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Case Series

Pathology Section

Histopathological Spectrum of Clinically Diagnosed Epidermoid Cyst: A Series of 20 Cases

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ABSTRACT

Epidermoid cysts are among the most common subcutaneous nodular lesions encountered in clinical practice and are often diagnosed clinically. However, a wide spectrum of benign and malignant cutaneous adnexal and soft-tissue tumours can closely mimic these lesions, posing significant diagnostic challenges. The present retrospective case series was conducted at a tertiary care hospital over a one-year period (January–December 2025) to evaluate the histopathological spectrum of lesions clinically diagnosed as epidermoid cysts. A total of 20 cases (12 males and eight females) were analysed. Clinical details were recorded and all excised specimens underwent histopathological examination. The majority of cases showed clinicopathological discordance. Skin adnexal tumours were the most frequent mimickers (11 cases), including nodular hidradenoma (n=5), pilomatricoma (n=3), eccrine spiradenoma (n=1), chondroid syringoma (n=1) and pilomatrix carcinoma (n=1). Peripheral nerve sheath tumours were identified in four cases. Other diagnoses included basal cell carcinoma (n=1), calcinosis (n=1), dermoid cyst (n=1), ganglion cyst (n=1) and papillary cystadenoma (n=1). Two cases were malignant. The present study highlights significant clinicopathological discordance and the risk of missed malignancies in clinically suspected epidermoid cysts. Histopathological examination {Haematoxylin and Eosin (H&E)} remains essential for definitive diagnosis and a multidisciplinary approach is critical for appropriate patient management.

Keywords: Calcinosis, Carcinoma, Peripheral nerve sheath tumour, Skin adnexal tumour

INTRODUCTION

Epidermoid cyst is one of the most frequent subcutaneous nodular lesions seen in clinical practice [1]. They can develop anywhere on the body, although they prefer to form on the face, neck and trunk. While the majority of epidermoid cysts develop naturally in hair-bearing regions, they can also develop as a result of trauma or on the palms and soles [2].

The diagnosis of epidermoid cysts is often made clinically, based on their characteristic appearance and location. However, this approach can be misleading, as other skin lesions can mimic epidermoid cysts. Skin adnexal tumours and soft-tissue tumours, in particular, can pose a diagnostic challenge, as they can present with similar clinical features.

The present article presents a series of cases in which patients were clinically misdiagnosed with epidermoid cysts and subsequent histopathological examination revealed a surprising diagnosis of skin adnexal tumours and soft-tissue tumours. These cases underscore the importance of a thorough histopathological evaluation in accurately diagnosing skin lesions, even with strong clinical suspicion.

CASE SERIES

The present case series was conducted at a tertiary care Hospital in Sonipat, Haryana from January to December 2025 and included 20 cases clinically diagnosed as epidermoid cysts that were subsequently identified as skin adnexal or soft-tissue tumours on histopathology. Patients of all age groups and both sexes, clinically diagnosed cases of epidermoid cyst and cases that underwent surgical excision and histopathological evaluation were included. Inadequate or poorly preserved tissue specimens and cases lacking complete clinical or histopathological data were excluded.

The present study included 20 patients, comprising 12 males and eight females, with an age range of 10-68 years. The most commonly involved site was the forearm 4 (20%), followed by the scalp 3 (15%). Other sites included postauricular region (n=2), scrotum (n=2), neck (n=2) and single cases involving the chest, thigh, arm, cheek, back, foot and infraauricular region [Table/Fig-1].

On clinical examination, the majority of lesions were firm in consistency 10 cases (50%) and presented as painless swellings 9 cases (45%). A central punctum was identified in 6 cases (30%). Pain was reported in 5 cases (25%) and signs of inflammation, such as local erythema, were observed in 3 cases (15%). Rapid increase in size was noted in 2 cases (10%), while surface changes, including hyperpigmentation or bluish discolouration, were also seen in 2 cases (10%). Overall, the majority of lesions were slow-growing 18/20 (90%) and clinically suggestive of benign pathology, whereas a small proportion 2/20 (10%) demonstrated rapid enlargement, raising clinical suspicion of possible malignancy [Table/Fig-1]. On gross examination, all lesions were skin-covered nodules measuring between 1 cm and 4 cm. Cut sections revealed solid to cystic areas with appearance varying from pearly white to brown [Table/Fig-1,2a-d].

