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Hydroadenocarcinoma, a rare tumor to be kept in mind

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ABSTRACT

Background: Nowadays, the incidence of skin cancer has increased, especially in the elderly population, probably due to increasing longevity and lifestyle changes. Sun exposure plays a pivotal role in the development of the skin tumors, among these basal cell carcinoma (BCC) is the most frequent with an incidence 4 times higher than that of squamous cell carcinoma (SCC) and it is 20 times more common than melanoma. On the other hand, skin adnexal tumors are extremely rare and hydroadenocarcinoma (HC) is generally considered a malignancy of eccrine cutaneous sweat glands. It occurs in 0.01% of skin cancers and often it can mimic other skin cancers, particularly BCC.

Case presentation: An 84-year-old woman come to our attention for a neof ormation on the upper lip. Seeing as she had previously undergone operations for removal of basaliomas on the face, the lesion was believed to be a recurrence. Facial and neck MRI and CT-scan analysis revealed that the lesion appeared in correspondence of the midline and paramedian site of the upper lip with extension into the left nasal cavity, not dissociable from the surrounding tissues. For this reason, the patient underwent an "en bloc" resection instead of Mohs' surgery. The definitive histological diagnosis concluded that the lesion was a hydroadenocarcinoma.

Conclusion: In front of a nodular lesion of the skin it is always advisable to perform a biopsy to type the neof ormation and also exclude rare tumors such us hydroadenocarcinoma.

1. Introduction

A greater incidence of dermatological problems has been observed in the elderly population, probably due to an increase in life expectancy. The age range of 50–70 year olds is the most affected and men approximately have a 1.6 fold increased risk compared to women. In addition to the normal ageing process, also environmental factors acquired over time, especially UV rays which cause cumulative damage, are involved in the development of skin cancers [1]. Skin cancers can arise from: epidermis, melanocytic, dermis,

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panniculus and pilosebaceous tissues [2]. Excluding non-melanoma skin cancers, an average of 80–85% are basal cell carcinomas (BCC) while squamous cell carcinomas (SCC) are less common but more aggressive [3]. Surgical excision often represents the primary therapeutic choice. Non-excisional options are represented by curettage, cryotherapy, radiotherapy, chemotherapy or topic application of agents such as 5-fluorouracil. Mohs' micrographic surgery is a promising surgical alternative which consists in a mapping of the concentrically excised tissue, intraoperatively examined under magnification, to establish the need for surgical removal [2]. The aim of this paper is to present a case report of an accidental diagnosis of hidradenocarcinoma (HC) in an elderly patient operated for BCC.

2. Case report

An 84-year-old woman was referred to the Maxillo-Facial Unit of the University of Campania "Luigi Vanvitelli" by her trusted dermatologist for a lump on the upper lip (Fig. 1a). The anamnesis of the patient reported a history of sun exposure for professional reasons. In the previous 20 years, she had undergone 6 surgeries for facial BCC removal in different areas, of which 3 on the left upper lip, next to the ipsilateral facial alar sulcus. For this reason, her dermatologist suggested Mohs' surgery due to the supposed diagnosis of BCC relapse. Extraoral examination showed a painless multinodular mass in the midline of the upper lip extending to the left nasal orifice. On palpation the lesion appeared to be hard in consistency and fixed to the underlying planes. Facial and neck CT scan, with and without contrast media, showed a heteroplastic lesion in correspondence of the midline and paramedian site of the upper lip with extension into the left nasal cavity, not dissociable from the surrounding tissues but without evidence of bone erosions. Bilateral cervical lymph nodes appeared inflamed. On MRI (Fig. 2a and b), with and without contrast media, this lesion appeared hypo-intense on T1- and T2-weighted images and hyper-intense on STIR (short time inversion recovery) sequence, with homogeneous enhancement. Due to the imaging evaluation we opted for a more radical approach, so an "en bloc" resection of the mass was performed instead of Mohs' surgery (Fig. 3). A sample of $3.5 \times 3 \times 1.5$ cm was resected with contextual radicalization of the margins for extemporaneous histological examination which resulted negative. Subsequently, after identification of the facial arteries, the reconstruction was based on 2 naso-labial sliding flaps (Fig. 4). The definitive histological examination showed spindle cells, foci of clear cells with basaloïd differentiation, and occasionally secreting cells with microvacuolated cytoplasm which were positive for CEA and EMA im-



Fig. 1. Frontal view. Preoperative (A), 4 months follow-up (B), 11 months follow-up (C).

