of inflammation is noticeable. In some cases, hyperplasia of epidermis, necrosis of follicular epithelia or sebaceous gland can be visible.

Fungal folliculitis is commonly seen in adult women living in warm and humid climates. Immunosuppression, diabetes and antibiotic use can be predisposing factors. The cause is



**Figure 1.** Mixed type inflammation that surrounded the follicle, attacked the follicular epithelia, and destroyed the hair follicle (HE  $\times 100$ ).





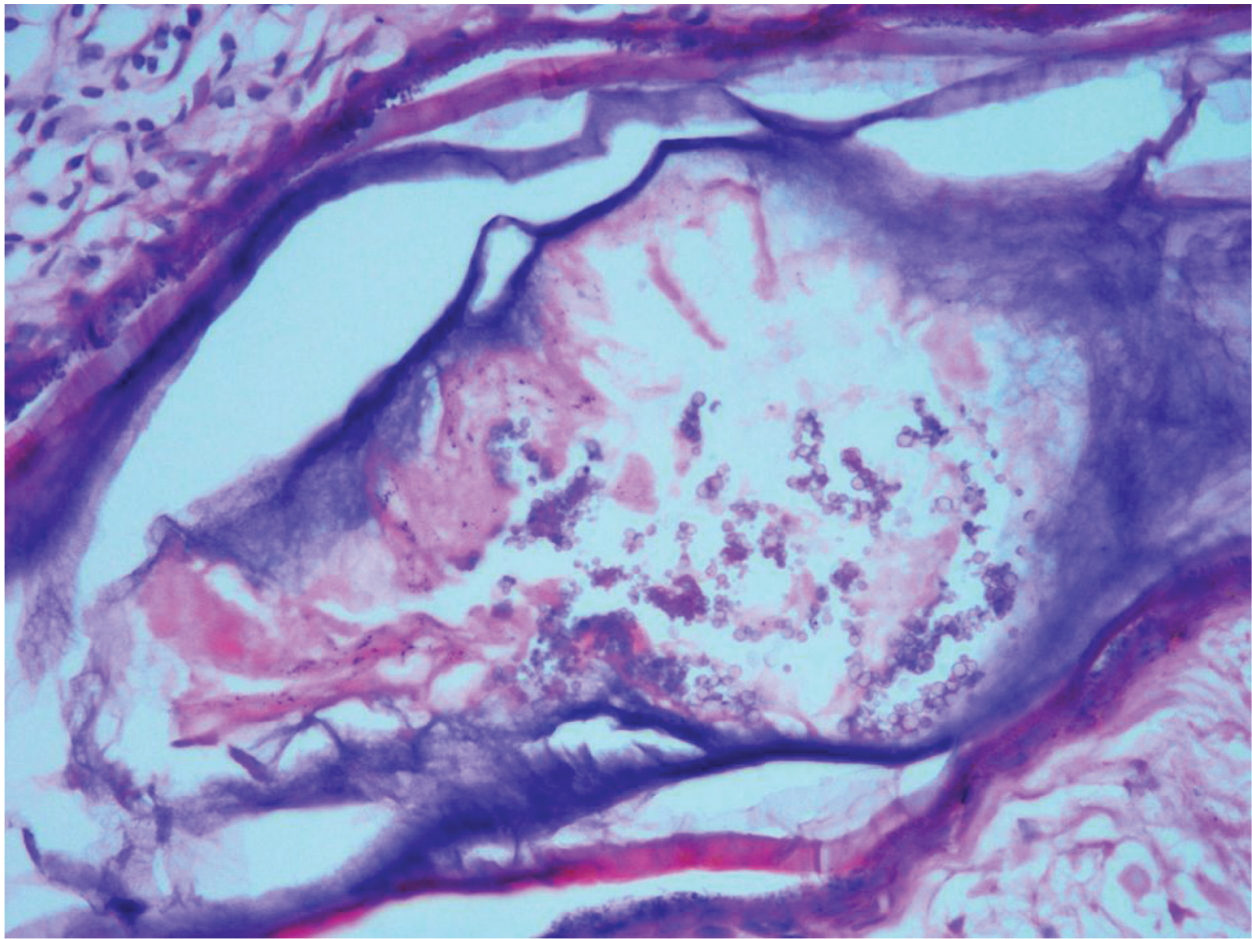
**Figure 2.** In a bacterial folliculitis case, predominantly neutrophilic infiltrate is present in the upper dermis and invades the follicular epithelia (HE  $\times 100$ ).

mostly *Malassezia globosa* (*Malassezia furfur*). Inside the dilated hair follicle due to keratin plug, numerous yeasts are visible (**Figure 3**). Around hair follicle mild chronic inflammation (including eosinophils) can be seen. The rupture of follicle transforms chronic inflammation to acute inflammation consequently abscess formation and granulation tissue can be seen [4].

In the syphilitic folliculitis, plasma cells are dominant [6].

There are some possible and practical methods for finding the cause of folliculitis such as: Gram staining (for bacteria), PAS or silver stain (for fungi) and immunohistochemistry (for viral causes). However, the sensitivity of these methods can be low. The more sensitive and specific methods such as fresh tissue culture, PCR, etc., can be used for microorganism typology [6].

Folliculitis can also be classified according to microanatomic structure of the skin which is involved. Most of bacterial folliculitis involves the superficial part of hair follicle that is why they are called superficial bacterial folliculitis. The superficial folliculitis caused by *S. aureus* is also called impetigo of Bockhart. In deep folliculitis tenderness, warmth, and erythema are visible in a wide area. Nodules are formed. They are most commonly seen in buttocks, axilla,



**Figure 3.** Keratin plug of hair follicle contains numerous yeast forms of fungi (HE ×400).

and legs. Furuncle: deep folliculitis includes only one hair follicle. More than one furuncle combines to form carbuncle [5].

In some textbooks the term “acneiform folliculitis” can be seen. This term means that there is an acneiform dilatation in the hair follicle (e.g., pityrosporum folliculitis).

In demodex folliculitis, besides the mites located inside the hair follicle, follicular spongiosis, perifollicular lymphohistiocytic inflammation also draws attention. An isolated folliculitis is generally self-limited. In old and advanced lesions of all folliculitis perifollicular fibrosis can be visible.

When clinically folliculitis is among the differential diagnosis but histopathologically the lesion is not seen in biopsy sections, deeper and serial sections must be taken. When histopathologically folliculitis diagnosis is made but no microorganism is detected, additional histochemical and immunohistochemical stains can be implemented. Acneiform lesions should be thought primarily when no microorganisms detected microscopically and by applying additional methods (culture, etc.). On the other hand, for diagnosis of acneiform lesions a hundred percent clinical correlation is required.



During investigation if a microorganism is detected, cure rate is very high with appropriate treatment (topical antibiotic, topical antifungal, and systemic antiviral drugs).

## 2.2. Special types of folliculitis and acneiform eruptions

Eosinophils are predominant in some kinds of folliculitis. When eosinophils are predominantly seen in folliculitis, the first step should not be searching for microorganisms. *Eosinophilic folliculitis* is mostly seen in HIV-positive patient whose CD4 T helper cell count <200–300/ $\mu$ l. *E. folliculitis* is characterized by severe pruritic papules and pustules. Bacteria and yeast fungi can accompany this clinic course. *Ofuji disease* (eosinophilic pustular dermatosis) is a rare disease generally detected in Japan, characterized by pruritic follicular papules and pustules located on the face and scalp [5].

Histopathologically follicle infundibulum is surrounded by inflammation which is predominantly composed of eosinophils and few lymphocytes. The follicle can be ruptured but granuloma formation is not expected. In the past few years, studies have recommended exclusion of fungal folliculitis with PAS-D and/or GMS (Gomori methenamine silver) staining. Eosinophilia in peripheral blood and increased serum IgE levels can be detected in eosinophilic folliculitis. There is also a self-limiting variant of eosinophilic folliculitis presenting on the scalp of children with numerous papules and pustules.

