Clinicopathologic Study of "Calcifying epithelioma of Malherbe" - Pilomatricoma - A Retrospective study in a Tertiary Care Hospital

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ABSTRACT

Background - Pilomatricoma, also known as pilomatrixoma, is a type of noncancerous (benign) skin tumor associated with hair follicles.It demonstrates a bimodal peak presentation during the first and sixth decades of life, 40% of cases occur in patients younger than 10 years of age and 60% of cases occur within the first two decades of life [1,2]. Pilomatricoma represents 0.12% of all skin tumors.[4]Its prevalence is poorly defined and its presentation varies and can simulate various other skin lesions also.

Materials and Methods - This retrospective study was conducted to evaluate the clinical and histomorphology of pilomatricoma along with it's incidence with respect to age, sex and site of lesion in a tertiary care hospital, Navi Mumbai. Following parameters were used to diagnose pilomatricoma
1. Shadow cells
2. Sebocytes
3. Matrical cells
4. Supramatrical cells
5. Isthmic differentiation
6. Infundibular differentiation
7. Calcification
8. Melanocytes
9. Basaloid epidermal proliferation
10. Trichohyaline granules
11. Outer sheath differentiation(clear cells)
12. Foreign body giant cells

Results – A female preponderance with maximum cases in the 31 – 45 years age group was found in our study. The predominant site of lesion was head more specifically scalp followed by upper arm. The clinical diagnosis comprised of spectrum of lesions including dermoid cyst, sebaceous cyst, unidentified lesion and inflammatory lymph node. Histological features of basaloid cells with eosinophillic ghost cells was found in almost all cases along with associated features of calcification and presence of giant cells.

Conclusion – Pilomatricoma is not rare in occurrence but rarely diagnosed because of lack of confirmation of excised swelling. These are often mistaken for small round blue cell tumours in children, or for merkel cell carcinoma, basolioma and metastatic small cell carcinoma in adults, with possible aggressive therapeutic approach and hence, it is imperative that it should be kept in the differential diagnoses of all superficial skin tumors by dermatologists and surgeons. This study also helped in finding the prevalence of this disease in India, as there is paucity of the same in our country. Thus overall, this study helped in finding the various histomorphological features which are diagnostic of pilomatricoma. It also adds to the data of the disease in our country and will help in better clinical management as well as triage of patients.

Keywords: Nodular Scalp swelling, Histopathology, Epithelioma of Malharbe

INTRODUCTION: Pilomatrixoma (Calcifying epithelioma of Malherbe) is a tumor of hair matrix that usually occurs in the first two decades of life and is almost always benign. Calcified lesions in the skin have been noted since ancient times.[1] The first complete work, based on a series of patients, was published by Malherbe and Chenantais in 1880. They described calcifying epitheliomas, initially thought to be tumors of sebaceous glands.[2] The term *pilomatrixoma*, to denote origin from hair matrix cells, was suggested by Forbis and Helwig in 1961. This was later corrected to *pilomatricoma*, as more etymologically correct.[3] These tumors have a wide variety of signs, which often causes misdiagnosis.[4]

It affects individuals at any age, with peak incidence in the first and sixth decades of life. It is more common in women (1.5 to 2.5:1) among young people, 40% occur before 10 years of age and 60% before 20 years.[3,5] New hair follicles are not formed after birth, only some are activated during puberty. If they are located in deep layers, differentiation induction agents will not act on them. These partially differentiated follicles would form the pilomatricomas.[6]

The most common sites are the head and neck area or upper extremities. Pilomatricoma usually presents as a hard, solitary, deep-dermal nodule with normal overlying skin, or occasionally as a more superficially located solitary lesion with discoloration of the overlying skin.[7]

Histological characteristics include pilomatricoma as a sac of epithelium that is infundibular above and matrical and supramatrical cells along the sides along with ghost cells in the center with basophilic nucleated cells in the periphery.[8] These basaloid cells are fairly uniform in size, with rounded nuclei, small nucleoli, fine granular/vesicular chromatin and delicate nuclear membranes. Calcification is present in 70%–95%. [9,10].
Pilomatricoma may be confused with small round blue cell tumours in children, or for merkel cell carcinoma, basolioma and metastatic small cell carcinoma in adults and many various other diseases, hence this study was conducted to categorize various histopathological features of pilomatricoma and their manifestations according to different age groups to obtain credible data of the patients. Although most pilomatricomas have firm calcified nodule, few of them look vascular with associated thinning of skin. Bowers and Millard[14,16] describe this variant in which the typical tumor is covered by irregular spaces that contain lymphatic fluid. Small blood vessels are also increased in number, and the overlying dermis and epidermis are atrophied