Histopathological examination revealed that the majority of lesions were benign (n=18, 90%), with only 2 malignant cases (10%). Skin adnexal tumours constituted the most common category (n=11, 55%), including nodular hidradenoma (n=5), pilomatricoma (n=3), eccrine spiradenoma (n=1), chondroid syringoma (n=1) and pilomatrix carcinoma (n=1) [Table/Fig-3a-d].

Peripheral nerve sheath tumours accounted for 4 cases (20%), comprising neurofibroma (n=2), schwannoma (n=1) and neuroma (n=1) [Table/Fig-4a-d]. Other histopathological diagnoses included dermoid cyst (n=1), papillary cystadenoma (n=1), ganglion cyst (n=1), calcinosis (n=1) and basal cell carcinoma (n=1). The two malignant cases identified were basal cell carcinoma and pilomatrix carcinoma and these were the cases that showed rapid enlargement clinically. All patients had an uneventful postoperative recovery. The follow-up duration ranged from four months to 12 months. No recurrence was observed in benign cases (n=18) during the available follow-up

S. No.	Age/ Sex	Site	Duration	Clinical findings	Clinical diagnosis	Gross findings	Histopathological diagnosis	Nature of lesion	Follow-up
1.	68/M	Right postauricular,	5 months	3 cm, painless, central punctum +	Epidermoid cyst	Skin covered, 3 cm in size, C/S- solid, cystic	Nodular hidradenoma	Skin adnexal tumour	Uneventful
2.	48/F	Scalp	3 months	1 cm, firm, slow growing	Epidermoid cyst	Skin covered, 1.5 cm in size, C/S- solid, cystic	Nodular hidradenoma	Skin adnexal tumour	Uneventful
3.	10/F	Scalp	6 months	1 cm, central punctum +	Epidermoid cyst	Skin covered, 1 cm in size, C/S- solid, cystic grey-yellow	Nodular hidradenoma	Skin adnexal tumour	Uneventful
4.	51/F	Chest	1 year	3 cm, firm, central punctum+	Epidermoid cyst	Skin covered, 3 cm in size, C/S- grey-white homogenous with cystic area	Nodular hidradenoma	Skin adnexal tumour	Uneventful
5.	34/M	Left thigh	6 months	2 cm, firm, local erythema +	Epidermoid cyst	Skin covered, 2.5 cm in size, C/S- solid, cystic	Nodular hidradenoma	Skin adnexal tumour	Uneventful
6.	44/F	Left arm	1 year	1.5 cm, painless, central punctum +	Epidermoid cyst	Skin covered, 1.5 cm in size, C/S- grey-white	Pilomatricoma	Skin adnexal tumour	Uneventful
7.	13/M	Nape of neck	2 year	3 cm, firm, mobile	Epidermoid cyst	Skin covered, 3 cm in size, C/S- grey-white	Pilomatricoma	Skin adnexal tumour	Uneventful
8.	17/F	Left forearm	6 months	2 cm, central punctum +	Epidermoid cyst	Skin covered, 2 cm in size, C/S- grey-white and gritty	Pilomatricoma	Skin adnexal tumour	Uneventful
9.	42/F	Left neck	5 months	3 cm, painful, local erythema +	Epidermoid cyst	Skin covered well-circumscribed, 3.5 cm in size, C/S- grey-white solid	Eccrine spiradenoma	Skin adnexal tumour	Uneventful
10.	25/F	Left forearm	4 months	2.5 cm, firm, bluish discolouration	Epidermoid cyst	Skin covered, 2.5 cm in size, C/S- grey-white solid with myxoid appearance	Chondroid syringoma	Skin adnexal tumour	Uneventful
11.	35/M	Right infraauricular	1 year	4 cm, rapidly growing	Epidermoid cyst	Skin covered, 4 cm in size C/S- grey-white solid with necrosis and calcification	Pilomatrix carcinoma	Skin adnexal tumour	Lost to follow up
12.	21/M	Left forearm	5 months	1.5 cm painful	Epidermoid cyst	Well-circumscribed, 1.5 cm in size	Neurofibroma	Peripheral nerve sheath tumour	Uneventful
13.	23/M	Back	7 months	2 cm, painful	Epidermoid cyst	Well-circumscribed, 2 cm in size	Neurofibroma	Peripheral nerve sheath tumour	Uneventful
14.	50/M	Scalp	1 year	2.8 cm, firm, slow growing, painful, local erythema +	Epidermoid cyst	2.8 cm in size, C/S- grey-yellow glistening	Schwannoma	Peripheral nerve sheath tumour	Uneventful
15.	40/M	Left forearm	6 months	1.5 cm, painful	Epidermoid cyst	Skin covered, 1.7 cm in size	Neuroma	Peripheral nerve sheath tumour	Uneventful
16.	23/M	Left postauricular	5 year	2 cm, central punctum +	Epidermoid cyst	Skin covered, 2 cm in size, C/S- hair +	Dermoid cyst	Benign cyst	Uneventful
17.	47/M	Right cheek	4 months	2 cm, rapidly growing, hyperpigmented	Epidermoid cyst	Skin covered with, 2 cm in size	Basal cell carcinoma	Skin non melanocytic tumour	Lost to follow up
18.	49/M	Scrotum	3 year	2 cm, firm, slow growing	Epidermoid cyst	Skin covered, 2.3 cm in size	Papillary cystadenoma	Benign tumour	Uneventful
19.	50/F	Right foot	5 year	2.5 cm, firm, slow growing	Epidermoid cyst	Skin covered, 2.5 cm in size	Ganglion cyst	Non neoplastic	Uneventful
20.	42/M	Scrotum	1 year	3 cm, hard in consistency	Epidermoid cyst	Skin covered, 3 cm in size, C/S- calcification +	Calcinosis	Inflammatory	Uneventful