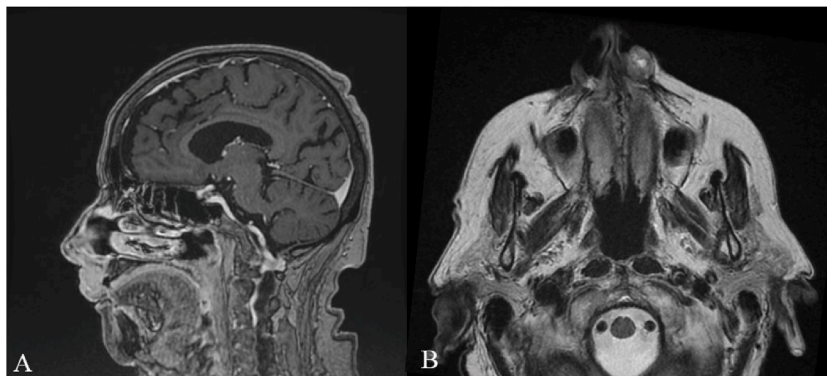


Fig. 2. MRI sagittal section (A) and axial section (B). Extension from the upper lip to the left nasal cavity is noticed.

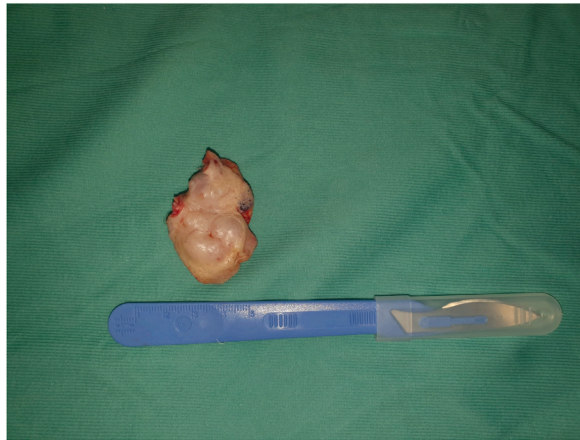


Fig. 3. “En-bloc” neoplasm resection.



Fig. 4. Intraoperative view of the resection and naso-labial harvesting.

munostaining. Further immunohistochemical investigations showed positivity for BerEp4 and negativity for S100 and chromogranin. In addition, perineural infiltration without evident vascular emboli was reported. The pathologist concluded with a diagnosis compatible with a malignant neoplasm of the skin appendages: hidradenocarcinoma (Fig. 5). At the fourth and eleventh month post-surgical follow-up the patient is fine and there are no signs of recurrences (Fig. 1b and c).

3. Discussion

BCC is the most frequent skin cancer which commonly affects white males with skin phenotype I and II in old age. The incidence of skin cancer has increased due to increasing longevity and lifestyle changes such as incorrect sun exposure behavior which represents one of the main risk factors. BCC mainly affects the photo-exposed areas and 80% of the lesions arise in the head-neck region. It has an incidence 4 times higher than SCC and it is 20 times more common than melanoma [4]. Some genetic diseases, such as xeroderma pigmentosum, predispose patients to the development of skin cancers (BCC, SCC and melanoma) [5]. In contrast, skin adnexal tumors are uncommon and there are difficulties in their classification [6,7]. Traditionally, they are subdivided into four groups: eccrine, apocrine, mixed origin (eccrine and apocrine) and un-classifiable sweat gland tumors [8,9]. According to histopathology, there are many types of sweat-gland carcinomas and HC is usually considered as a malignancy of eccrine cutaneous sweat glands [10]. It is an extremely rare tumor of the eccrine sweat glands and it accounts for less than 0.01% of skin cancers [8]. This tumor is commonly