AIMS/OBJECTIVES OF STUDY:
Aim : Clinicopathologic study of Calcifying Epithelioma of Malharbe
Objectives:
1.To find the frequency of pilomatricomas out of the total nodular lesions of skin.
2.To find the frequency in relation to age, sex and site of lesion.
3.To find the correlation between clinical diagnosis and histopathological diagnosis.
4. To study the histopathologic features of pilomatricoma with an emphasis on the occurrence of other forms of differentiation.

MATERIALS AND METHODS
A retrospective study was undertaken in the department of pathology in a tertiary care hospital in Navi Mumbai on nodular lesions of skin. Total 1500 nodular lesions were received out of which 20 cases of clinically suspected or diagnosed as pilomatricoma, for a period of 5 years from January 2016 to December 2020. Excision biopsy and in some cases punch biopsy was taken from the lesion, in the department of surgery and dermatology of the same hospital. All biopsies were fixed in formalin and processed in histopathology section of the Central Laboratory. The sections were stained with routine hematoxylin and eosin stain and various histopathological features were studied.

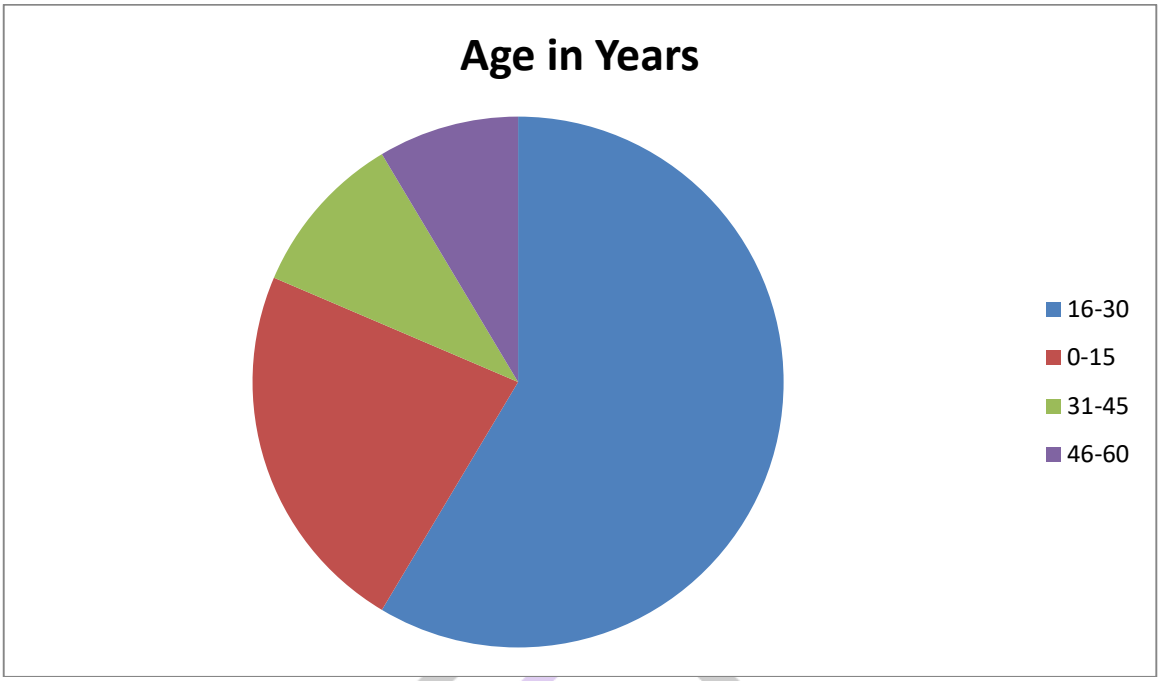
INCLUSION CRITERIA: All the nodular skin biopsies received in the section of histopathology with provisional and differential diagnosis of Pilomatricoma.
Patients of all age groups and both genders were included in this study

EXCLUSION CRITERIA: All skin biopsy samples other than nodular lesions. Inadequate biopsy samples (biopsies showing only dermis or epidermis on histologic examination).
OBSERVATIONS and RESULTS

Table 1. Location of presenting nodular lesion

Location of lesion	Number of Cases / Percentage
	Total 20
Head (Forehead,occipital region ,scalp) Neck (Submental/submandibular region) Upper extremities (Forearm) Trunk (Chest and Back)	10 (50.6%) 2 (10%) 7(35%) 1 (5%)

Table 1.The lesions were maximally seen in the region of head, followed by upper extremity and least affected was trunk.



