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Squamous cell carcinoma arising in an epidermal inclusion cyst

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ABSTRACT

Squamous cell carcinoma (SCC) arising from an epidermal inclusion cyst (EIC) is uncommon. We present a case of a 70-year-old man with a scalp nodule with persistent discharge that was resected based on the clinical impression of an EIC. Histopathologic exam showed an infundibular EIC with an epidermal type of squamous epithelium; however, some of the cyst lining and lumen was replaced by squamous proliferation with malignant features. There are 56 cases of SCC arising in EICs reported in the English literature. Though suspected EICs are commonly benign, a thorough pathologic evaluation is required to rule out malignancy.

KEYWORDS Diagnostic errors; epidermal cyst; neoplastic cell transformation; squamous cell carcinoma

Epidermal inclusion cysts (EIC) account for 90% of all excised cysts and are characterized as subepidermal nodules filled with keratinous debris and lined by stratified squamous epithelium with a granular layer.[1,2] Rarely, this benign neoplasm can transform into a malignancy including squamous cell carcinoma (SCC), basal cell carcinoma, and Merkel cell carcinoma.[2–6] SCC is the most frequent tumor that arises from an EIC, with an incidence ranging between 0.011% and 0.045%.[7–13] Herein, we report a case of an SCC incidentally discovered after excision of a clinically suspected EIC.

CASE REPORT

A 70-year-old man without prior history of skin cancer presented to our clinic with a 7-month history of a scalp nodule with persistent discharge. A 2 cm firm, subcutaneous, mobile, draining nodule was found on the posterior vertex of the scalp. There was no appreciable bony involvement. At the patient's request, an excision was performed to treat the suspected EIC.

Histopathologic examination revealed a dermal cyst with an epidermal type squamous lining with preserved granular layer. Most of the cyst wall showed exuberant squamous proliferation, ranging from well to moderate to poorly differentiated SCC. The epithelium of the SCC was contiguous with the cyst wall without involving the overlying epidermis *(Figure 1a)*. The SCC showed nuclear pleomorphism with prominent nucleoli, mitotic activity, and moderate cytoplasm with keratin *(Figure 1b)*. In other areas, the neoplastic cells were poorly differentiated with marked pleomorphism, large and bizarre nuclei, and prominent nucleoli *(Figure 1c)*. An immunostain for p40 was positive in the tumor, consistent with the diagnosis of SCC. Multifocal invasion into the connective tissue with a desmoplastic stroma was also present *(Figure 1d)*. The surgical margins were free of tumor.

The patient was referred to otolaryngology for further management. Imaging studies revealed no evidence of metastatic disease or skull invasion. The patient was eager to pursue maximal therapy and was further treated with adjuvant electron radiotherapy (50 Gy in 20 fractions in 4 weeks). There was no evidence of recurrence at 1-year follow-up.

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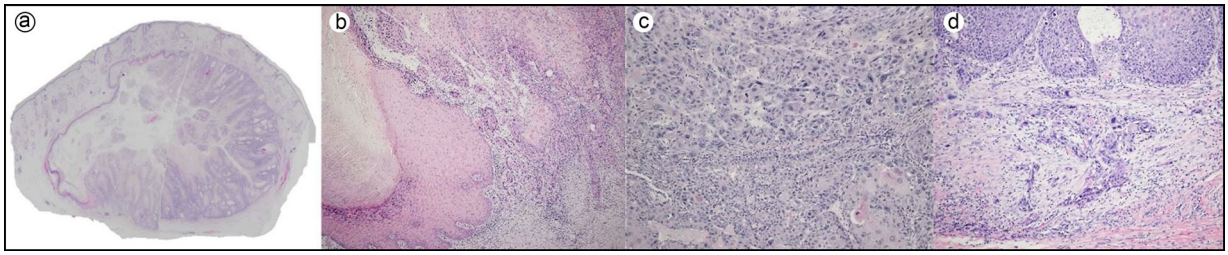

Figure 1. **(a)** The whole mount composite of the dermal cyst with the squamous carcinoma arising from the cyst wall occupying the lumen of the cyst. The epidermis is uninvolved. Hematoxylin and eosin (H&E). **(b)** Squamous-lined cyst with preserved granular layer (bottom left) and the invasive squamous carcinoma (right) contiguous with the cyst wall. H&E 40×. **(c)** Poorly differentiated squamous cell carcinoma in the upper portion and moderately differentiated squamous carcinoma with cytoplasmic keratin in the bottom. H&E 100×. **(d)** Invasive squamous cell carcinoma with desmoplastic reaction in the surrounding soft tissues. H&E 100×.

