Pilomatricoma: histopathologic evaluation of 100 cases and introduction of new features

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Background: Pilomatricoma is a benign skin adnexal neoplasm. Various histological features are observed on microscopic examination. We aimed to evaluate this tumor's demographic and histological features in detail.

Methods: One hundred cases with a diagnosis of pilomatricoma were selected, and demographic and clinical data were entered into a checklist. The pathology slides were reviewed to confirm the diagnosis. The demographic profile of all patients, including age and gender, primary clinical impression, multiplicity of the tumor, microscopic features, and location of tumoral involvement, were extracted. Qualitative data were summarized using frequencies and percentages. Regarding descriptive analysis, the frequency of each histopathologic feature was calculated.

Results: Two groups of patients were identified regarding age. This tumor was more common in males among adult patients, while a female preponderance was seen in those under 18. Most lesions were located on the face (40%), followed by upper (32%) and lower (10%) limbs. In addition to well-known histological features, we observed intraepidermal pilomatricoma in two cases presenting unique histopathologic features. Both showed foci of suprabasal cleft formation, while one showed the Borst-Jadassohn phenomenon. These features, in addition to sebaceous differentiation and acantholysis of ghost cells, were not addressed in previous literature.

Conclusion: Understanding the diverse and new histological features of pilomatricoma is necessary for differentiating it from other adnexal and soft tissue tumors.

Keywords: adnexal tumor, pilomatrixoma, histopathology, Neoplasms

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INTRODUCTION

Pilomatricoma or pilomatrixoma is a benign calcifying skin adnexal neoplasm originating from hair follicles' matrix cells [1]. The lesion is mostly centered in the lower dermis, extending to the subcutaneous fat [2]. Although it emerges at any age,

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approximately 40% of pilomatrixomas are seen in children and younger adults. The definite predisposing causes of pilomatricoma are unknown. It could be associated with an insect bite, trauma, and surgery. Pilomatricoma is typically presented as a hard, tender, solitary, and mobile nodule with faceted edges, mostly seen on the head and neck and less frequently on the limbs. The nodules do not attach to deeper tissue and are usually covered by normal-color skin, although anetoderma can also be seen in the covering skin. The lesions are mostly asymptomatic, although pain and swelling are sometimes observed due to itching or palpation [3]. The presentation of multiple lesions is associated with the familial form of pilomatricoma. The familial form is rarely detected and closely associated with known syndromes such as Turner syndrome, Gardner syndrome, basal cell nevus syndrome, Rubinstein-Taybi syndrome, and myotonic dystrophy [4-6].

On microscopic examination, pilomatricoma is characterized by basaloid cells transforming into transitional cells, sometimes achieving squamoid features. Ghost cells with light or disappeared nuclei and extensive eosinophilic cytoplasm are also seen. Several histopathologic features have been evaluated in several studies so far [1,2,7]. This study evaluated clinicopathological characteristics of 100 cases of pilomatricoma from 98 patients to seek new histopathologic features of pilomatricoma alongside previously known features.

METHODS

Study materials

This cross-sectional study was conducted on 100 cases of pilomatricoma in 98 patients. The cases were selected from the pathology department of Razi Hospital in Tehran (the capital of Iran) between 2016 and 2020. Nighty-eight patients diagnosed with pilomatricoma based on prior pathology reports were evaluated.

Data collection

Based on the information recorded in the pathology results, cases with a diagnosis of pilomatricoma were identified, and demographic and clinical information were extracted and entered into a checklist. The pathology slides were reviewed to confirm the diagnosis. In cases with inappropriate low-quality slides, paraffin blocks were sectioned to obtain an appropriate pathology slide.

The inclusion criteria encompassed all cases with the final diagnosis of pilomatricoma registered in the archive system of the hospital's pathology department between 2016 and 2020. Cases with incorrect diagnoses and missing files were excluded.