Graph 1: Age Distribution

The graph shows maximum incidence in the age group of 15-30 years and least in age group of 45-60.

Table: 2 Clinical /Preoperative diagnosis

Clinical diagnosis	
Preoperative diagnosis	Number of cases
Pilomatrixoma	5 (25%)
Unidentified mass	1 (5%)
Epidermoid cyst	5 (25%)
Sebaceous cyst	4 (20%)
Dermoid cyst	4 (20%)
Inflammatory lymph node	1 (5%)

The most common clinical diagnosis was of Sebaceous cyst and Pilomatricoma. One clinical diagnosis of inflammatory lymph node was also observed.

Table 3. Microscopic features N=20

Microscopic Features	Number of Cases/(%)
Basaloid epidermal proliferation	20 (100)
Shadow cells	20 (100)
Matrical cells	20 (100)
Supramatrical cells	15 (75)
Isthmic differentiation	12 (66)
Infundibular differentiation	8 (40)
Sebocytes	4 (20)
Calcification	5 (25)
Foreign body giant cells	8 (40)

The above table shows maximum microscopic features of Basaloid epidermal proliferation Shadow cells and Matrical cells . Least incidence was presence of sebocytes.

Table 4. Clinicopathologic Correlation

Case no.	Age in years	Sex	Location	Size (cm)	Duration	Clinical diagnosis	Histopathology diagnosis
1.	24	M	Scalp	1	1 year	Dermoid cyst	Pilomatricoma
2.	28	F	Scalp	2	4 months	Sebaceous cyst	Pilomatricoma
3.	04	F	Preauricular	2.5	6 months	Unidentified mass	Pilomatricoma
4.	31	F	Left posterior neck	1.8	3 months	Epidermal inclusion cyst	Pilomatricoma
5.	47	F	Scalp	2	6 months	Pilomatricoma	Pilomatricoma
6.	21	M	Arm	4	1year	Sebaceous cyst	Pilomatricoma
7.	22	F	Arm	2	1 month	Sebaceous Cyst	Pilomatricoma
8.	23	M	Scalp	2.5	2 months	Epidermoid cyst	Pilomatricoma
9.	24	F	Scalp	2cm	15 days	Dermoid cyst	Pilomatricoma
10.	28	F	Arm	2.8cm	6 months	Dermoid cyst	Pilomatricoma
11.	30	M	Head	1.9cm	8 months	Pilomatricoma	Pilomatricoma
12.	30	F	Scalp	1.5cm	2years	Epidermoid cyst	Pilomatricoma
13.	12	M	Neck	3cm	1years	Unidentified mass	Pilomatricoma
14	15	F	Neck	2.9cm	4years	Pilomatricoma	Pilomatricoma
15.	20	M	Arm	1.9	2years	Pilomatricoma	Pilomatricoma
16.	14	F	Scalp	1.8	4 months	Skin tumour	Pilomatricoma
17.	49	F	Scalp	1.5cm	2 months	Epidermoid cyst	Pilomatricoma
18.	27	F	Arm	1.5	3 months	Dermoid cyst	Pilomatricoma
19.	39	F	Scalp	1.8	8 months	Pilomatricoma	Pilomatricoma
20.	21	M	Preauricular	2.1	1year	Epidermoid cyst	Pilomatricoma

Clinical Presentation

Out of the total 1500 nodular lesions received 20 cases (1.3%) were diagnosed as pilomatricoma. The main presenting symptom was a hard, subcutaneous, slowly growing mass. In 5 cases (25%), the lesion was associated with pain and tenderness. In 3 cases, the pilomatrixoma was warm to the touch. The pilomatrixomas presented with discoloration of the skin, blue being the color most often noted. In one case the region had previously been infected and one case had history of trauma . Tumor size in the greatest dimension ranged from 1 to 45 mm. The average tumor size in the greatest dimension was 12 mm.

