International Journal of Surgery Case Reports 114 (2024) 109085

Contents lists available at ScienceDirect

International Journal of Surgery Case Reports

journal homepage: www.elsevier.com/locate/ijscr

Case series

Peri-ocular proliferative apocrine hidrocystoma (cystadenoma): A clinicopathological case series

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ARTICLE INFO

Keywords:
Apocrine cystadenoma
Hidrocystoma
Eyelid
Periocular
Skin
Histopathology

ABSTRACT

Introduction: Apocrine cystadenomas are rare, benign tumors that might arise in the periocular region from glands of Moll. They characteristically demonstrate proliferative features on histopathological examination, which differentiate them from simple hidrocystomas.

Presentation of cases: We retrospectively identified 4 consecutive cases of apocrine cystadenomas in male patients with a mean age of 48.5 years (range 20–62). One of the cases was a recurrent lesion. The Preoperative clinical diagnosis was mostly hidrocystoma. All patients agreed on complete surgical excision of their cystic lesions. Histopathological review of the excised cysts confirmed the diagnosis of apocrine cystadenoma based on the presence of proliferative features with no atypia or infiltrative behavior. Cases are summarized in Table 1 and the histopathological appearance is demonstrated in the included figure.

Discussion: Apocrine cystadenoma is rare. It occurs in the areas of skin with hair follicles, such as the axilla, neck, and trunk, and may be mistaken for other skin lesions, such as nevi or syringomas. In the eyelid region, they are commonly missed and frequently diagnosed as simple hidrocystoma due to the presence of bluish hue such as in our series. Recurrence is rare but was found in one of our patients at initial presentation. Our series included unique locations of this lesion in the medial canthus in one patient and near the eyelid tarsus in another.

Conclusion: Ophthalmologist should be aware of the rare occurrence of this lesion in the periocular region. Further studies to explain the etiology of such proliferative nature in apocrine cysts would be interesting.

1. Introduction

Apocrine cystadenomas are rare, benign tumors that arise from sweat glands in various parts of the body [1]. Apocrine cystadenomas display proliferative features on microscopy, which distinguishes them from the more common hidrocystomas [2]. They represent an adenomatous cystic proliferation of apocrine glands, which are found mainly in areas rich with hair follicles, such as the face, neck, axilla, and trunk [3]. In the periocular region, they originate from the glands of Moll along the eyelid margin and canthi.

This retrospective study presents a series of four cases of eyelid and periocular cystadenomas. The study focuses on describing their clinical and histopathological characteristics with brief literature review on similar cases in the periocular location. The aim of this study is to attract the attention of ophthalmologists and oculoplastic surgeons to this rare ocular tumor.

2. Methods

No IRB approval is needed for case reports. However, this retrospective case series was prepared according to the ethical standards of the human ethics in accordance with the Helsinki Declaration. Written informed consent was obtained from the patients for publication of this case series and accompanying images. A copy of the written consent is available for review by the Editor-in-Chief of this journal on request.

Research registry of the case series: researchregistry# 9653. We

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https://doi.org/10.1016/j.ijscr.2023.109085
Received 30 October 2023; Received in revised form 16 November 2023; Accepted 17 November 2023
Available online 20 November 2023

retrospectively report four cases with identical histopathological features to this described entity. All lesions were similarly treated with complete surgical excisional biopsy in 2 centers. The surgical procedure was performed under topical anesthesia in each corresponding center where the patient originally presented by the primary caring consultant ophthalmologist/oculoplastic surgeon. The obtained specimens were histologically examined by the senior author for confirmation of the peculiar entity of apocrine cystadenoma. This case series has been prepared and reported according to the PROCESS criteria [4].

