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# Unusual age and unusual localization: the eye-catching histology makes the diagnosis.

**Case Presentation:**

A54-year-old man suffered of several angiolipomas on the forearms and upper body. The surgeon observed at time as well a tumor lesion on the right upper eyelid. An additional angiolipoma was suspected as well at this localization. Due to the localization the patient was referred the ophthalmology clinic.

The patient presented with a painless, gradually enlarging mass on his right upper eyelid. He denied any history of trauma or rapid growth. Beside his angiolipomas he had no significant medical history and was not taking any medication.

On examination,0.8x0.5cm, well-circumscribed, firm, non-tender nodule was noted on the right upper eyelid. The overlying skin appeared slightly erythematous. There was no ulceration. The mass was not attached to the underlying structures, suggesting it was subcutaneous.

A differential diagnosis of sebaceous cyst, chalazion, and benign neoplasm was considered. The patient was advised to undergo an excisional biopsy to establish a definitive diagnosis.

*Histology*

Histopathological analysis revealed a tumor predominantly consisting of shadow cells. There was a small proportion basaloid cells and focal calcification. The sparse soft tissue around the tumor cells showed a lymphohistiocytic inflammation with foreign body giant cells. There was no increased mitotic activity and no cellular pleomorphism of the few basaloid cells. The remarkable shadow cells made straightforward the diagnosis

*Diagnosis*

Pilomatrixoma (PMX)

**Discussion**

PMX was first described by Malherbe and Chenantais in 1880 and is as well called calcifying epithelioma of Malherbe. It is a benign adnexal neoplasm with differentiation mainly to the matrix of the hair follicle and the hair itself.

While it can develop anywhere on the body, it exhibits a predilection for the head, neck (>50%) and upper limb regions (≈25%). PMX can occur at any age but is more commonly observed in children and adolescents. About 60% of the cases are diagnosed in the first 2 decades of life. In a series of 209 cases, the lesions occurred with a bimodal peak of presentation in the first and sixth decade with a female preponderance (2:1 to 3:1)[1]. In the periocular region the eyebrow is mostly involved. In contrast, eyelid PMX is less common, and often clinically misdiagnosed. There are several case reports. A recent retrospective study reported 19 clinicopathological PMX of the eyelid from the Wilmer Eye Institute, Johns Hopkins Hospital, Baltimore, diagnosed between 1981 and 2022[2].The mean age was 24 years (range 2–63 years) with 8 (42%) and 4 (21%) of patients in the first and second de cades of life, respectively. There were 12 (63%) females and 7 (37%) males. Tumors were

most common on the upper (n = 14) as compared to the lower (n = 5) eyelid The lesions varied from 2 mm to 12 mm in maximum dimension.

PMX generally presents as a fairly well-circumscribed, smooth -surface, cystic, or firm slow growing nodule. The consistency of the nodule is dependent on the degree of calcification. Most examples range in size from 1-3cm in largest dimension. Rapid growth may result from hemorrhage or give a clinical impression of malignancy. However rare variants such as giant forms (up to 15 to 20 cm)[3], bullous, pigmented or exophytic exist.

*PMX Histology*

- Well-circumscribed, dermal to subcutaneous nodule
- 2 cell types: Basaloid cells and shadow cells
- Lesion often surrounded by fibrous connective tissue capsule
- Newer lesions may be cystic
- Dystrophic calcification or ossification is commonly seen

PMXs are usually solitary, though multiple lesions may be associated with certain genetic conditions such as Gardner's syndrome, myotonic dystrophy, Turner's syndrome, Sotos syndrome, trisomy 9 and other rare disease [4,5]. Most sporadic cases possess a mutation in CTNBB1 (β-catenin), resulting in the activation of Wnt signaling [6,7]. Interestingly, of all above mentioned diseases Wnt signaling pathway is just activated in Gardner's syndrome. Therefore, whether multiple PMX have a genuine association to the mentioned diseases or represent a coincidence is yet to be determined; however, this mutation is identified in a range of other neoplasms as well. The reported relapse rate is between 2% and 6% possibly due to incomplete excision[7]

A clinicopathologic correlation of 485 eyelid tumors in childhood and adolescence at the University Eye Hospital Bonn from 1998-2023 found PMX in 2.1%. The most frequent tumor was chalazion (57.3%), followed by dermoid cysts (16.7%) and molluscum contagiosum (9.6%)[8].

*Subtypes of Pilomatrixoma*

Proliferating PMX occurs in elderly patients (mean age70 years

Atypical features: Large size, variable nuclear atypia, and mitotic figures. The lesion imitates pilomatrical carcinoma and perhaps represents an intermediate precursor lesion.

Aggressive Pilomatrixoma

Reported in a small group of children and young adults

Higher mitotic rate (7/10HPF), more basaloid cells, conventional 1-2/10HPF), atypia, prominent nucleoli, single cell necrosis. Presence of invasive cords of benign tumor cells into adjacent dermis.

Pigmented Pilomatrixoma

Melanin is present in shadow cells or stromal melanophages. May be focal and very prominent and give the tumor a "vanilla fudge" gross appearance. Rarer than melanin pigment is proliferation of conspicuous dendritic melanocytes within PMX providing a degree of overlap with melanocytic matricom (most probably a variant of PMX).

Perforating Pilomatrixoma

PMX is extruded from the upper dermis to the skin surface through a perforating epidermal or infundibular channel. Atypical clinical feature with rapid development and reddish, exophytic appearance with surface alteration

Unusual stromal changes

Prominent desmoplastic stromal reaction, resembling a malignant mesenchymal tumor.

Anetodermic variants the surrounding stroma is remarkably oedematous, and vascular-rich with abundant mucin

Extramedullary hematopoiesis

Found in 6% 11

**Differential**

Pilomatrical Carcinoma [12]

May develop from a preexisting benign PMX

- Often connected to epidermis
- Ulcerated, asymmetrical, dermal to subcutaneous nodule
- Poorly circumscribed, hypercellular, and infiltrative tumor
- Focal areas of true tumor necrosis
- Basophilic cells with prominent nucleoli and numerous mitoses
- Foci of shadow cells are helpful in diagnosis
- Vascular/lymphatic invasion (rare)
- Melanocytes and melanin pigment within some tumors (malignant melanocytic matricoma)

Mainly local aggressive, which often recurs following simple or incomplete removal. Metastatic disease occurs in about 15% of cases.[12]

**Conclusion**

PMX is a rare but important diagnosis to consider when evaluating eyelid masses. While it can resemble other benign conditions, its distinct histopathological features aid in definitive diagnosis. Surgical excision is the treatment of choice, with a low recurrence rate following complete removal. This case emphasizes the importance of considering pilomatrixoma in the differential diagnosis of periocular masses, even in adult patients.

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