Statistical analysis

The demographic profile of all patients, including age and gender, primary clinical impression, the multiplicity of the tumor, microscopic features, and location of tumoral involvement, were extracted and entered into a checklist. SPSS version 16 (SPSS Inc., Chicago, IL, USA) was used for data analysis. Qualitative data were summarized using frequencies and percentages. Regarding descriptive analysis, the frequency of each histopathologic feature was calculated. Continuous parameters are presented as mean ± SD. Two groups of patients were identified regarding age based on the model-based clustering method by using the mclust package in R software. The Kolmogorov-Smirnov test was used to evaluate the normality of the data. Also, the chi-squared test was used to check the demographic differences between the two age groups. P-values < 0.05 were considered significant.

Ethical consideration

This investigation was performed in accordance with the ethical standards of the Tehran University of Medical Sciences Ethics Committee and are compatible with the Helsinki Declaration.

RESULTS

Patient's basic information

One hundred lesions obtained from 98 patients were studied. All the patients, except for two, had solitary lesions. Multifocality was observed in two patients, each with two tumors in different anatomic locations. Regarding the first clinical impression, 48 (48%) cases were clinically diagnosed as pilomatricoma. Fifty-four patients (55%) were females, and the patients' range of age was 1 to 79 years, with a mean age of 27.1 ± 20.7. Two groups of patients were identified regarding age based on the model-based clustering method by using the mclust package in

R software (loglikelihood = -401.33, N = 95, df = 5, BIC = -825.42): A children group (< 18) with a mean age of 9.35 ± 4.45 and an adult group with a mean age of 39.23 ± 18.34 years.

In the adult group, lesions were more frequent in males ($P = 0.013$, OR = 2.19, 95% CI: 1.24–6.81), while females were predominantly affected in the children group. Most lesions were located on the face (40%), followed by upper (32%) and lower (10%) limbs. Other anatomical locations included neck (7%), hand (3%), scalp (3%), and back (2%), while ear, foot, and abdomen involvement each were seen in one patient. Face lesions were significantly more common in children than in adults (OR = 2.33, $P = 0.046$, CI: 1.01–5.38). However, there was no significant difference in the involvement of upper and lower limbs between the children group and the adult group (upper limbs: $P = 0.575$, OR = 1.286, 95% CI: 0.534–3.094, lower limbs: $P = 0.29$, OR = 3.043, 95% CI: 0.598–15.469). Likewise, no association was found between gender and the location of the lesions ($P = 0.512$).

Microscopic features

The main microscopic features of pilomatricoma included cellular composition and various differentiations, tumoral connection to the epidermis, transepidermal elimination of tumoral elements (Figure 1), ulceration of tumoral surface, cyst

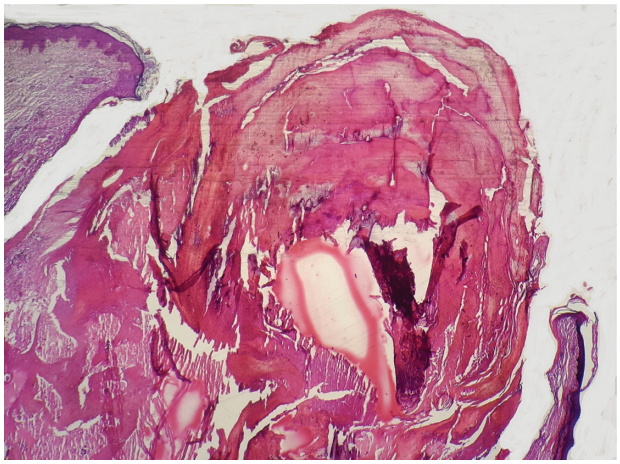

Figure 1. Transepidermal elimination of a large mass of keratinized shadow cells is seen at the center. The overhanging epidermis is evident at the periphery (H & E stain)