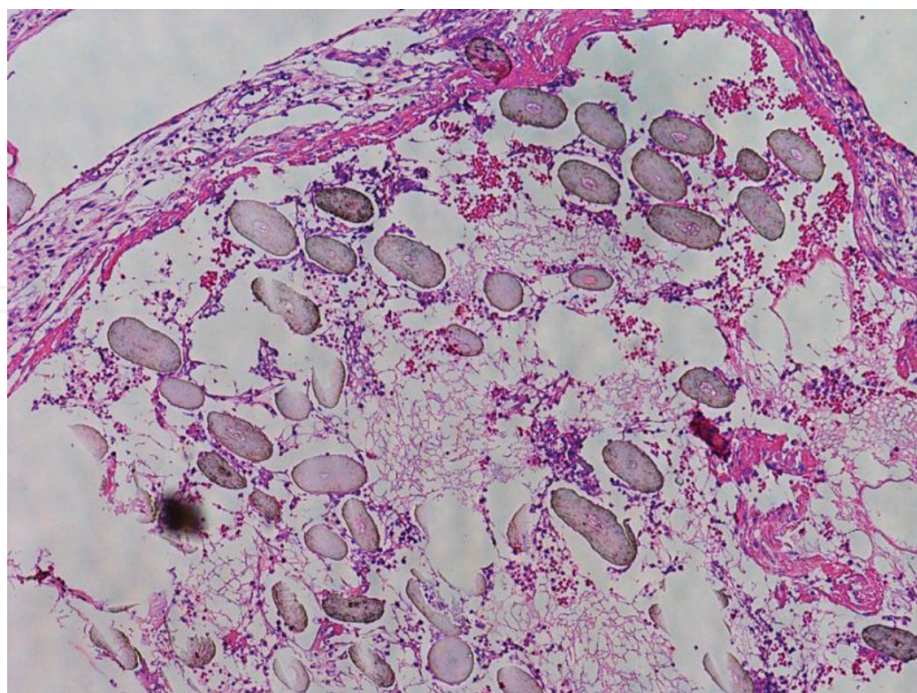
*Folliculitis decalvans* (*perifolliculitis capitis abscedens et suffodiens/dissecting cellulitis of scalp*): is a type of deep folliculitis, generally affects the scalp and commonly seen in black race. In the year 1952, Brunstig described folliculitis decalvans a component of the *follicular occlusion triad*. Other components of the triad include: acne conglobata (a kind of nodulocystic acne) and hidradenitis suppurativa (acne inversa or apocrine acne). The histology of these disorders is similar. In all three disorders, abscess formation, suppurative granulomas, and finally sinus tracts are formed as a result of follicular hyperkeratinization [3]. Generally, culture is negative in these three disorders.

*Acne conglobata*: giant comedones, cysts, and nodules are located on the neck and chest. These lesions leave large irregular scars and can end up with epidermal cysts.

*Hidradenitis suppurativa* is actually a wrong nomenclature because apocrine and eccrine sweat glands are generally affected secondarily. It favors axilla and groins. Histopathologically, the hair follicle is dilated and the apocrine gland duct is plugged with keratin.

Some authors accept *pilonidal sinus* as a component of *follicular occlusion triad*. In pilonidal sinus disease, hair shafts are embedded in fibrosis they continue growing and elongating inside fibrosis (**Figure 4**). Histopathologically dense suppurative inflammation, fragmented hairs, abscess formation, and necrosis are seen one within the other.

*Acne keloidalis nuchae* and acne conglobata (component of follicular occlusion triad) are frequently seen together and generally seen in the black race. Acne keloidalis nuchae favors posterior part of scalp and neck. Lesions end up with scars. In the beginning, discrete papules and pustules are detected [5]. This condition is also called *folliculitis keloidalis nuchae*. This is among the causes of scarring alopecia [4]. In curly hairs, the hair infundibulum is believed to grow backwards



**Figure 4.** Chronic abscess which is formed by hair shafts and chronic inflammatory cells (HE  $\times 100$ ).

and cause a reaction in dermis which in turn triggers scarring. Follicle is surrounded by lymphocytes and plasma cells. Inflammation is observed in the upper part of the follicle. Ruptured follicles cause secondary granuloma formation. Abscess formation and sinus tracts can also be formed. Dense hypertrophic scar and collagenosis is noticeable (**Figure 5**). Exactly a true keloid formation is not seen [6]. Dystrophic calcification can be seen in scarring acne lesions.

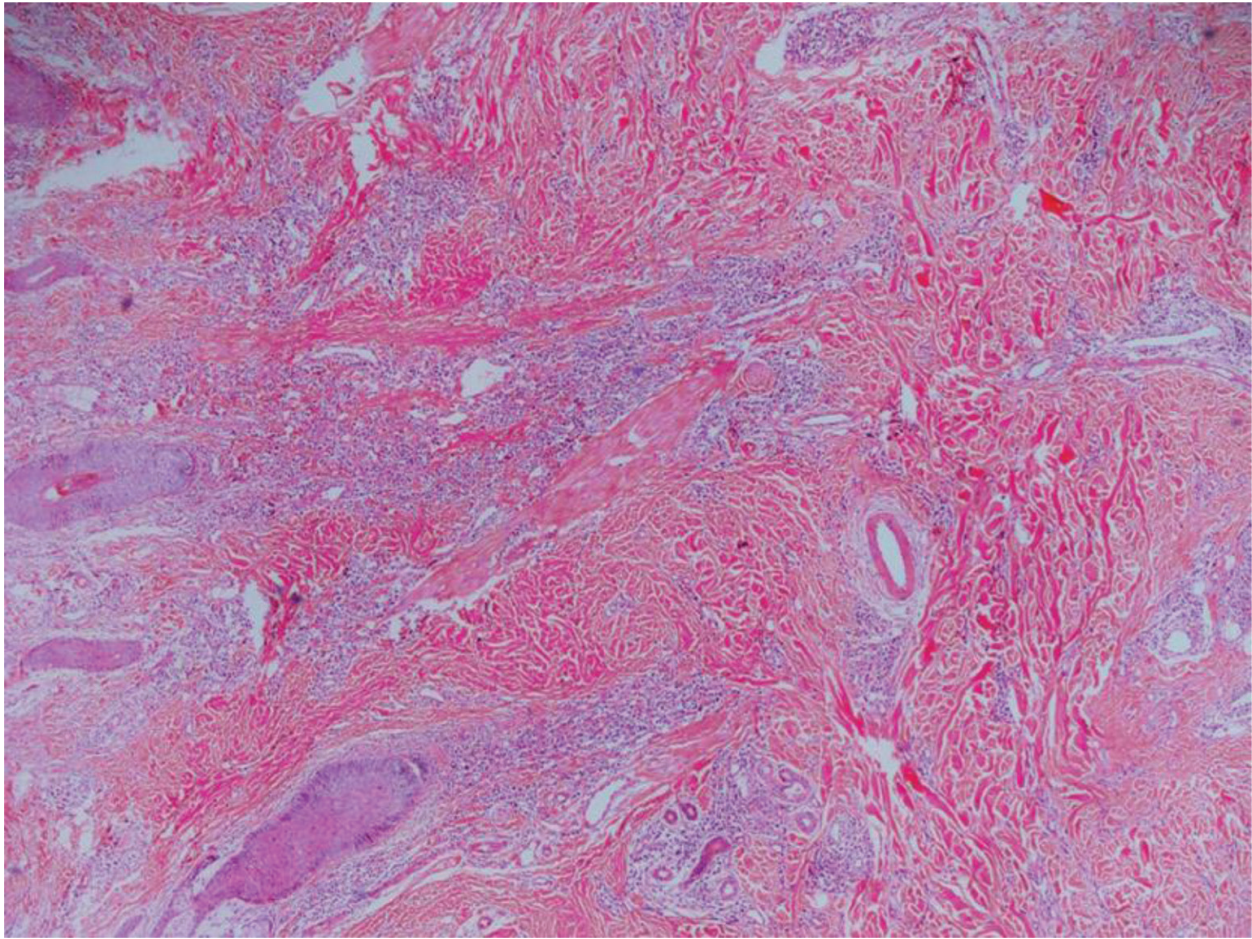
*Pseudofolliculitis barbae* is another entity which has similarities with acne/folliculitis keloidalis nuchae [5]. *P. barbae* is seen in people who have thick and curly hair in beard area. The lesions are formed due to the transition of hair from infundibulum to the surrounding epidermis. Histopathologically mixed type inflammatory cells and foreign-body-type giant cells are seen in the intrafollicular and perifollicular area.

*Acne/folliculitis necrotica (acne varioliformis)*: It is a folliculitis that ends up with scarring and alopecia. The lesions present as umbilicated erythematous papules and pustules. The lesions are located in the follicle. Comedones are not expected [2]. The term acne is misnomer. Histopathologically perifollicular lymphocytic infiltrate is seen. This infiltrate makes exocytosis into follicular epithelia and causes dense necrosis in keratinocytes. In advanced lesions, necrosis of the follicles can be confluent and clinically ends up with formation of depressed scars [6].

There are some acne forms that are induced or developed by drugs, sunlight exposure, impulsive skin picking, or different materials.

*Acne cosmetica (pomade acne)*: this clinical entity is a temporary follicular occlusion that ends up with acneiform eruption. Acne cosmetica is caused by dense cosmetic usage. The follicle infundibulum is dilated and thin.





**Figure 5.** Fibrosis in the dermis which can turn into a hypertrophic scar (clinically an acne keloidalis nuchae case) (HE  $\times 100$ ).

Overuse of bromides triggers severe acneiform lesions which is called *halogenoderma/iododerma/bromoderma/fluoroderma*. Histopathologically in addition to classical acne findings, pseudoepitheliomatous hyperplasia, intraepithelial small abscess and granulomatous inflammation can be seen [3].

Chemical exposure to mineral oils and dioxin can cause acneiform eruptions predominantly comedones, this is called *chloracne*. The comedones are shaped as a bottle or column. Follicular keratin stasis and increased melanocytic activity is detected in epidermis and hair infundibulum [7]. *Steroid-induced acne* is caused as a result of high dose corticosteroid treatment. In contrast to chloracne comedones are not expected. Generally monomorphic pustules are observed [8]. EGFR inhibitors can cause acneiform drug reaction [3].

