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CASE REPORT

Squamous Cell Carcinoma Arising on an Epidermal Inclusion Cyst: A Case Presentation and Review of the Literature

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KEYWORDS

Epidermal inclusion cyst;
Squamous cell carcinoma

Abstract

Epidermal inclusion cysts are very common lesions that very rarely undergo malignant transformation—in the English-language literature we have only found 18 adequately documented cases. We present the case of a man with a 2-month history of a retroauricular skin lesion in which histological study revealed squamous cell carcinoma arising on an epidermal inclusion cyst. Cysts that grow rapidly, reach a large size, ulcerate, develop a fistula, or that do not respond to medical treatment, and those that recur should be excised completely and histological study performed of the whole lesion.

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PALABRAS CLAVE

Quiste de inclusión epidérmica;
Carcinoma epidermoide

Carcinoma epidermoide desarrollado sobre quiste de inclusión epidérmica cutáneo. Presentación de un nuevo caso y revisión de la literatura

Resumen

El quiste de inclusión epidérmica es una lesión muy común, siendo muy poco frecuente la transformación maligna del mismo. En la bibliografía en lengua inglesa solamente hemos encontrado 18 casos publicados que estuvieran adecuadamente documentados. Presentamos el caso de un varón con una lesión cutánea retroauricular de dos meses de evolución, cuyo estudio anatomopatológico mostró un carcinoma epidermoide que tenía su origen en un quiste de inclusión epidérmica. Los quistes de crecimiento rápido, aquellos que alcanzan gran tamaño, los que se ulceran, los que fistulizan y no responden al tratamiento médico y aquellos que presentan recurrencias deben extirparse completamente y estudiarse histológicamente en su totalidad.

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Introduction

Epidermal inclusion cysts and squamous cell carcinoma of the skin are very common lesions. There have been a number of reports of malignant and premalignant lesions arising in cutaneous epidermal inclusion cysts, including squamous cell carcinoma, Merkel cell carcinoma, basal cell carcinoma, Bowenoid papulosis, Bowen disease, Paget disease, and mycosis fungoides. There have also been reports of squamous cell carcinomas arising in noncutaneous epidermal inclusion cysts; this has occurred mainly in intracranial lesions, though also at other sites (precoccygeal, presacral, hepatic, splenic, and orbital). However, the association of epidermal inclusion cysts and squamous cell carcinoma in the skin is very rare. As malignant transformation is unusual and unexpected, it is recommended that large or rapidly growing cysts, those that ulcerate, and those that do not respond to medical treatment be completely excised and sent for histological study of the whole lesion. We present the case of a man with a retroauricular cystic lesion of the skin that had appeared 2 months earlier. Pathological study revealed a squamous cell carcinoma that had arisen in an epidermal inclusion cyst with no signs of dysplasia.

Case Report

The patient was a 65-year-old man who presented a fistulating cystic lesion that had appeared 2 months earlier in the right retroauricular-mastoid region. The lesion did not improve with antibiotic treatment and excision biopsy was performed in various fragments. Analysis of the biopsy was difficult due to the fragmentation of the material. However, one of the fragments contained a moderately differentiated, infiltrating squamous cell carcinoma on the walls of an epidermal inclusion cyst (Figures 1 and 2). The tumor had areas with a conventional pattern and others with an adenoid pattern; the change between the normal cyst wall and tumor was sharp, with no zone of dysplastic transition. The tumor was in contact with the surgical margins. Examination of multiple serial histological sections showed that the tumor did not arise from the epidermis. The other fragments were practically all of the tumor and showed no other relevant findings.

Reoperation was performed to extend the surgical margins, and microscopic examination only revealed persistence of microscopic tumor deposits.

Two months later, the lesion reappeared and the excision was repeated; histology findings were identical to those of the previous surgery and the surgical margins were once again involved.

Ten months later the tumor had regrown. It had the same characteristics and extended towards the mastoid process and external auditory canal. After repeat excision, pathology findings were identical to the previous occasions. The analysis was completed using immunohistochemistry for cyclin D1 (Neomarkers; clone: SP4, EnVision), p53 (Dako; clone DO-7, EnVision), and Ki67 (Dako; clone Mib-1;

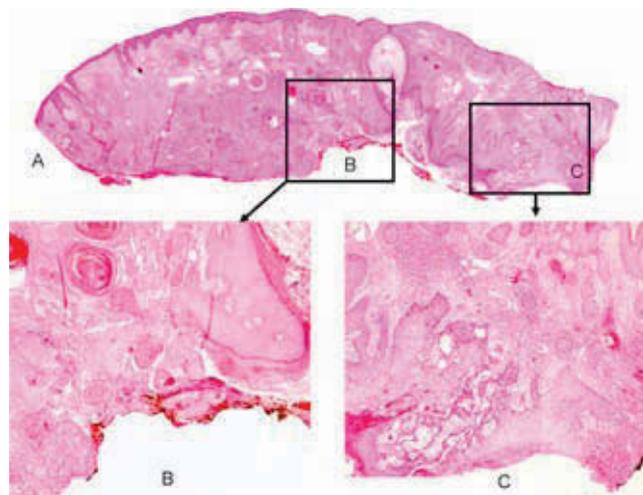


Figure 1 A, Full-thickness section of skin that shows the malignant transformation in the wall of the cyst in the deep margin and the fistulous tract in the center. No contact was seen between the tumor and the epidermis (Hematoxylin-eosin). B and C, Squamous cell carcinoma growing in the wall of the cyst, in contact with the deep surgical margin (Hematoxylin-eosin, $\times 2.5$).