3. Results

Four consecutive cases have been included and summarized in Table 1. The age range was wide (20 to 62 years) with a mean of 48.5 years. Three out of the 4 cases were diagnosed as simple hidrocystoma and the remaining case (Case 3) was diagnosed as epidermal cyst. The cystic lesion was recurrent in a single patient (Case 1) following excision elsewhere. All cases were males, underwent surgical excisional biopsy of the cystic lesions by experienced oculoplastic surgeon. The patients tolerated the procedure well with no complications, and had short term follow up duration of approximately one year. The characteristic histopathological features in the excised tissue were irregular cystic structure, primarily lined by myoepithelial cells, and inner columnar cells with apical decapitations. The epithelial cyst wall demonstrated papillary projections with connective tissue cores representing true adenomatous hyperplasia (Fig. 1A & B). Therefore, all cases were diagnosed as apocrine cystadenoma. The following is brief description of individual cases.

4. Case 1

A 59-year-old male with a medical history of diabetes and hypertension presented with a left medial canthal cyst that has been present for one year. The cyst measured 3 mm × 3 mm and had a bluish tinge, with a history of previous surgical excision 2 years before. The bluish color owing to the Tyndall light effect was highly supportive of the clinical diagnosis of a recurrent hidrocystoma. The lesion was carefully removed surgically to ensure complete excision of the cyst wall, and histological assessment was performed. The sections showed pieces of skin with unremarkable keratinizing stratified squamous epithelium. The underlying dermis displayed an irregular cystic structure, which was primarily lined by myoepithelial cells, and inner columnar cells with apical decapitations. Papillary projections representing adenomatous hyperplasia of the epithelial cyst lining were also noted. The overall histopathological appearance was consistent with hidrocystoma of the apocrine type, which demonstrated proliferative features, thus consistent with apocrine cystadenoma.

5. Case 2

A 53-year-old male with no known medical problems presented with a painless cyst in the nasal fornix of the left upper lid, which has been present for two years. A computerized tomography (CT) scan showed a fluid-filled cyst of approximately 2 cm × 0.8 cm in size, slightly abutting the superior globe, and located superior to the orbital septum over the oblique tendinous insertion. No deeper extension or other complications were present. The clinical diagnosis was either hidrocystoma or epithelial cyst. Excision of the cyst was done through a conjunctival approach under general anesthesia. The cyst was found to be strongly adherent to the tarsus but was entirely removed. The cyst was lined by apocrine type of epithelial cells and showed similar histopathological appearance. Surgical excision site healed nicely with no recurrence noted.

6. Case 3

A 20-year-old male with no medical history presented with a 4-year history of a painless subcutaneous cystic mass near the right superior orbital rim. The mass was firm, mobile, and transilluminating. It was not associated with erythema or discharge and did not change in size over the disease's duration. Interestingly, the magnetic resonance imaging in this case showed mildly complex cystic lesion in the right eyelid inferior to the superior orbital rim measuring 13.6 mm × 6.8 mm demonstrating fine internal septations with faint marginal enhancement. The clinical diagnosis was more in favor of an epidermal cyst considering the complexity of the mass that was showing solid and cystic components. The lesion was excised completely through a lid crease incision with similar tissue diagnosis. The proliferative nature of the lesion might explain the unique complex appearance, presence of septations and compartment-like configuration by the radiological study.

7. Case 4

A 62-year-old diabetic male presented with a 6-month history of a left upper lid cystic lesion located close to the eyelid margin, measuring 2mmx2mm with positive transillumination and no destruction of the surrounding anatomical structures. The clinical diagnosis was simple hidrocystoma. The lesion was surgically excised by the oculoplastic surgeon without complications. The histopathological examination of the excised cyst revealed proliferative findings consistent with apocrine cystadenoma. No recurrence occurred within a follow up period of one year.