*Acne aestivalis* (Mallorcan acne): presents with papules and pustules, favors head and neck, sun exposure triggers the lesions. Histopathologically folliculitis and necrosis of follicular epithelia is noticeable [9, 10].

Acneiform lesions can be seen both in Behcet's and Wegener's diseases.

*Morbus Morbihan (Morbihan disease)*: is a clinical form of severe acne which presents with solid facial edema and favors primarily the central face area.

*Acne fulminans*: characterized by abrupt onset of tender nodules, plaques, and ulcers. Clinically fever, lymphadenopathy, hepatosplenomegaly, weight loss, etc., can accompany.

*Acne Excoriee*: scratched acneiform lesions seen in young women due to impulsive picking emotion.

*Acne mechanica*: acneiform lesions are observed secondary to hair friction caused by hat, helmet, etc. [3].

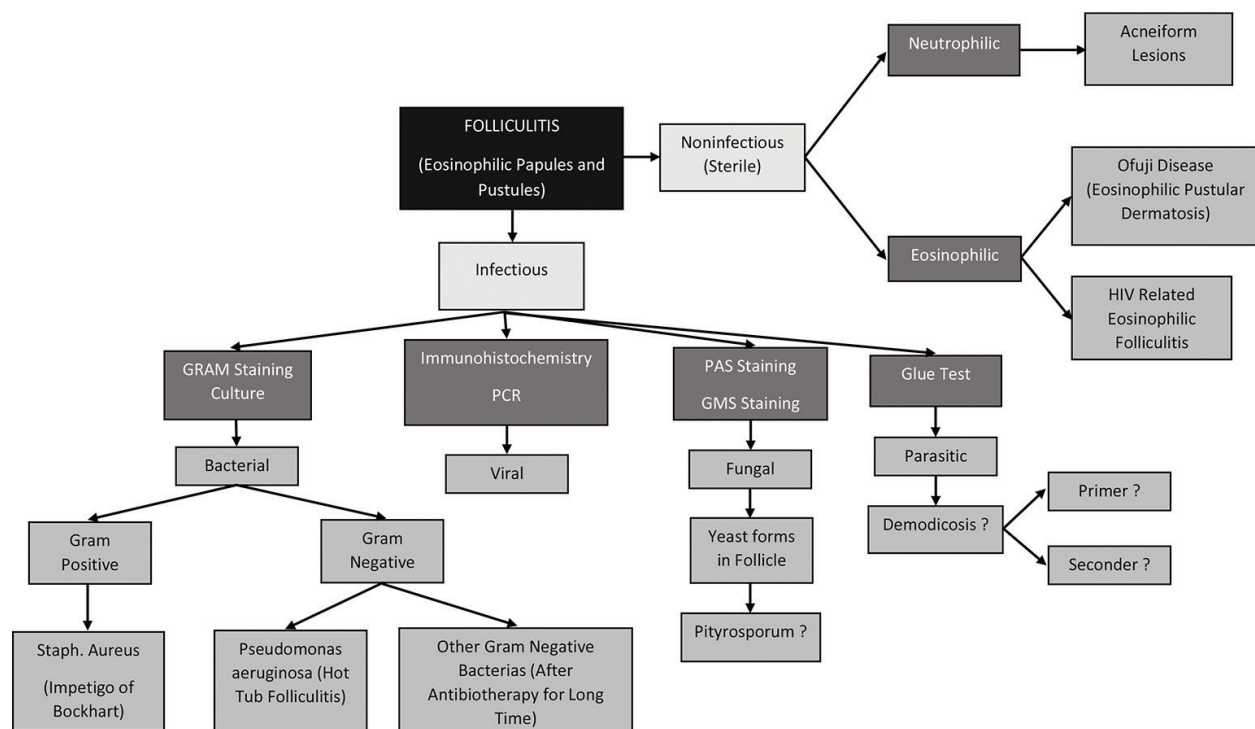
*Nevus comedonicus (acne nevus)*: is a term used when multiple open comedones are gathered together on a plaque lesion [3]. This lesion can also be evaluated as a hamartoma made up of small infundibular cysts [6].

In conclusion, a comprehensive dermatological examination and detailed history taking is indispensable in all clinical entities mentioned above.

**Flowchart 1** summarizes all the above-mentioned clinical entities.

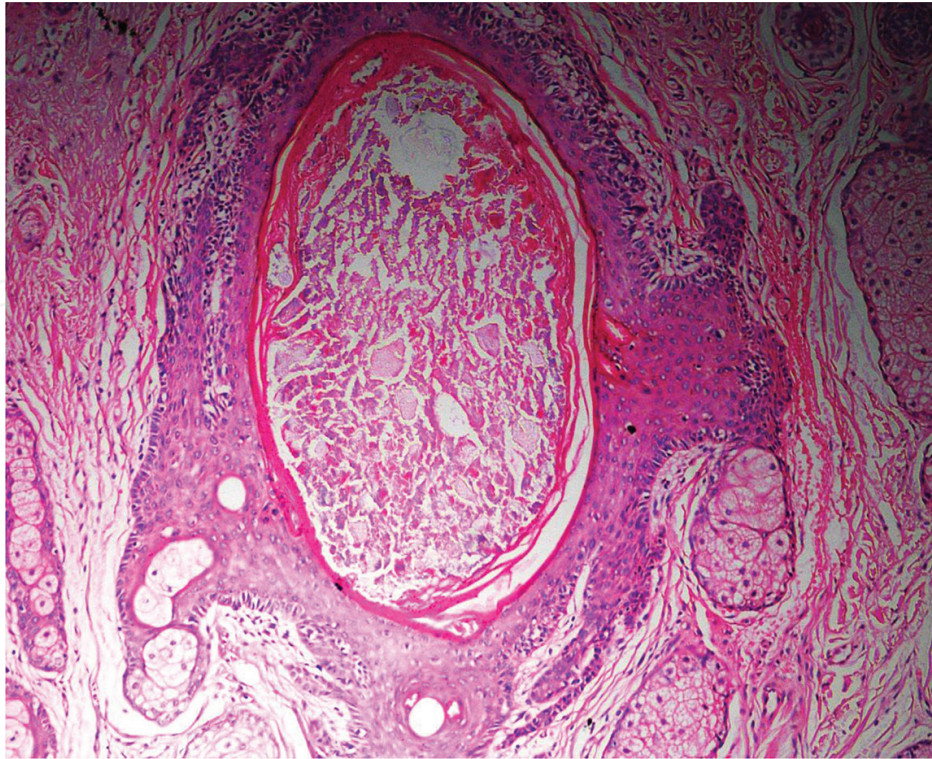
### 2.3. Acne vulgaris/pimples

Acne vulgaris is the prototype of acneiform lesions and is the inflammatory disease of sweat glands and pilosebaceous units, mostly observed in teenagers and young adults. In contrast to age predilection, race and sex predilection do not exist. The clinical course is severe in male



**Flowchart 1.** A simple, practical approach to basic kinds of folliculitis.

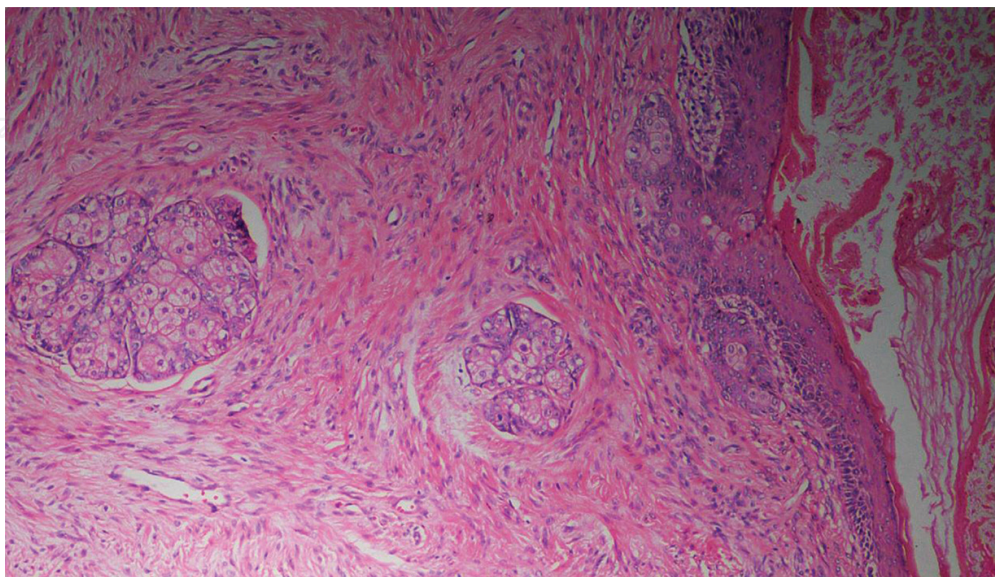




**Figure 6.** Pilosebaceous unit has started to be dilated with keratin plugging, also a mild perifollicular inflammation can be seen (HE  $\times 100$ ).