[Table/Fig-1]: Clinicopathological correlation of clinically suspected epidermoid cysts (N=20).

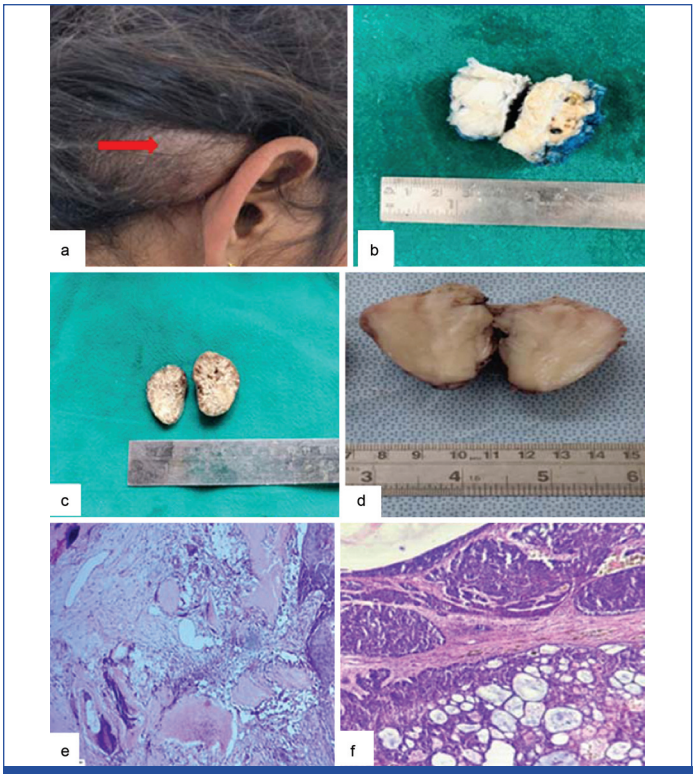
period. The two malignant cases were referred to an oncology centre for further management but were subsequently lost to follow-up.