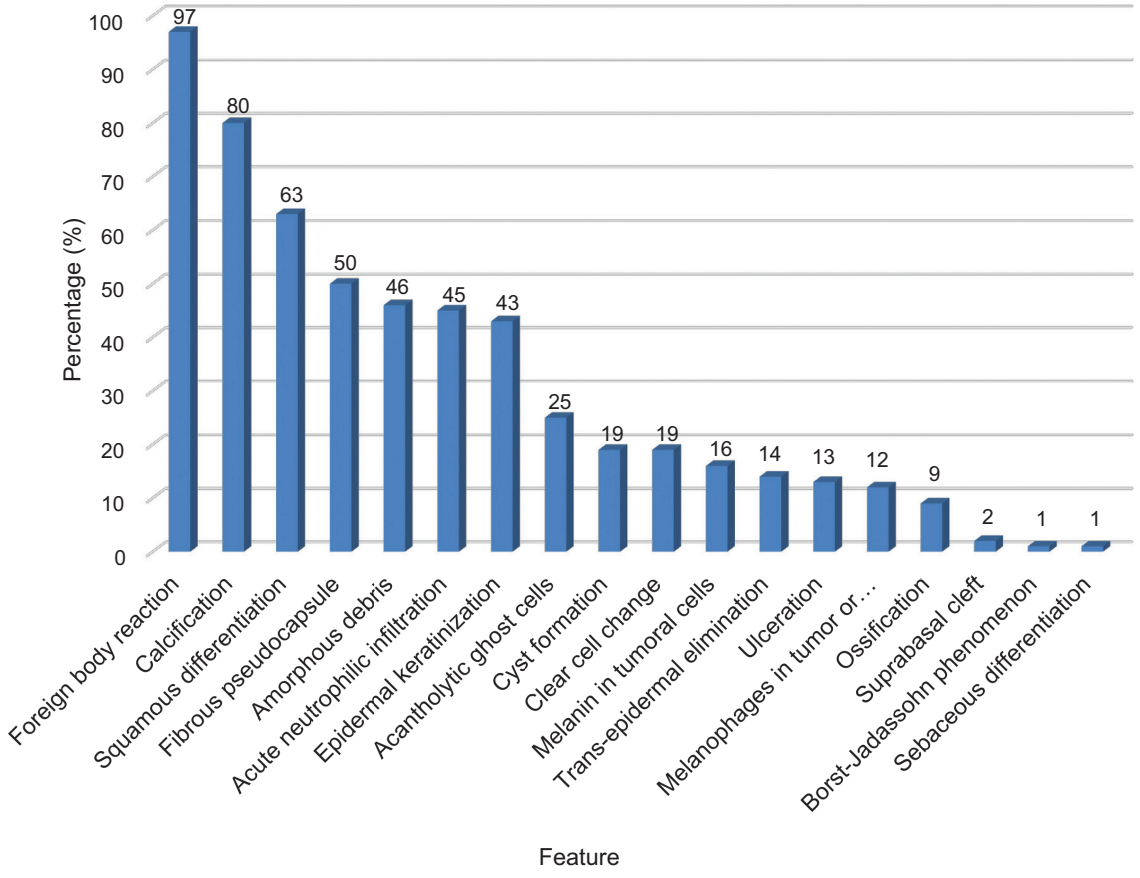

Figure 2. The microscopic features of pilomatricoma (%)

formation within the tumor, and inflammatory and stromal responses within and around the tumor such as foreign body reaction, fibrous pseudocapsules, and neutrophilic infiltration. Melanin deposition in melanophages and epithelial cells (including ghost cells), calcification, and ossification are also shown in Figure 2.

We observed intraepidermal pilomatricoma in two cases with unique histopathologic features. Both showed foci of suprabasal cleft formation, while one showed the Borst-Jadassohn phenomenon (Figures 3 and 4).

Regarding the tumor's average cellular composition, ghost cells constituted 82 ± 21.74% of tumoral cells, followed by basaloid cells (10.61 ± 14.49%) and transitional cells (5.08 ± 6.02%). Epidermal type keratinization was seen in 43%. Twenty-nine percent of the tumors were fully keratinized, composed only of ghost cells. In 25% of the tumors, the ghost cells showed acantholysis (Figure 5).