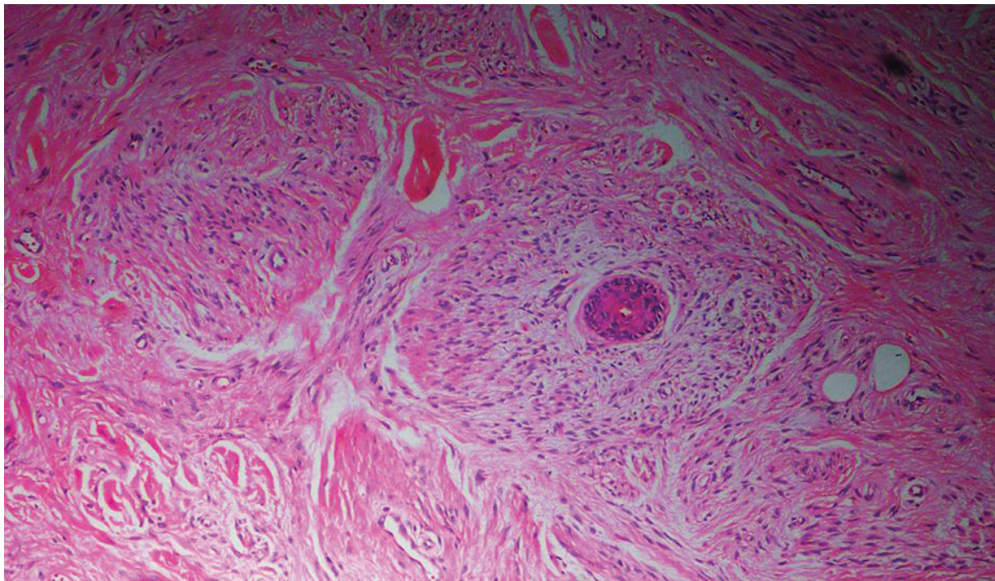
patients [2]. Acne lesions favor forehead, chin, cheek, chest, shoulder, and back. Family history may be present. In most patients, the lesions regress in a few years period.

The lesions are generally presented as erythematous papules, pustules, blackheads, and whiteheads. In severe cases, tender and painful nodules and cysts can be apparent. Because hair follicle is plugged with keratin, excreted sebum is accumulated in addition to *P. acnes*



**Figure 7.** A kind of fibrotic process at the neighborhood of dilated follicle can be noticed (HE  $\times 100$ ) (Same case with Figure 6).

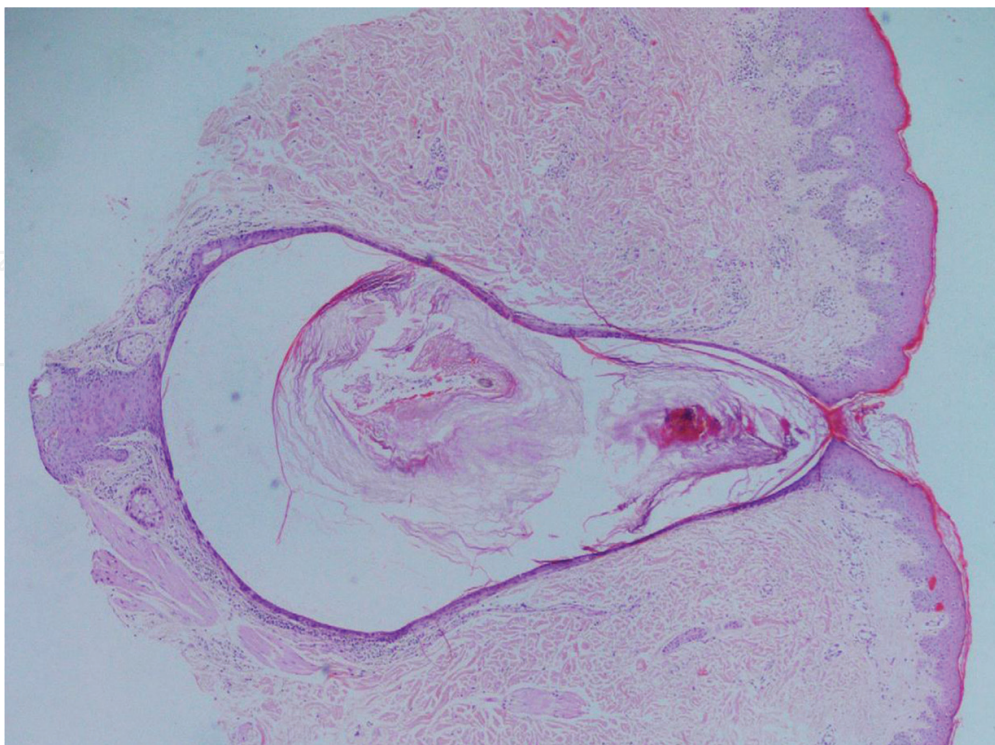




**Figure 8.** Deeper part of the same lesion in Figures 6 and 7. Scar formation and an entrapped tiny hair follicle can be defined (HE ×100).

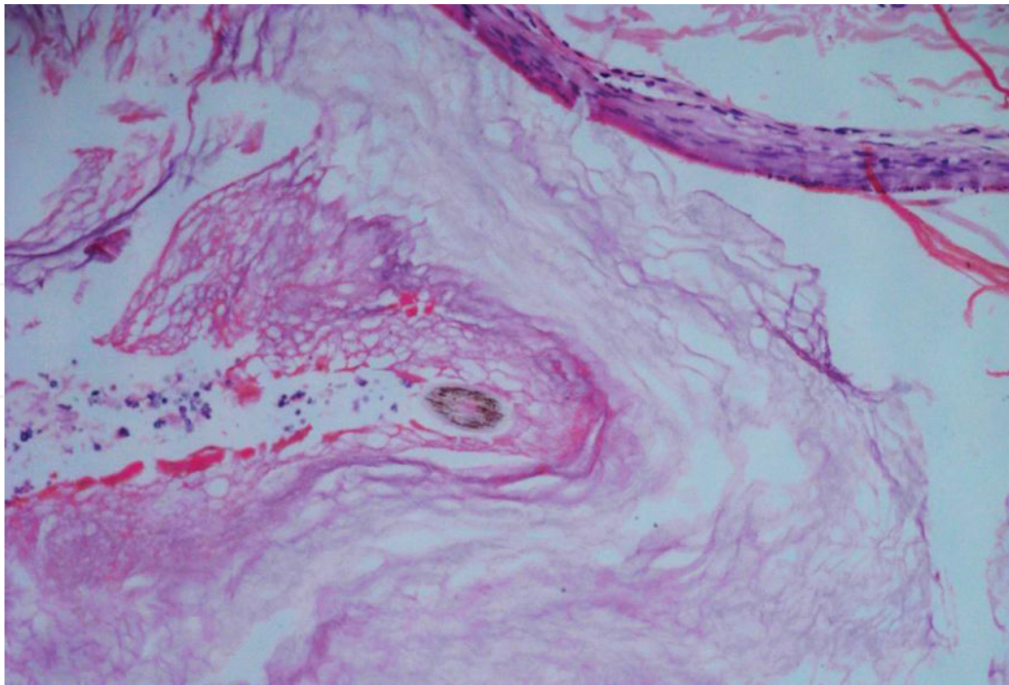
colonization and all these steps lead the follicle to folliculitis. Severe desquamation of follicle epithelia and sebaceous gland epithelia also plays a role in pathogenesis.

Acne vulgaris lesions are studied in two groups: noninflammatory (blackheads and whiteheads or comedones) and inflammatory (folliculitis, etc.). Acne lesions can end up with postinflammatory hyperpigmentation and scars (**Figures 6–8**). Keloid formation is quite rare.



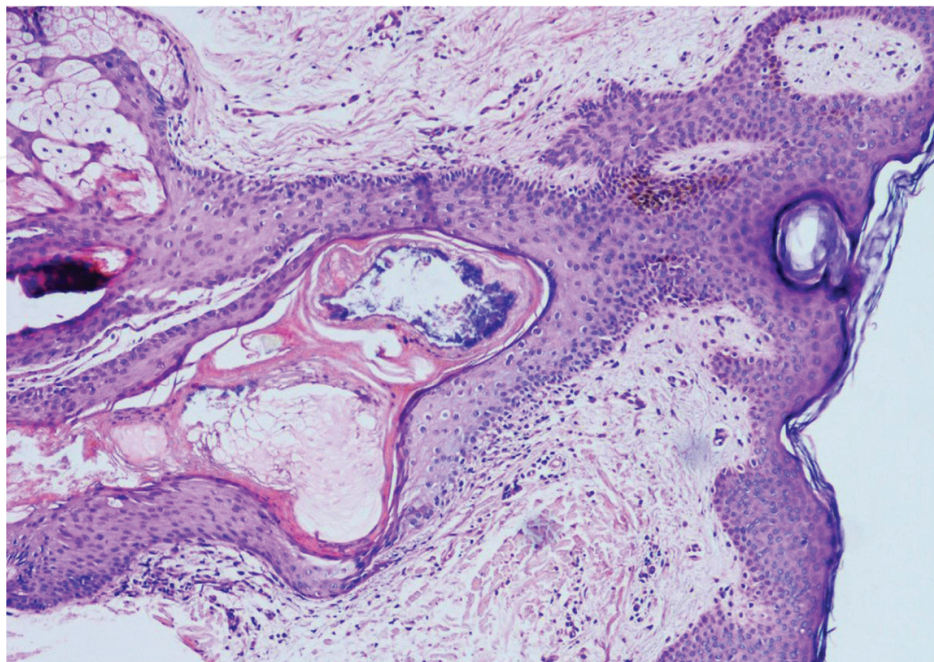
**Figure 9.** A closed comedone that has a narrow orifice on epidermal side (HE ×40).