DISCUSSION

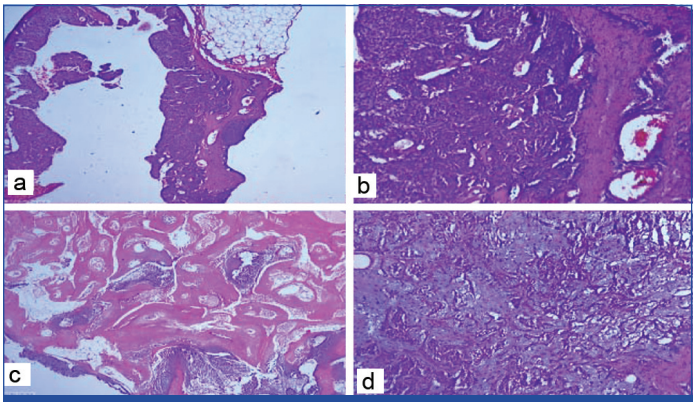
Epidermoid cysts are among the frequent clinical diagnoses for cystic skin lesions that are frequently seen in clinical practice. The exact nature and origin of these lesions is still the subject of much discussion and misunderstanding [3]. Adnexal and soft-tissue tumours, as well as cysts such as dermoid cysts, ganglion cysts, calcinosis cutis and infrequently, malignancy, are among the many differential diagnoses that can be made for a clinical suspect [4].

In the present series, most lesions lacked a classical punctum and demonstrated firm consistency rather than typical cystic fluctuation. However, central punctum was noted in six cases which is characteristic of epidermoid cyst and hence it was misleading clinically. Two cases showed rapid growth which on histopathology turned out to be malignant. Such subtle features, though often overlooked, may help identify cyst mimickers. Absence of a central punctum, increased firmness, rapid enlargement, or occurrence at unusual anatomical sites should prompt consideration of alternative diagnosis [5].

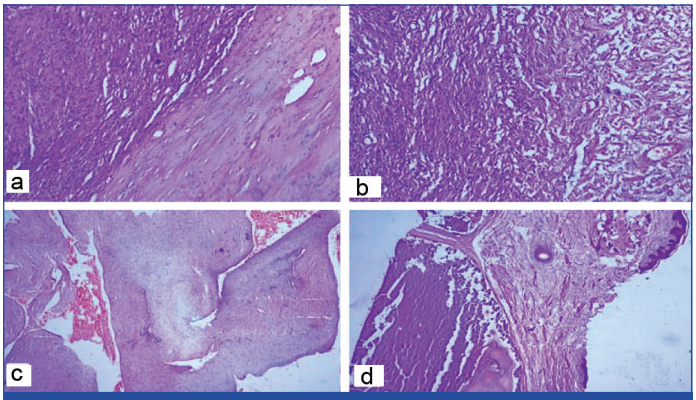
Histopathology remains the diagnostic gold standard. Epidermoid cysts show stratified squamous epithelium with a granular layer and lamellated keratin, without adnexal structures. Skin adnexal tumours display characteristic patterns: nodular hidradenoma with solid-cystic nodules and ductal differentiation; pilomatricoma with basaloid and ghost cells, often calcified; eccrine spiradenoma with dual cell lobules. Peripheral nerve sheath tumours include neurofibroma with spindle cells in myxoid stroma and schwannoma with Antoni A/B areas and Verocay bodies. Malignant lesions such as basal cell carcinoma and pilomatrix carcinoma show infiltrative growth, cytologic atypia and increased mitoses [6]. Immunohistochemistry is useful in challenging cases: S100 positivity supports schwannoma and neurofibroma; Ber-EP4 aids in diagnosing basal cell carcinoma; cytokeratin and EMA highlight adnexal differentiation [7]. Complete surgical excision is usually curative. No recurrence was observed in