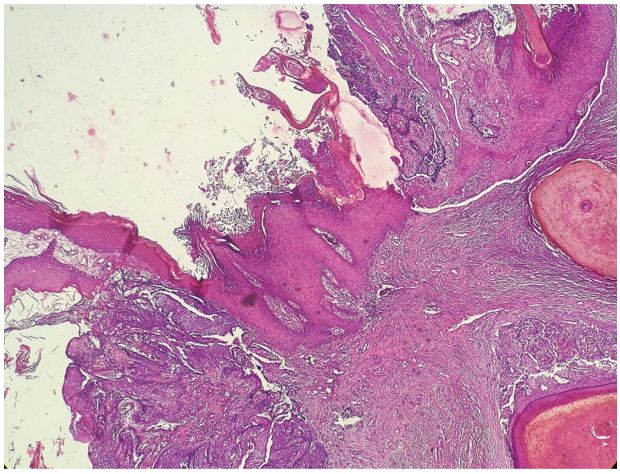

Figure 3. The intraepidermal component of this pilomatricoma shows suprabasal clefts with mild acantholysis (H&E stain)

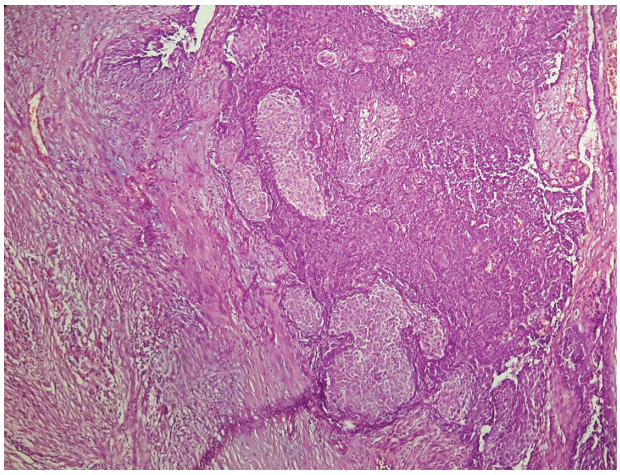

Figure 4. The Borst-Jadassohn phenomenon is seen in the intraepidermal component of the tumor as well as suprabasal clefts (H&E stain)

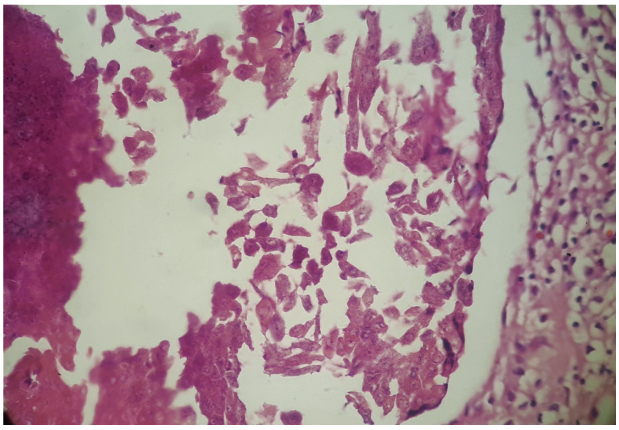

Figure 5. Acantholysis was a frequent finding in shadow cells (H&E stain)

Regarding cellular differentiation, squamous differentiation was detected in 37%, followed by clear cell changes in 19% and sebaceous differentiation in 1%.

Atypical nuclear morphology, including pleomorphism and loss of polarity, was seen in 4% and 2% of cases, respectively. In 89% of the cases, the mitotic count was less than 1/mm^2, and only 11% showed higher mitotic counts (2–5/mm^2), although none of them were atypical mitosis.

Necrosis was not observed, but amorphous eosinophilic debris was found in 46%.

Most of the tumors (72%) were located in the dermis, extending into the subcutis. The isolated involvement of dermis or subcutaneous fat was observed in 28% of the tumors (14% for each). Surgical excision was incomplete in 72%, meaning margins were involved in these cases.

In our statistical analysis, we could not find any significant relationship between most histological features and demographic variables. However, there was a significant association between age and transepidermal elimination, which was more common in adults than children (P = 0.015, OR = 5.85, 95% CI: 1.23–27.83).

DISCUSSION

This cross-sectional study evaluated the clinicopathological features of 100 lesions diagnosed

as pilomatricoma. Approximately half of them were correctly diagnosed as pilomatricoma by clinicians prior to the biopsy. This tumor was more common in males in adult patients, while a female preponderance was seen in children.