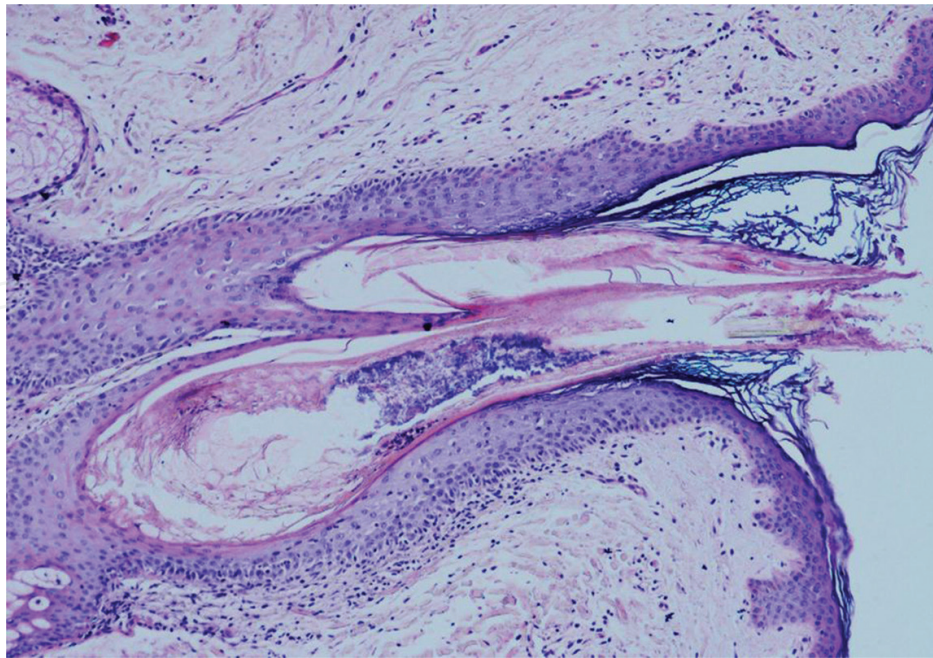


**Figure 10.** Comedone consists of lamellar keratin, hair shaft, and some bacteria (HE  $\times 200$ ).

Acne is diagnosed clinically, and biopsy confirmation is generally not required. Histopathologically noninflammatory lesions (comedones) are a kind of follicular retention cysts. These tiny cysts may consist of cornified cells, hair shafts, sebum, *P. acnes*, and other bacteria. Closed comedones' orifices on epidermis can be normal in size, mild wider, or narrower (**Figures 9–11**). However, open comedones' orifices on epidermis are definitely dilated (**Figure 12**) [6]. The precursors of inflammatory lesions are generally closed comedones or subclinical microcomedones. Open



**Figure 11.** Microcomedone that has a smaller dilatation of follicle opening and a few mononuclear inflammatory cells basically around the follicular epithelia (HE  $\times 100$ ).



**Figure 12.** An opened comedone with keratin plugging, wider orifice on epidermis, and mild perifollicular inflammation (HE  $\times 100$ ).

comedones do not trigger the inflammatory process. In comedonal lesions around the affected hair follicle, few inflammatory cells may be present.

Inflammatory lesions may progress in the following pattern: papule→pustule→nodule→cyst.

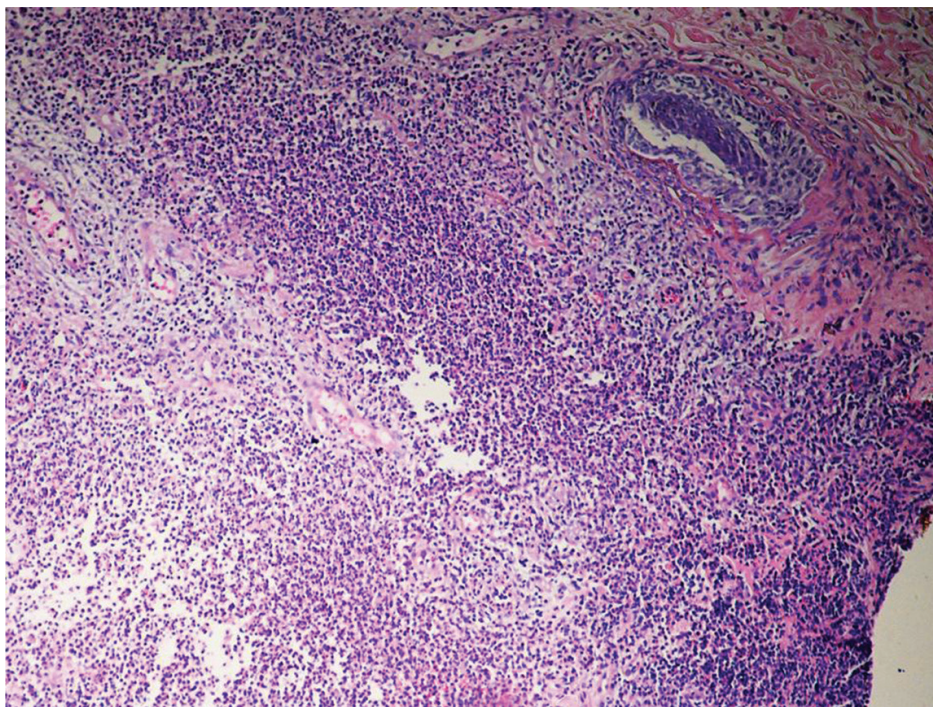
Comedonal lesions due to retention the follicular wall is quite thin and the follicular content oozes into adjacent dermis which in turn causes accumulation of inflammatory cells in dermis. This process plays the major role in the formation of inflammatory lesions. When the follicle wall becomes much thinner, the follicle may rupture and lead to pustule (**Figure 13**) and by the time, nodule formation is in deep dermis. Depending on follicular damage and severity of inflammatory response scar formation, dermal necrosis, and confluent abscesses formation can be observed. Perifollicular elastolysis can be noticed in acne vulgaris scars [8].

In a noninflammatory lesion if the follicular opening does not expand the follicular wall becomes thinner thus follicular rupture becomes inevitable [8]. Spongiosis is noticeable in follicular epithelia of both inflammatory and noninflammatory lesions. In inflammatory lesions the inflammatory cells attacking follicular epithelia or perifollicular inflammatory cells are composed of mixed type cells (polymorphonuclear leucocytes, lymphocytes, histiocytes). Foreign-body-type multinuclear giant cells and/or granulomatous reactions can be observed as a result of follicular rupture (**Figure 14**).

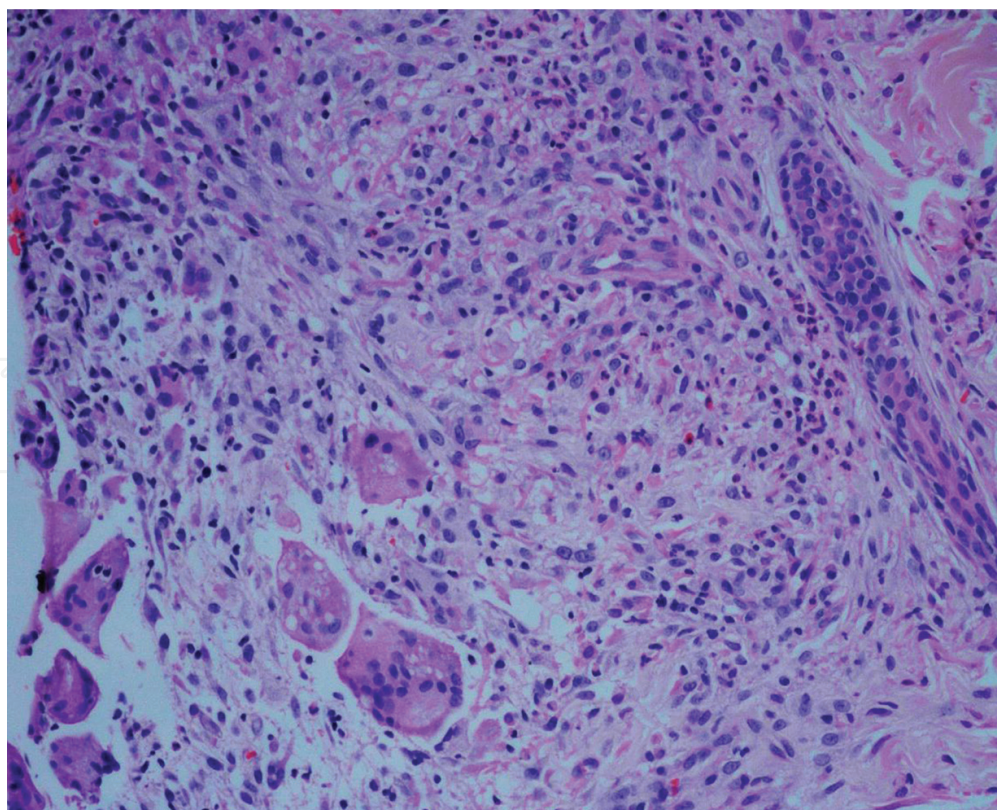
#### **2.4. Acne rosacea (adult onset acne)**

Rosacea is a disease characterized by macular erythema and flushing of central face generally affecting adult population. Some authors classify acne rosacea as a vascular and follicular disease. In a true rosacea, typical acneiform lesions such as papules and pustules are observed. However, comedones are not an important component of acne rosacea. In contrast to acne vulgaris, increased sebum is not the subject in acne rosacea. Sometimes acne rosacea can lead





**Figure 13.** A deep ruptured folliculitis, severe mixed type inflammation and a destroyed hair follicle (HE  $\times 100$ ).