Sex

Out of total 20 patients diagnosed as pilomatrixoma, 13 were female (64 percent) and 7 were male (36 percent) showing male-to-female ratio as 1:1.75.

Age

The age at the time of diagnosis ranged from 4 months to 30 years. 2 cases of males affected were of age 47 and 49 years respectively. (Graph 1).

Sites of Origin

The most commonly affected region was the head and neck (50 percent), with the scalp being the most frequently affected site. The upper extremity was the second most common area (35 percent). Other areas of involvement included neck and trunk areas. (Table I).

Preoperative Diagnoses

The preoperative diagnosis in each case was obtained from the patient's operative report.
The postoperative diagnosis in each case was obtained from the patient's pathology report.
The preoperative diagnosis was accurate and consistent with the pathological diagnosis of pilomatrixoma in 5 cases (25 percent). The chart review revealed 5 other possible diagnoses. Of the 20 confirmed cases of pilomatrixoma, 4 cases (20 percent) were erroneously diagnosed as dermoid cysts, 4 (20 percent) were diagnosed as sebaceous cysts, and 1 (5 percent) was diagnosed as unidentified mass (Table 4.)

Pathological Findings

The microscopic features seen in pilomatricoma are summarized in Table 3.

Pathology reports were reviewed for all 20 patients.
The classic appearance of **basaloid and eosinophilic cells** was seen in all cases [Figure 1], with the mature ones being composed only of **eosinophilic "ghost" cells** [Figure 2].

Matrical differentiation, as characterized by areas showing closely packed basaloid cells having round, pale staining and finely stippled nuclei with prominent nucleoli, [Figure 2a].
Supramatrical differentiation i.e. cellular areas with pale staining cells having a moderate amount cytoplasm and a not very crowded appearance as compared with the areas of matrical differentiation was seen in all of the cases [Figure 3].
I**nfundibular differentiation** (in 40% cases) including keratohyaline granules.
Basket woven orthokeratosis [Figure 4].
Calcification and ossification were frequently seen.
Foreign body reaction was common.

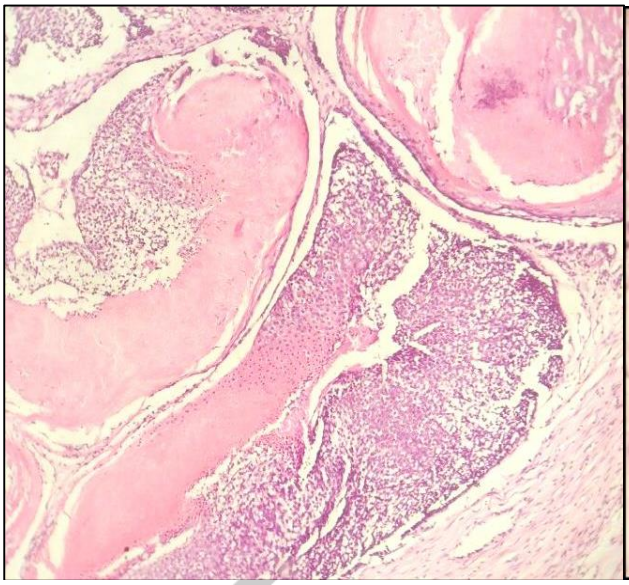


Fig 1. Basaloid areas with eosinopohillic cells (H&E 10 x)

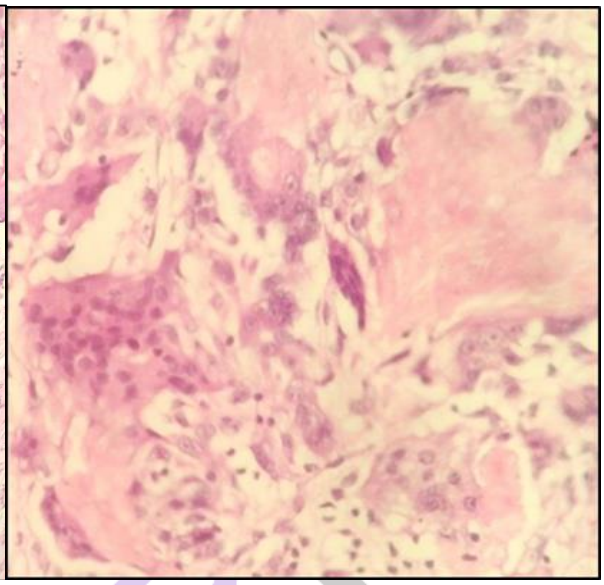


Fig 2. Multinucleated giant cells with inflammatory cells. (H&E 40 x).