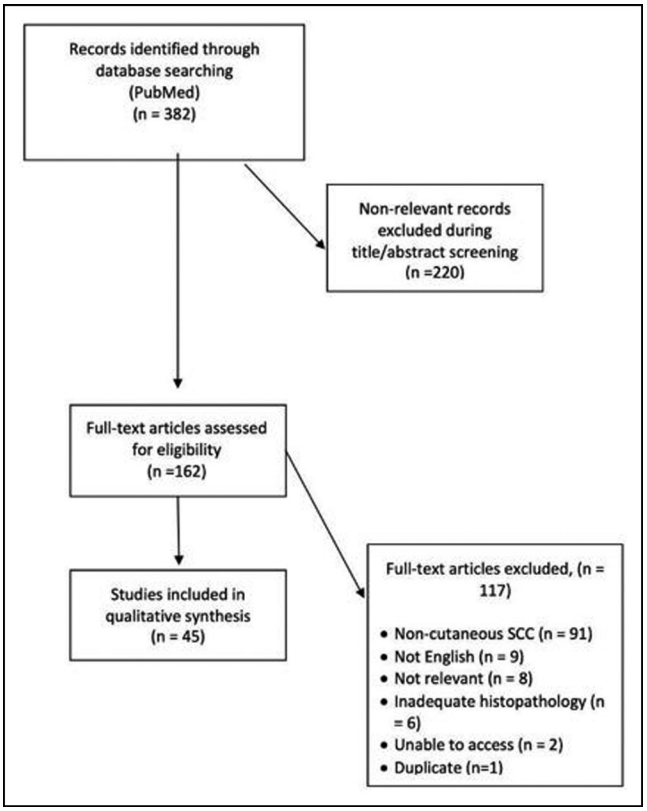

Figure 2. PRISMA flow chart, adapted from Moher et al.[14]

DISCUSSION

Although EICs are usually benign and asymptomatic, they may secondarily become inflamed, infected, or, rarely, develop into a malignancy.[2] Our review of the literature between 1976 and 2021 yielded 56 cases (including ours) of SCC arising in an EIC *(Figure 2)*.[14] The average duration of the lesion prior to presentation was 7 years. The most frequent location was on the head and neck. All lesions were primarily managed by excision, with some cases requiring adjuvant chemotherapy, adjuvant radiation therapy, re-excisions, or amputations. Three patients had metastases and died within 5 to 10 months of presentation, and one patient had recurrence with metastases and survived following chemotherapy.

Clinically, it is difficult to distinguish between benign and malignant cutaneous cystic lesions. Certain EIC characteristics should raise suspicion for indolent malignancy and include recurrence, rapid growth, size >2 cm, heterogeneous content, pain, erythema, ulceration, persistent drainage, or failure to respond to antibiotics.[2,15] However, a malignancy can still be present in the absence of these clinical signs/symptoms. Histopathology is imperative for diagnostic confirmation. All surgically removed EICs at our institution are confirmed by histopathology. Having this protocol in place allows for earlier detection of a malignancy and the initiation of appropriate care vital to patient outcomes.[16,17]

The pathologic differential diagnostic considerations of a dermal cystic lesion lined by squamous epithelium include an inclusion cyst of epidermal or pilar type. The epidermal type shows squamous lining epithelium with preserved granular layer and lumen with epidermal-type keratinous material. The pilar type cyst epithelium shows squamous cells with absence of granular layer, and lumen with eosinophilic pilar-type keratinous material with cholesterol clefts/calcification. Squamous lined cysts secondary to human papillomavirus infection have been reported[18–20] and are more commonly on the palms and soles and rarely the scalp. These cysts show squamous lining epithelia with papillomatosis, hypergranulosis, parakeratosis, and, rarely, cytoplasmic inclusions. Proliferative changes in the cyst wall occupying the cyst lumen can be seen in proliferating trichilemmal or epidermal cysts, or malignancy arising in epithelial cysts. Proliferating trichilemmal tumors, commonly seen in the scalp, show a wide spectrum of squamous proliferation. Epithelial proliferation with pleomorphism and surrounding stromal invasion is seen in carcinomas arising in trichilemmal cyst. A proliferating epidermal cyst shows squamous proliferation with epidermal-type keratinization. Atypia of the squamous cells can be seen.

Malignant transformation of a cyst should be diagnosed when the malignant cells are contiguous with the cyst wall without connection to overlying epithelium.[16,17] Cellular pleomorphism, mitotic activity, and stromal invasion with desmoplasia is seen. To avoid misdiagnosis and prevent potentially fatal outcomes, we strongly recommend that all providers and institutions send all excisions of suspected EICs for histologic analysis, regardless of clinical features.

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