**Figure 14.** After the rupture of hair follicle, foreign body type inflammatory reaction can be seen (HE  $\times 200$ ).



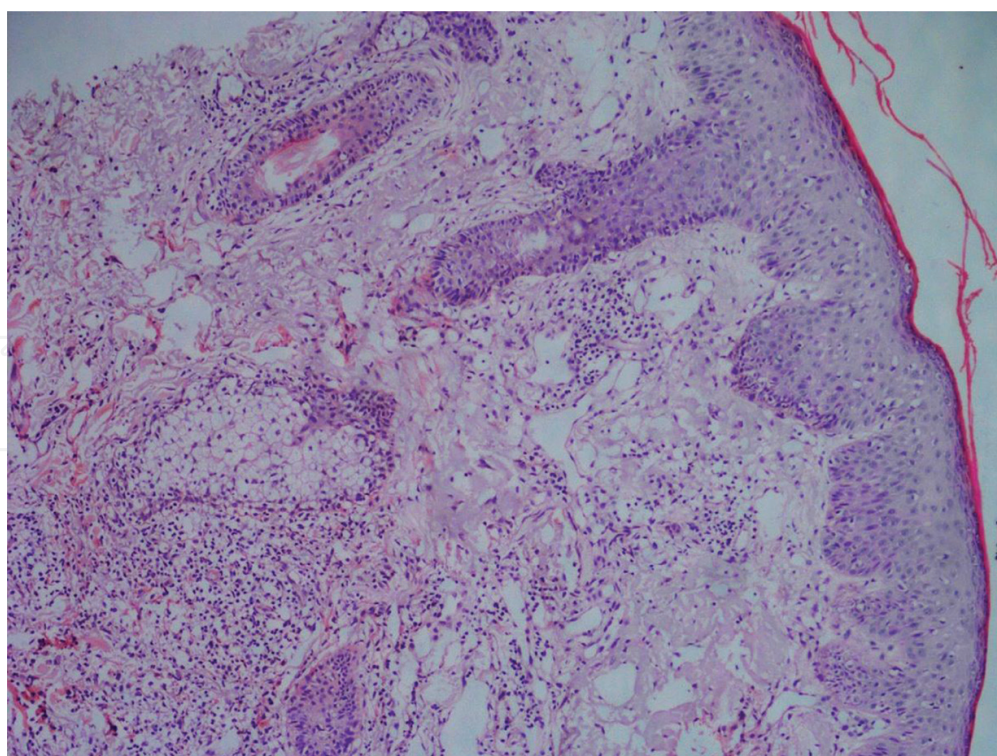
to blepharitis and phyma formation. In acne rosacea, flushing can be triggered by warmth, cold, alcohol intake, and spicy foods. Granulomatous lesions can be confronted within acne rosacea which present as yellow-brown nodular lesions [5].

Histopathological findings differ according to the stage of disorder.

In early nonpustular lesions, telangiectasia is in the foreground also perifollicular and perivascular mixed type inflammation (lymphocytes, plasmocytes, macrophages, eosinophils, and polymorphonuclear leucocytes) draw attention (**Figures 15** and **16**). Abnormal dermal vessel regulation hypothesis is postulated but there is no objective method for evaluating telangiectasia [11, 12]

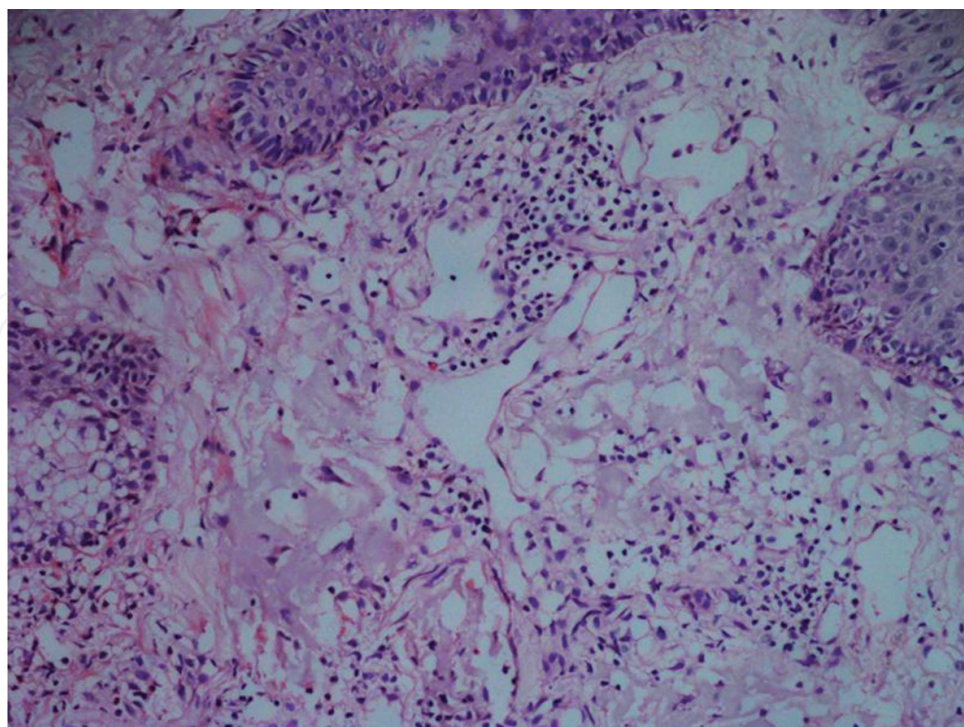
Acne rosacea can rarely be extrafascial and/or generalized [2]. Acne rosacea more commonly affects women who have type 1 celtic descent skin phenotype. Some methods are present for clinical staging and severity scoring of acne rosacea [2, 13].

In pustular lesions, an increased amount of polymorphonuclear leucocytes are observed. In severe rosacea (rosacea fulminans, pyoderma faciale), polymorphonuclear leucocytes are predominant cells. In the epithelia of hair follicle, spongiosis can be seen in infundibulum part (**Figure 17**). Follicular rupture can cause granulomatous reactions. Sometimes caseification necrosis can be observed in the center of granulomatous reaction. Solar elastosis can be generally present in rosacea lesions. However, solar elastosis can be a coincidence rather than a specific finding of acne rosacea because solar elastosis is generally present in patients above 40 years of age, in addition to central face is under dense exposure of sunlight throughout life [2].