[Table/Fig-2]: a) Clinical photograph showing an ovoid swelling (marked) in right postauricular region measuring 3x2.5 cm with normal overlying skin; b) Gross specimen of nodular hidradenoma, cut surface shows solid cystic areas; c) Gross specimen of pilomatrix carcinoma- cut surface is grey-white with areas of necrosis and calcification; d) Gross specimen of schwannoma with homogenous grey-yellow glistening appearance on cut section; e) Pilomatrix carcinoma composed of shadow cells, trichilemmal type of keratinisation, calcification and atypical basaloid cells with mitosis and focal areas of necrosis (H&E, 100X); f) Basal cell carcinoma showing large basaloid lobules with peripheral nuclear palisading and cleft formation with marked mucin production gives rise to pseudoglandular appearance (H&E, 100X).



[Table/Fig-3]: Skin adnexal tumours: a) Histomorphology of nodular hidradenoma (H&E, 100X); b) Hidradenoma showing polyhedral basophilic cells and hyalinised stroma (H&E, 400X); c) Pilomatricoma with ghost cells and basaloid cells (H&E, 100X); d) Chondroid syringoma showing a biphasic proliferation comprised of epithelial cells forming ducts in a background of chondroid matrix (H&E, 100X).



[Table/Fig-4]: a) Schwannoma with hypercellular Antoni A and hypocellular Antoni B areas (H&E, 400X); b) Neurofibroma showing spindle cells with thin wavy nuclei and collagenous stroma (H&E, 400X); c) Ganglion cyst with myxoid change (H&E, 400X); d) Calcinosis cutis showing basophilic, finely granular deposits (H&E, 400X).

our follow-up; however, malignant lesions require adequate margins and long-term surveillance due to risk of local recurrence [8].

Gaffoor N et al., conducted a study which aimed to investigate the diagnostic discrepancies between clinically suspected epidermoid cysts and their actual histopathological diagnoses, emphasising the importance of routine microscopic evaluation post-excision. This study retrospectively analysed 42 cases initially diagnosed as epidermoid cysts based on clinical assessment. Upon histopathological examination, only 29 cases were confirmed as epidermoid cysts, while the remaining 13 revealed a diverse spectrum of non neoplastic and neoplastic lesions, including pilomatricoma, trichilemmal cyst, spiradenoma, nodular hidradenoma, ancient schwannoma and even adenoid cystic carcinoma. In the present study, the authors are presenting 20 such cases which were clinically diagnosed as epidermoid cyst but later on diagnosed as skin adnexal tumours and peripheral nerve sheath tumours [1].

Mittal N and Gupta N published a case report on ossifying pilomatricoma masquerading as epidermoid cyst. In the present study, we have three cases of pilomatricoma and one case of pilomatrix carcinoma which were initially diagnosed as epidermoid cysts based on clinical assessment [9]. Ashby HE et al., reported an unusual case of Merkel cell carcinoma in a 42-year-old man that clinically mimicked an epidermal cyst and rapidly evolved into a painful lesion over the antecubital fossa [10]. Likewise, Ingale YP et al., described a case of Trichilemmal carcinoma in a 67-year-old woman presenting with a scalp swelling initially diagnosed as an epidermoid cyst [11]. These reports parallel the findings of the present study, where two malignant tumours (basal cell carcinoma and pilomatrix carcinoma) were also clinically presumed to be benign epidermoid cysts.

The present study highlights the importance of histopathological examination in accurately diagnosing skin lesions. Despite clinical diagnoses of epidermoid cysts, histopathology revealed unexpected findings of skin adnexal tumours and peripheral nerve sheath tumours. This discrepancy underscores the limitations of clinical diagnosis alone and emphasises the need for histopathological confirmation. Clinicians should consider a broad range of differential diagnoses and utilise histopathology to ensure accurate diagnosis and appropriate management.

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CONCLUSION(S)

In conclusion, the findings emphasise the crucial role of histopathology in accurately diagnosing skin lesions. Clinically diagnosed epidermoid cysts may conceal underlying skin adnexal or peripheral nerve sheath tumours, highlighting the need for histopathological confirmation. The present study underscores the importance of integrating clinical and histopathological findings to ensure precise diagnosis and optimal patient care.

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