8. Discussion

Apocrine cystadenoma is a rare benign skin tumor first described by Mehregran et al. [1]. It is characterized by distinctive histological features, including papillomatous and adenomatous growth of luminal cells, leading to the formation of cystic lesions that often have a bluish hue. These cystic growths can sometimes be mistaken for other skin lesions, such as nevi or syringomas. While apocrine cystadenomas most frequently occur in the eyelid region, they have also been reported in areas with a high density of hair follicles, such as the axilla, neck, and trunk [3]. One of the challenges in diagnosing apocrine cystadenoma is that it can be easily confused with apocrine hidrocystoma, which lack the characteristic proliferative features of apocrine cystadenomas. Clinical differentiation between apocrine cystadenoma and its non-proliferative counterpart is nearly impossible, making histopathological examination a necessity for an accurate diagnosis. In our series three out of the 4 cases were diagnosed pre-operatively as hidrocystomas. Thus, none of the ophthalmic surgeons has been eager to obtain clinical photos for such a common simple lesion.

Table 1
Summary of 4 cases of apocrine cystadenoma:

Case #	Age (years)	Gender	Location	Size (mm)	Duration	Pre-operative clinical diagnosis
1	59	Male	Left medial canthus	3 × 3	1 year	Hidrocystoma
2	53	Male	Left upper lid, adherent to the tarsus	20 × 8	2 years	Epithelial cyst Hidrocystoma
3	20	Male	Right upper lid, subcutaneous. Near the superior orbital rim	13.6 × 6.8	4 years	Epidermal cyst
4	62	Male	Left upper lid	2 × 2	6 months	Hidrocystoma

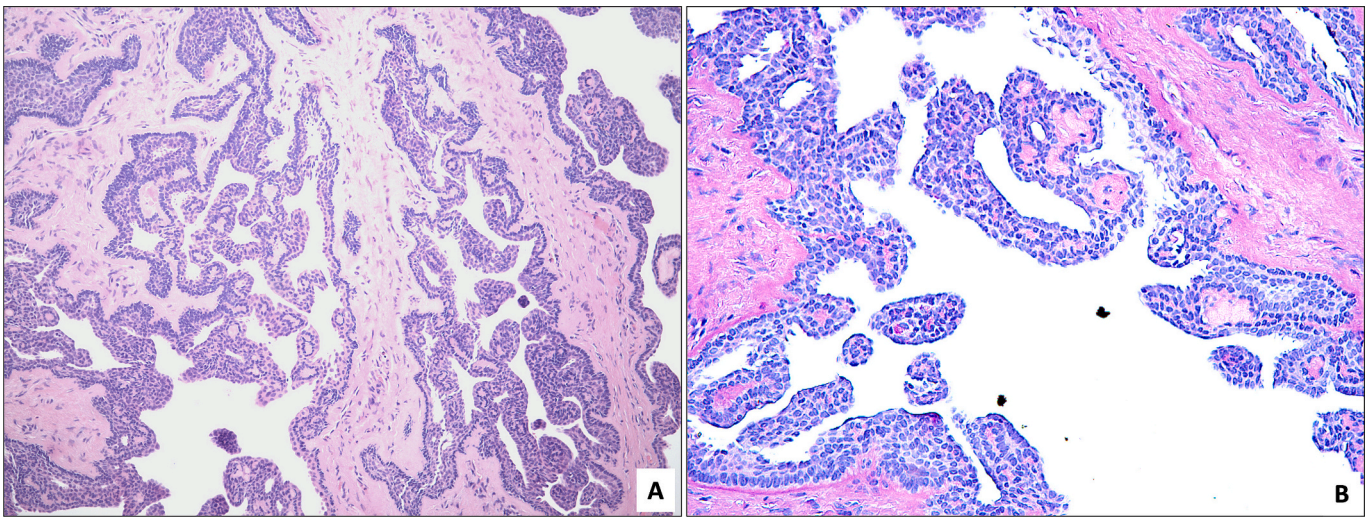

Fig. 1. A: The histopathological appearance of the irregular cystic structure, lined by myoepithelial cells, inner columnar cells, and papillary projections (Original magnification ×100, Hematoxylin and eosin). B: Higher power appearance of the papillary proliferations with connective tissue cores representing apocrine cyst adenomatous lesion (Original magnification ×200, Periodic Acid Schiff).