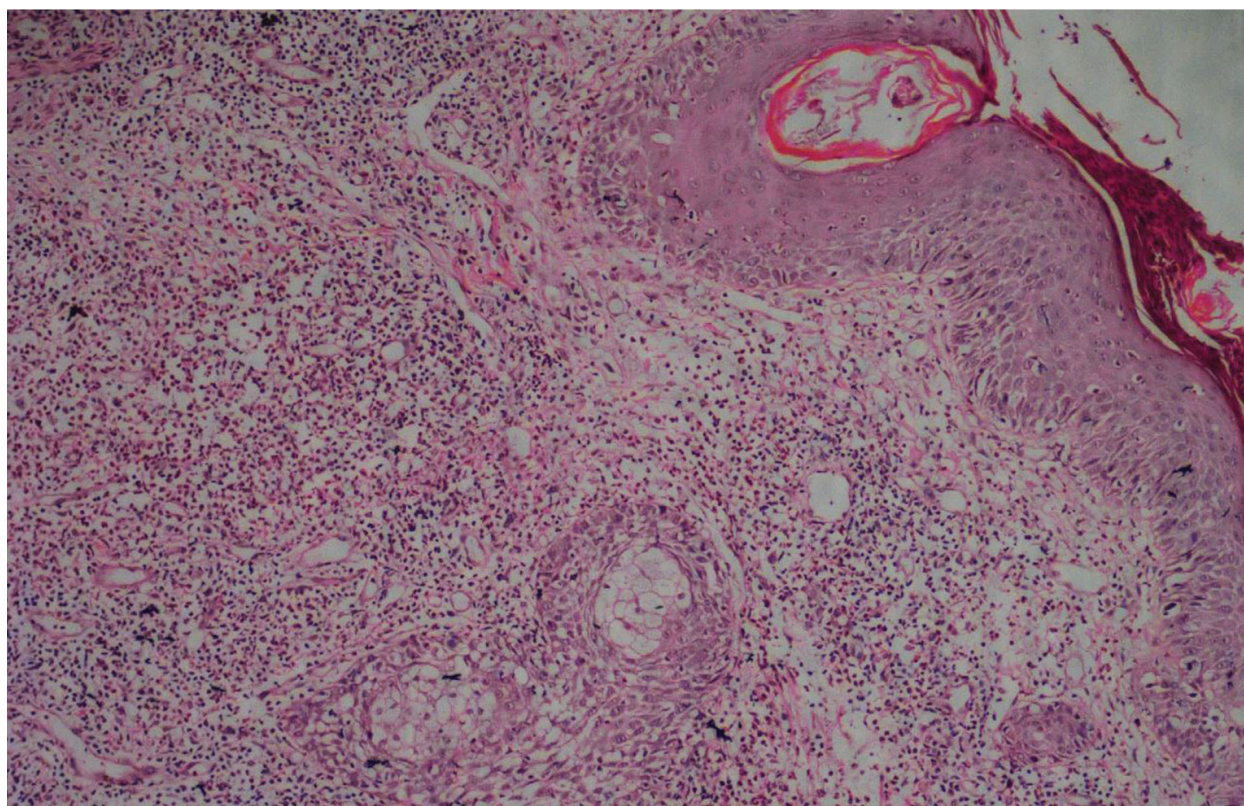


**Figure 15.** There is a mild-moderate inflammation in dermis and also telangiectatic vascular structures with solar elastosis in the upper dermis (HE ×100).





**Figure 16.** Lymphocyte predominant inflammation in the upper dermis, around the telangiectatic vessels (HE  $\times 200$ ).



**Figure 17.** A severe rosacea case that has intensive inflammatory infiltrate (polymorphonuclear leucocytes are dominant) (HE  $\times 100$ ).



Most of resources use the clinical classification method [14, 15] that has four types of acne rosacea:

1. Erythematotelangiectatic
2. Papulopustular
3. Phymatous
4. Ocular

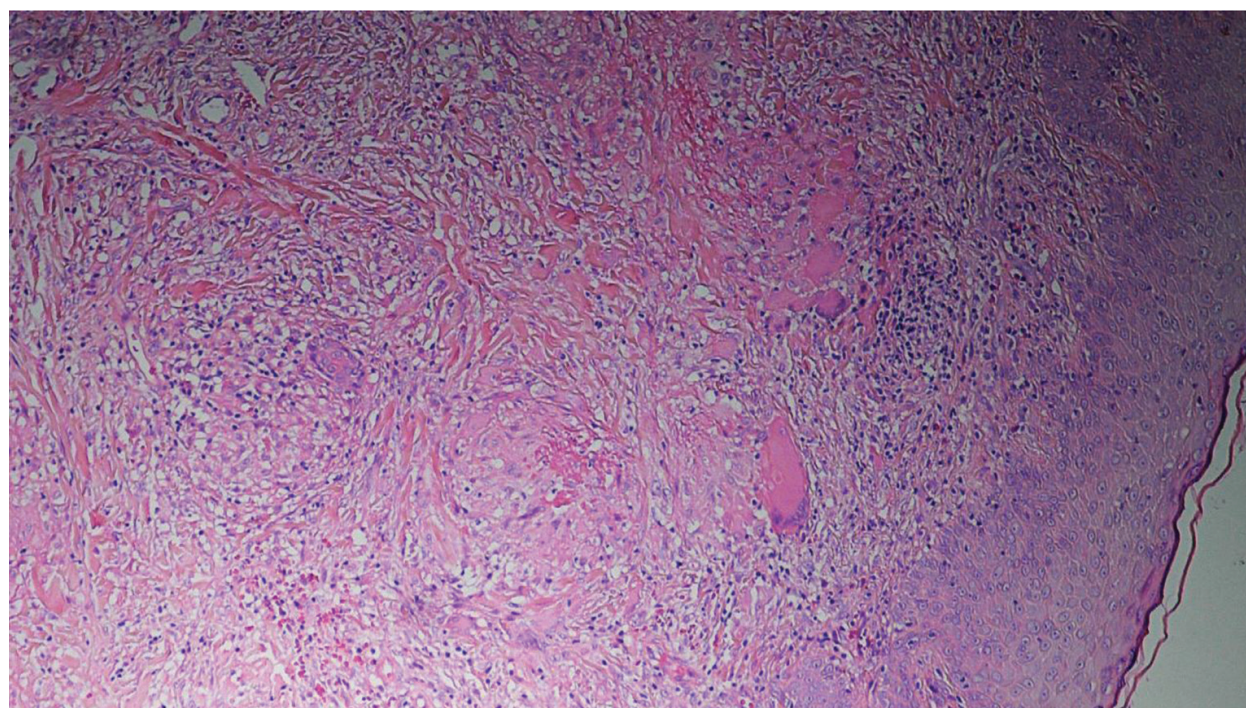
*Rhinophyma* or phyma formation (*nose, chin, auricle, and forehead*) can be seen in the most advanced stages of acne rosacea.

In order to reach this stage, episodic flushing → persistent flushing → papulopustular stages must be passed.

In the histopathologically evaluation of rhinophyma, different amounts of lymphocytic inflammation, sebaceous hypertrophy, nodular ectatic vessels, hyperkeratosis [4], fibrosis, solar elastosis [6], and mucin accumulation can be observed [8]. Rhinophyma is generally irreversible and surgical intervention is required.

Telangiectatic vascular structures surrounding the rhinophymatous papules may evoke the suspicion of basal cell carcinoma for a clinician [16]. In this case, a biopsy can be done for the exclusion of basal cell carcinoma.

In granulomatous rosacea where long-term phymatous lesions are present in the face, *acne agminata* (*lupus miliaris disseminatus faciei, acnitis*) [5] or FIGURE (*facial idiopathic granuloma with regressive evolution*) [2] can also be observed. In this disease, caseification necrosis is seen in the



**Figure 18.** There are granulomas that have caseification necrosis in their center and multinuclear histiocytic giant cells in dermis (HE ×100).

center of pealike granulomas (**Figure 18**). The granulomas are ARB (acid resistant bacteria) negative; no microorganisms are found in PCR. Because of the caseific and amorphic eosinophilic material, the morphology of the granuloma is similar to that of rheumatoid nodule [17]. Acne agminata is the best identified form of granulomatous rosacea. Acne agminata do not involve extrafascial areas, within years the lesions undergo resolution.

*Perioral-periocular dermatitis*: is very similar to acne rosacea, some authors acknowledge this as the same entity with acne rosacea [5]. Symmetrically distributed erythematous papules and pustules are observed around mouth and eyes. Steroid abuse can induce perioral-periocular dermatitis. Telangiectasia is not expected in perioral dermatitis. Histopathologically mild acanthosis in epidermis, parakeratosis (especially in the ostium of hair follicle) with perivascular and perifollicular lymphocytic inflammation is present. The presence of a relation between demodex mite and acne rosacea or other acne forms has been observed.

### 3. Demodex and demodicosis

Demodex can be found in the normal fauna of the pilosebaceous unit. For this reason, generally it is not mentioned in the pathology reports. However, changing degrees of inflammatory reactions (from accumulation of lymphocytes up to suppurative and granulomatous reactions) are related to demodex mites [3]. Demodex favors sebaceous areas. Density of demodex mites increases with age.

Two species of demodex inhabit in human: *Demodex folliculorum* and *Demodex brevis*.

Life cycle of demodex mite is as follows: ova→larvae→protonymph→nymph→adult [16].

The aid of its mouth, *D. folliculorum* moves inside the follicle. The tail is in the caudal part (**Figure 19**). *D. folliculorum* has eight ova, and each ovum has an arrowhead-like structure and is big in size. *Demodex folliculorum* is the most frequent demodex living on human beings. In each hair follicle so many *D. folliculorum* can live.