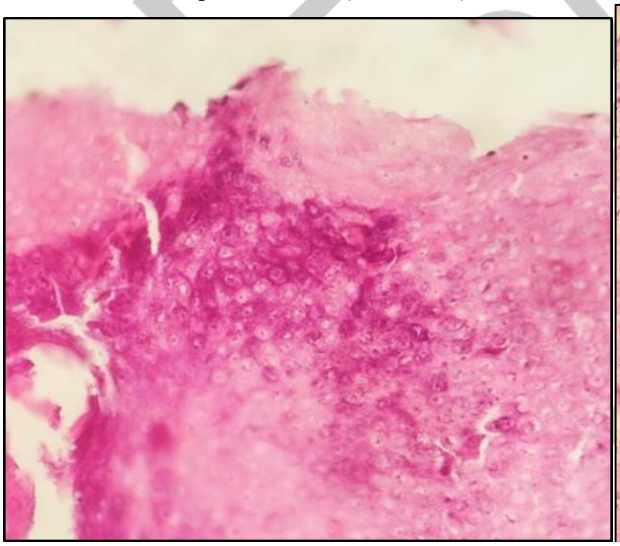


Fig 3. Eosinophillic ghost cells (H&E 40x)

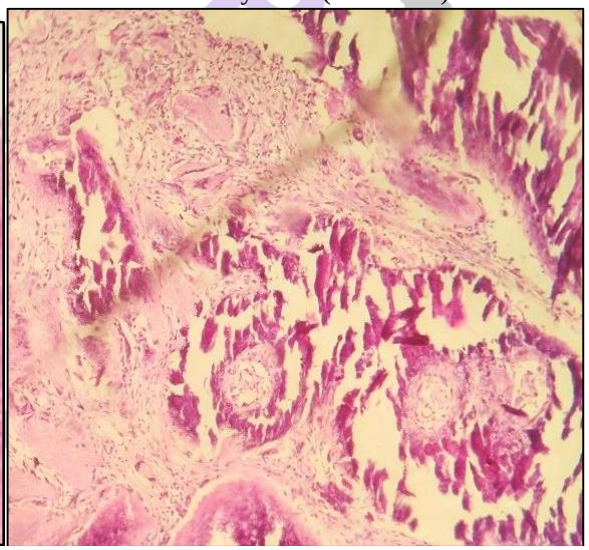


Fig 4. Calcification (H&E 40x)

DISCUSSION:
Pilomatricomas formerly called as Pilomatrixoma are superficial benign skin tumours mostly located in head and neck. They are the second most excised superficial masses in children after epidermoid cyst and excluding lymph nodes [11]. Clinically, these lesions present as solitary, firm, painless or subcutaneous masses. Growth is slow and may occur over a period of months to years. Pilomatrixoma are generally solitary tumors, but multiple tumors have been reported to occur in 2% to 3% of cases.[12] Multiple or recurring tumors may be found in association with Gardner syndrome,[13] myotonic dystrophy,[14] or Turner's syndrome.[15] Most of the worldwide studies showed a low incidence of pilomatricoma, representing about 0.12% of neoplasms involving the integument [18]. Since studies conducted in India are fewer in number an accurate assessment of its occurrence in general population cannot be made.

CONCLUSION:

Pilomatricoma, is usually surrounded by a fibrous capsule, typically occurs in the lower dermis and extends into the subcutis. However, if it occurs in the superficial papillary and mid-dermis it may perforate the epidermis through a process called transdermal elimination[17].According to Moehlenbeck, the incidence of pilomatricoma is low, representing about 0.12% of neoplasms involving the integument [18]. PMX is occasionally misinterpreted as squamous cell carcinoma,[19] but the young age of most patients, uniformity of the basaloid cells, and lack of significant nuclear atypia in the nucleated squamous cells facilitate differentiation between the two lesions. Malignant transformation of pilomatricoma is rare,[20] with fewer than 20 cases described in the world literature. Many tumors occurred on the head and neck, a cosmetically sensitive area. Consideration of this essentially benign tumor, with careful clinical and histopathologic examination, will lead to increased diagnostic accuracy. This is particularly important for young women in whom most of these tumors occur.

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Conflict of Interest: None

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