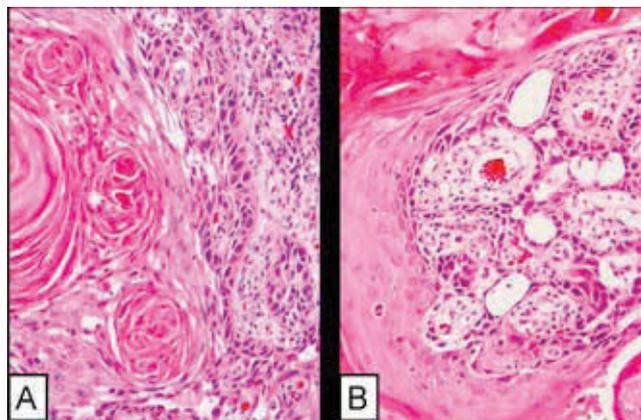


Figure 2 Squamous cell carcinoma. A, Conventional pattern (detail of Figure 1B). B, Adenoid pattern (detail of Figure 1C) (Hematoxylin-eosin, $\times 10$).

EnVision). All of the antibodies showed intense labeling within the tumor and no staining in the walls of the cyst. The border between the immunopositive and immunonegative regions was sharply defined, with no progressive transition between the 2 tissues.

Computed tomography (CT) showed involvement of the mastoid process and, in view of the difficulty for performing complete excision of the tumor, the patient was treated with radiotherapy, but no response was achieved.

Finally, 6 months later, radical resection of the auricle and of the mastoid process was performed (Figure 3), and the specimen was sent together with other small fragments of the mastoid bone for histological study.



Figure 3 Amputation of the auricle of the ear. Asterisks (*) indicate absent cartilage as a consequence of the previous surgery; narrow arrow, cyst; thick arrow, fistula.

Between the auricle and the external auditory canal there was a cystic cavity with a diameter of 2 cm and with a very thick and irregular white wall. The cavity was connected to the epidermis by a fistulous tract. Around the cavity there were several areas in which the cartilage was absent, probably due to earlier biopsies. Microscopy revealed that the cavity corresponded to an epidermal inclusion cyst with an inflammatory infiltrate and alterations secondary to the previous surgery; there was no evidence of tumor remnants or of dysplasia. Microscopic remnants of squamous cell carcinoma were only observed in some of the fragments from the mastoid process that had been sent separately.

The study was completed by CT to stage the disease, and there were no signs of tumor spread. At the time of writing, 18 months after the radical surgery, the patient was well and was free of disease.

Discussion

Epidermal inclusion cyst of the skin is a very common lesion. There have been a number of reports of malignant and premalignant lesions arising in the wall of these cysts.¹ However, such malignant transformation is very rare or, at least, there are very few references to this finding in the literature. The diagnosis of squamous cell carcinoma in an epidermal inclusion cyst must be differentiated from a squamous cell carcinoma with cystic changes, and it is therefore essential to demonstrate that there is no connection between the tumor and the epidermis, as we showed in our case after the study of multiple serial histological sections. In a review of the English-language literature, we only found 18 adequately documented cases of squamous cell carcinoma arising in the wall of an epidermal inclusion cyst of the skin.¹⁻⁷ We excluded those cases in which the description did not provide conclusive evidence of the presence of an epidermal inclusion cyst,

for example, sebaceous cysts in which the epithelium did not have a stratum granulosum, and those in which the histological description was more in line with a pilonidal cyst. The clinical data available from those reports and from this new case are shown in the Table.

The incidence of epidermal inclusion cysts with malignant transformation to squamous cell carcinoma is very difficult to determine as the reports are almost all of isolated cases. In the pathology department of Hospital Povisa, 3700 cutaneous epidermal inclusion cysts were diagnosed between January 1987 and May 2009, and this type of malignant transformation was only observed in one of them (0.027%). In the same period, 905 squamous cell carcinomas of the skin were diagnosed, and only one, the case presented in this report, arose in an inclusion cyst (0.11%).

Based on the data in the Table, the mean age at presentation of squamous cell carcinoma arising in an epidermal inclusion cyst is 43.2 years (range, 21-80 years), and it is more common in men (68.4%). The region most frequently affected is the head and neck, which was involved in 42.1% of cases. The mean diameter of the lesions was 5.7 cm (range, 1.5-13 cm), and the mean time to diagnosis after appearance of the lesion was 101 months (range, 2-480 months). The degree of differentiation of the tumor or histological variant was not reported in the majority of cases, although they tend to be moderately or well differentiated and present a conventional histological pattern.