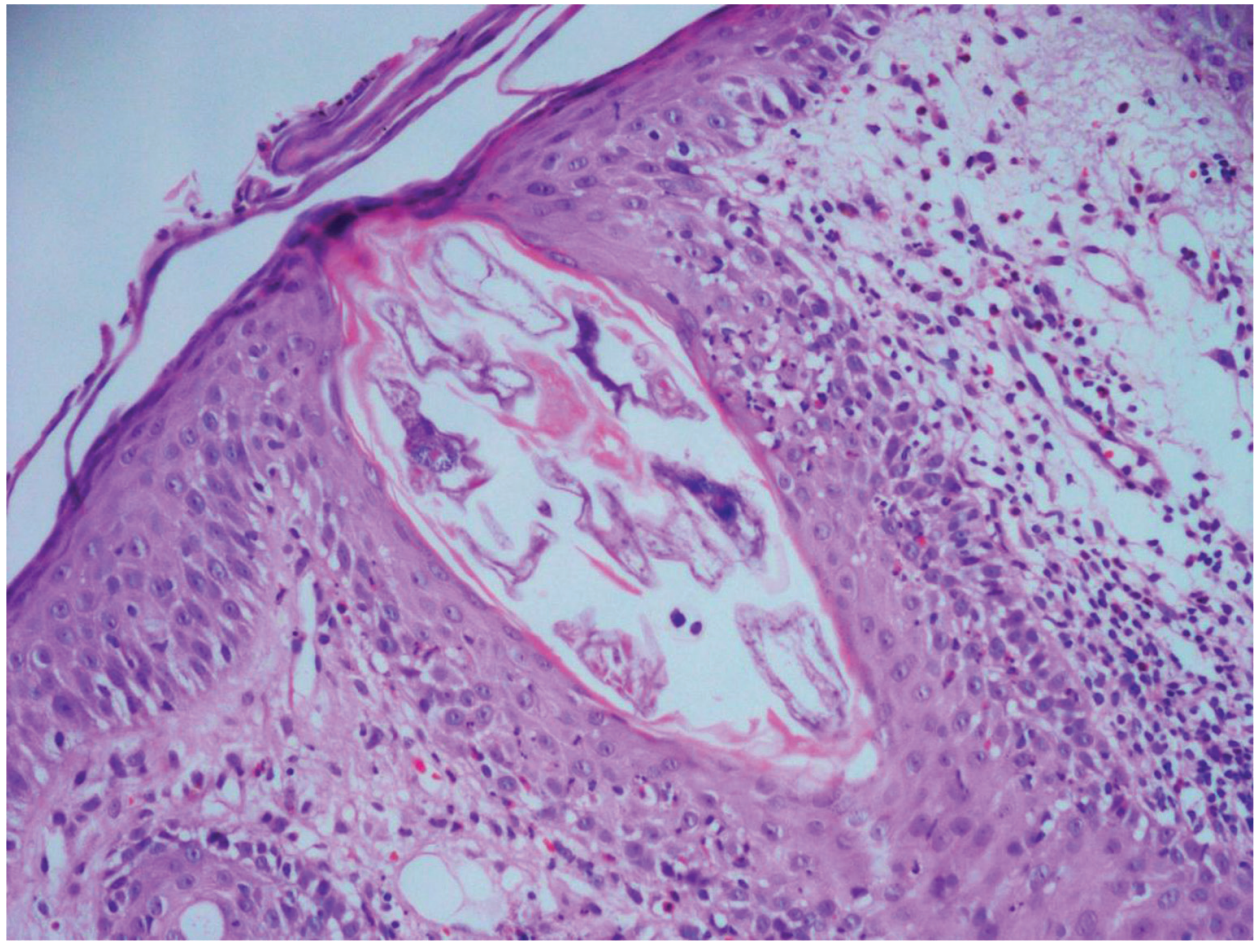
*D. brevis* is smaller than *D. folliculorum*, and the ovum is oval shaped. This type is not as frequent as *D. folliculorum*. In each follicle, one or two *D. brevis* can inhabit. *D. folliculorum* and *D. brevis* can live together in the same host. Mites are nourished from epithelial and glandular cells.

In 1993 Bonnar et al. [18], removed the stratum corneum of the skin by the help of cyanoacrylate glue and investigated the follicular contents. The mite count was significantly increased in patients who had acne rosacea compared to normal people. This study showed the relation between acne rosacea and demodex mites. This study is one of the studies that conclude the relationship between acne rosacea and demodex mites [17].

The pathogenetic mechanisms of Demodex in rosacea can be:

- foreign body reaction against the parasite
- immune reaction of the host toward the parasite
- the parasite serving as a vector for bacteria [18].





**Figure 19.** Demodex mites inside the hair follicle, perifollicular inflammatory cells and exocytosis of these inflammatory cells (HE ×200).

Clinically demodicosis also can be divided into primary and secondary demodicosis.

Primary demodicosis: *D. folliculorum* is found in the disease-free T region of the face (there is no sign and symptom).

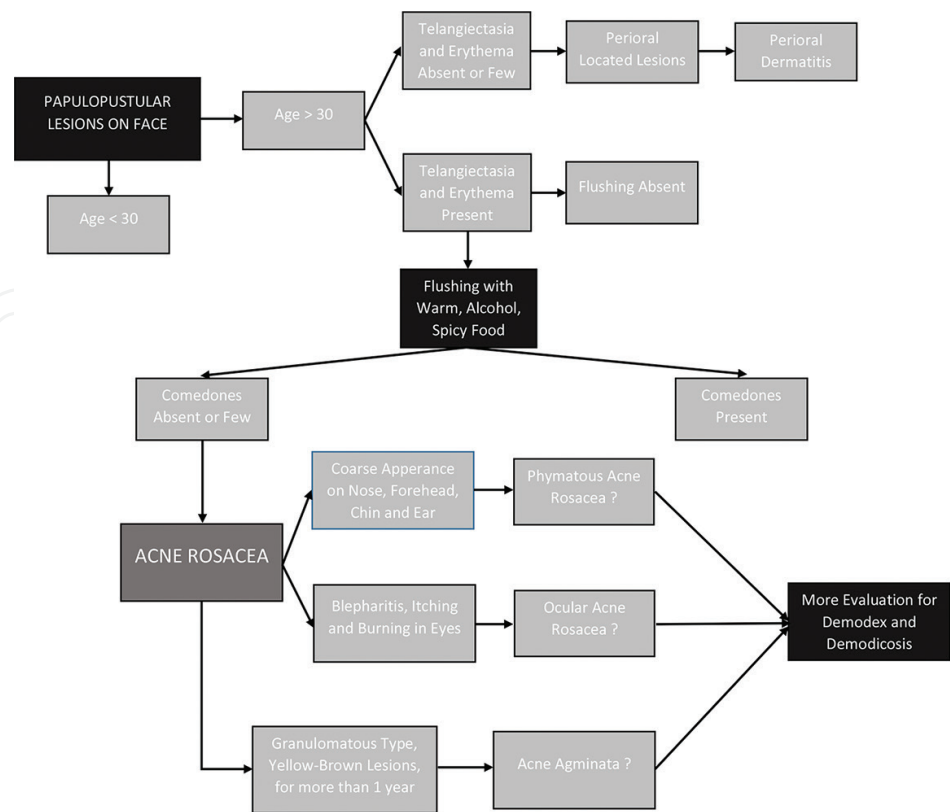
Secondary demodicosis: more than 30% of the face is affected. Signs and symptoms of the disease are present (erythema, pruritus, etc.), this clinic course is thought to be induced by *D. brevis* [19].

Furthermore, there are three forms of traditionally identified demodicosis:

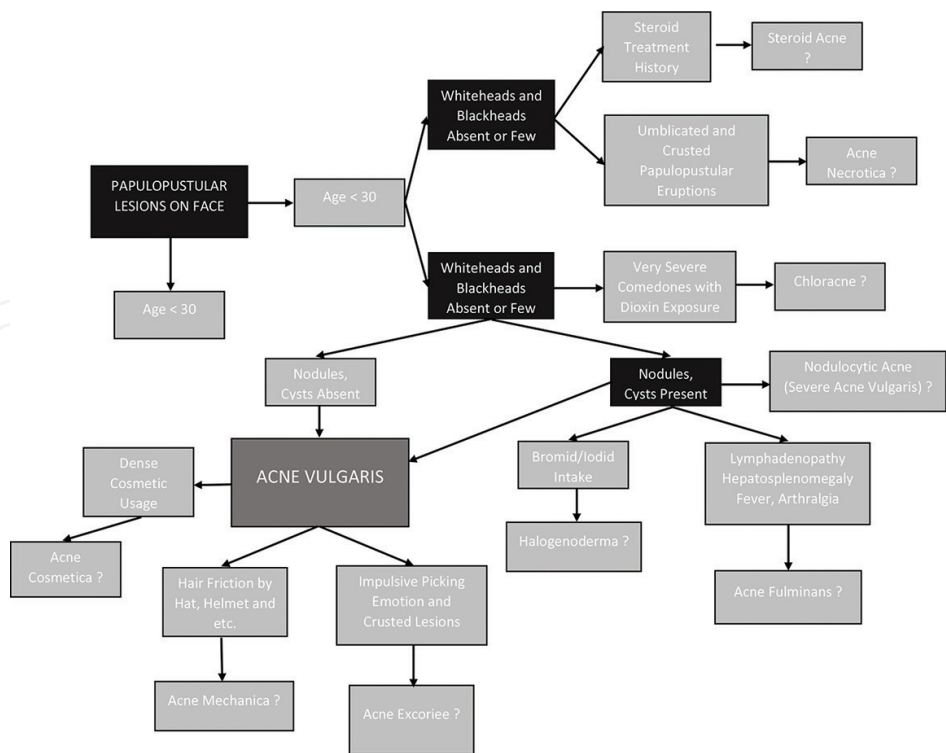
- pityriasis folliculorum,
- rosacea like demodicosis,
- demodicosis gravis [2].

In **Flowcharts 2** and **3**, we tried to establish a simple algorithm for making diagnosis easier.





Flowchart 2. A simple clinicopathological approach to central facial lesions.



Flowchart 3. Acne vulgaris and related diseases.

## Author details

Murat Alper\* and Fatma Aksoy Khurami

\*Address all correspondence to: [muratalper70@gmail.com](mailto:muratalper70@gmail.com)

Diskapi Yildirim Beyazit Research and Training Hospital, Altindag, Ankara, Turkey

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