In an effort to clearly differentiate these lesions, Sugiyama et al. [2] attempted to categorize apocrine hidrocystomas in a practical format histologically by their papillomatous or adenomatous growth patterns. This growth can be either diffuse throughout the lesion or localized within it. The presence of true papillae with connective tissue cores and lumen-forming units categorizes the lesion as an apocrine cystadenoma, which has been evident in our cases. In contrast, lesions that contain pseudo-papillae (epithelial projections into the lumen without connective tissue cores) are classified as "non-proliferative" hidrocystomas. Cystic lesions lined by a double layer of cuboidal epithelium are categorized as having "no growth".

Although periocular apocrine cystadenomas are more commonly found in the eyelid region, it is noteworthy that they can present in other anatomical locations, which is peculiar in our series. For example, in the cases discussed above, one patient had a medial canthal lesion, and another had a firm cystic mass adherent to the tarsus, both of which deviate from the typical anatomical locations reported in the literature. Additionally, Case 1 presented with a recurrent lesion two years after removal, suggesting that recurrences of apocrine cystadenoma can still occur, albeit infrequently [5,6]. The importance of properly diagnosing these cases and planning for complete excision apart from the possibility of recurrence is the significance of the presence of atypia or infiltrative pattern. It has been suggested that hidrocystoma is a precursor lesion that may progress to adenoma then carcinoma particularly endocrine mucin producing sweat gland carcinoma [7]. The authors demonstrated strong diffuse reactivity of the adenomatous epithelium in 80 % of the proliferative hidrocytomas to estrogen and progesterone receptors (ER and PR) by immunohistochemical staining. This type of staining was lacking in the non-proliferative simple cysts.

Limitations of the study include its retrospective nature and the small number of cases owing to the rarity of this lesion. However, attracting the attention to the differentiating features radiologically of these cystic lesions and the careful histopathological examination are essential.

9. Conclusions

Apocrine cystadenoma is a unique benign skin tumor characterized by papillomatous and adenomatous growth of luminal cells. Accurate diagnosis relies on histopathological assessment, which can distinguish it from non-proliferative hidrocystoma. While these tumors are most commonly found in the eyelid region, they can appear in other locations such as the canthal areas and tarsal plate. Recurrence is rare but still possible. Further research is recommended on the patho-etiology of such lesions, their immunohistochemical characteristics, and proliferative behavior in relation to the suggested hypothesis of being a precursor to carcinoma. Better clinical differentiation between the simple hidrocystoma and its proliferative counterpart is essential to identify and to manage these unusual lesions properly especially in view of the above-mentioned possibility.

Consent

General informed written consent was obtained from the patients including permission for anonymous use of photos and for reporting. A copy of the written consent is available for review by the Editor-in-Chief of this journal upon request.

Provenance and peer review

Not commissioned, externally peer reviewed.

Ethical approval

IRB is not required for case reports in our institute according to the Research/Human Ethics Committee. However, information was obtained and reported in a manner that was compliant with the standards set forth by the Health Insurance Portability and Accountability Act, and the Declaration of Helsinki as amended in 2013.

Funding

This research did not receive any specific grant from funding agencies in the public, commercial, or not-for-profit sectors.

Author contribution

FMA & AMA: Data collection and writing the first draft of the manuscript. **AMYM**: Histopathological diagnosis and images. **HMA**: Critical review of the manuscript for submission as Corresponding and Senior author.

Guarantor

Prof. Hind Manaa Alkatan.

Research registration number

1. Name of the registry: Research Registry.
2. Unique identifying number or registration ID: researchregistry9653.
1. Hyperlink to your specific registration (must be publicly accessible and will be checked): https://www.researchregistry.com/browse-the-registry#home/.

Conflict of interest statement

Authors have no conflicts of interest in relation to this work.

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