We observed a higher rate of face involvement in children compared to adults. Previous reports found pilomatricoma mostly in the head and neck region [5,7]. This is while some studies found that most lesions were on the upper limbs [1,8]. Similarly, our study found that the face was the most common region involved, followed by the upper extremities.

In 1961, Forbis and Helwig used the term 'pilomatricoma' to describe groups of tumors that arise from the hair follicle matrix [9]. Previous studies showed a female predominance of pilomatricoma in the first and second decades of life, similar to our findings [4,7]. In this series of cases, we found more male cases of pilomatricoma in the adult group, in accordance with the previous report by Guinot-Moya *et al.* [3].

Multiple lesions are most commonly seen in patients with the underlying syndrome, including Gardner syndrome, Turner syndrome, Sotos syndrome, Rubinstein-Taybi syndrome, medullary thyroid carcinoma, sarcoidosis, and Steiner syndrome [6,7,10,11]. Multiple lesions were seen in 2.04% of our cases. However, these patients had no accompanying syndromes. Our result is similar to the Moehlenbeck study, which described 2,000 patients with pilomatricoma [12]. The highest recorded prevalence of multiple pilomatricoma in the literature is 26.7% [13].

Histologically, pilomatricoma is characterized by a sharply demarcated lesion, including ghost and basaloid cells, besides other features such as calcification and foreign body reaction. During lesion progression, basophilic basaloid cells turn into ghost cells. The ghost cells, also named shadow cells, are eosinophilic cells with lost nuclei, mostly seen in keratinized areas [5]. Clear cells that indicate outer sheath differentiation were seen in about 20% of our cases, while other studies reported figures of 30 to 40% [1].

Secondary changes occur in varying degrees in most pilomatricoma lesions. Previous reports documented that calcification ranged from 19–85%, and ossification reached a maximum of 10% [1,7]. In this study, we found a high rate of calcification. Regarding ossification, our result aligns with an Indian report of about 10%. Foreign body reaction, another secondary change, was seen in 97% of our cases.

We introduced some novel histopathologic features not addressed in the previous literature. These include acantholysis with suprabasal clefting and the Borst-Jadassohn phenomenon in intraepidermal components of pilomatricomas, as well as sebaceous differentiation and acantholysis of ghost cells.

Clinicians and pathologists should be aware of the key differential diagnoses of pilomatricoma. For instance, dermoid cysts are common in children and present with regular and immobile nodules. Epidermal cysts are often seen in the older age group, presenting as firm, mobile, and round lesions. Imaging studies could help to rule out malignancy [10,14]; sonography can investigate the depth of the lesion [10]. It is crucial to differentiate pilomatrix carcinoma from benign nodules in the adult group, especially in men. Pilomatrix carcinoma is an extremely rare tumor that frequently involves lymph nodes; local recurrence and systemic organ metastasis tend to occur [15]. Mutations in exon 3 of the β-catenin gene (CTNNB1) are a predisposing factor for both malignant and benign pilomatricoma [16,17]. On the histopathological examination, the carcinoma usually exhibits the characteristics of various degrees of anaplasia, a high degree of mitotic rate (about 8 to 10 mitoses per high-power field), and atypical mitotic figures [16]. We observed some nuclear atypia in the histological evaluation of our cases, but none fulfilled the malignancy criteria.

The main limitation of our study was the limited sample size, which may affect the results, especially the frequency of rare features such as intraepidermal components and sebaceous differentiation.

CONCLUSION

Pilomatricoma is a well-known adnexal tumor with characteristic clinical and histological features. In the present study, in addition to well-known histologic features, we found some new histological features, such as suprabasal cleft formation, Borst-Jadassohn phenomenon, sebaceous differentiation, and acantholysis of ghost cells. Understanding this tumor's diverse and new histological features is necessary to differentiate it from other adnexal and

soft tissue tumors.

Authors contributions

Alireza Ghandan, Kambiz Kamyab, Vahidehsadat Azhari, Anahita Borzouei and Shirin Taraz Jamshidi contributed in histological evaluation of the specimens. Hamidreza Mahmoudi conducted clinicopathologic correlation. Ali Nili drafted the manuscript. All authors carefully reviewed and approved the final manuscript.

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Conflict of Interest: None declared.

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