It has been suggested that the triggering factor in the pathogenesis of malignant change could be chronic irritation of the lesion. Rapid growth of a pre-existing lesion has been reported in several cases,^{4,7} and progression was clearly related to trauma in one case.⁷ Actinic damage is also a possible factor, particularly given that the majority of these lesions arise on the head and neck. All of these possible mechanisms would suggest the presence of an intermediate step, with dysplasia appearing in the cyst before the carcinoma develops. However, it is clear that in some cases, including the present one, there is an abrupt transition between the wall of the cyst and the tumor, with no intermediate dysplastic changes between the 2 components.¹ Immunohistochemical analysis can be of great help in this situation. In our case, analysis with cyclin D1, p53, and Ki67 showed that the transition between the wall of the cyst and the tumor was very abrupt, without no demonstrable dysplastic changes between the 2 tissues. Morgan et al² reviewed 5 cases in an attempt to determine whether human papillomavirus could be involved in the origin of this transformation, but they were unable to demonstrate the presence of the virus in the lesions. However, this result cannot be considered conclusive due to the small number of cases studied.

With regard to the clinical course of the lesion, it is striking that 3 cases (12%) presented very aggressive disease with metastases and death within 5 to 10 months.^{1,5,7} Of those 3 cases, 2 were women and the mean age was 51.7 years (range, 48-59 years). The lesions were situated on the thigh, the abdomen, and the buttock, and the mean

Table Clinical Details of the Epidermal Inclusion Cysts Found in the Literature Review

Cases	No. of cases	Age, y	Sex	Site	Cyst diameter, cm	Time Since Onset, mo	Differentiation/ Histological Type/ Dysplasia	Treatment	Outcome
1 ¹	1	32	M	Left index finger	NS	120	NS	Amputation+RT	No recurrence
2 ¹	1	55	F	Left buttock	10	6	NS	Excision	NS
3 ¹	1	59	F	Left thigh	5	3	Well differentiated.	Excision and inguinal lymphadenectomy	Metastasis in 1 lymph node. Death at 6 mo
4 ¹	1	58	M	Right ear	2.5	132	No dysplasia	Excision	No recurrence
5 ¹	1	34	M	Left retroauricular	8	NS	NS	Excision+RT	No recurrence
6 ¹	1	68	M	Right preauricular	3	4	NS	Excision+parotidectomy	No recurrence
7 ¹	1	52	M	Right ear	2	132	NS	Excision	No recurrence
8 ¹	1	66	M	Left retroauricular	1.5	2	Well differentiated	Excision	No recurrence
9-13 ²	5	56.7 (range, 21-80)	3 M, 2 F	Left facial, Cervical 1, Trunk 3	NS	NS	Well differentiated.	NS	NS
14 ³	1	67	M	Right temporal	3	3	Not well differentiated	Excision	6 mo, no recurrence
15 ⁴	1	38	F	Left buttock	Very large	NS	SCC in situ	Excision	12 mo, no recurrence
16 ⁵	1	48	F	Abdomen	9.2	>120	Poorly differentiated	Excision+CT	Multiple metastases. Death at 10 mo
17 ⁶	1	74	M	Left thigh	13	480	Well differentiated	Excision	24 mo, no recurrence
18 ⁷	1	48	M	Buttock	5	336	Well differentiated	Excision+RT+inguinal lymphadenectomy	Inguinal and pulmonary metastases. Death at 5 mo
Our case (Povisa)	1	65	M	Right retroauricular	2	2	Moderately differentiated. Adenoid. No dysplasia	Excision+RT+ amputation of the ear	18 mo, no recurrence

Adapted from López-Ríos F et al.¹

Abbreviations: CT, chemotherapy; F, female; M, male; NS, not specified; RT, radiotherapy; SCC, squamous cell carcinoma.

diameter was 6.4 cm (range, 5-9.2 cm). The time since onset was 3 months in 1 case, more than 120 months—without being able to be more precise—in another, and 336 months in the third. The squamous cell carcinomas were well-differentiated in 2 cases and poorly differentiated in the other. One of the patients presented a single metastasis in an inguinal lymph node and the other 2 presented lymph node and systemic metastases. However, taking into account that there were only 3 patients involved, it would be unwise to attempt to extrapolate these data. For this same reason, it does not appear appropriate to make recommendations concerning the diagnosis, treatment, and follow-up of these patients beyond the current guidelines for conventional squamous cell carcinoma.

Finally, as a brief conclusion, we would like to recommend that malignant transformation should be suspected in cases with large epidermal inclusion cysts, those that present rapid growth, ulceration, or fistulas with persistent drainage of the cystic contents, and those that do not respond to medical treatment or that recur. In such cases, complete excision of the lesion is recommended, with detailed microscopic study of the whole lesion, paying particular attention to the thicker areas of the wall. It is therefore very important that the lesion reaches the pathologist intact; fragmentation can make pathological study difficult and lead to a loss of detail or even affect the final diagnosis.

Conflicts of Interest

The authors declare no conflicts of interest.

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