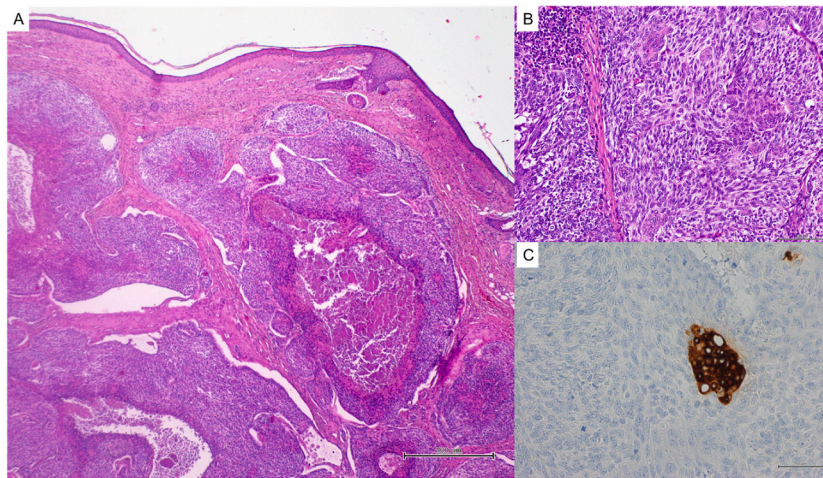


Fig. 5. (A) Dermal tumor with nodular and lobular growth pattern. Note the central necrosis (comedocarcinomatous variant) (Hematoxylin and Eosin, 10X). (B) The tumor cells have clear cytoplasm and vesicular nuclei with small nucleoli (Hematoxylin and Eosin 40X). (C) CEA immunohistochemical evaluation highlight ducts and intracytoplasmic lumina (Avidin-Biotin Complex, 40X).

known as malignant nodular hidradenoma, clear cell eccrine carcinoma, malignant clear cell acrospiroma, malignant clear cell hidradenoma, or primary mucoepidermoid cutaneous carcinomas. HC is extremely rare and has an aggressive behaviour. The incidence rate is about 0.001% of all malignant tumors and it represents approximately 6% of malignant eccrine cancers. The first case of sweat gland carcinoma was reported in 1865 by French pathologist Victor Andre Cornil [11] but it was only in 1954 that Keasby and Hadley described HC as a clear cell eccrine tumor [12]. HC can mimic other skin cancers, particularly BCC; in fact, it often appears as a lump in the dermis [8]. Generally, the diagnosis occurs in the fifth to seventh decade of life with a similar incidence in men and women [13]. Other authors suggest a higher incidence in women, and the delayed diagnosis is probably due to the fact that the lesion remains asymptomatic for a long time [14]. It occurs more frequently on the head and neck region, particularly on the face, but lesions have also been reported in other districts such as the abdomen, scalp, groin, trunk, elbow and digits [13]. It more frequently arises *de novo* compared to a malignant conversion of benign hidradenomas [14]. Lymphatic spread is the most common route for metastatic dissemination nevertheless, hematogenous metastasis have also been reported [10]. The definitive diagnosis is based on histological and immunohistochemical analysis. Generally, as in other eccrine tumors, HC expresses cytokeratins, EMA, CEA and S100 protein. It appears to originate from the intradermal duct of the eccrine sweat glands [11]. In 2009, Cohen et al. showed a case of a patient with a HC with apocrine features in the scalp region which probably derived from a pluripotent precursor cell with the capacity for multiple lines of adnexal differentiation. Aggressive surgical excision is generally considered the standard treatment [10]. Some authors suggest that the lesion should be excised with 3 cm margins and, precisely because of the high risk of recurrence and metastasis, sentinel lymph node biopsy should be performed [15]. A local recurrence rate of 10%–50% and metastasis rate of 21% are estimated. Promising results have been obtained with Mohs' surgery in order to avoid major surgical defects and to have easier reconstruction options [16]; although a more aggressive approach such as the “en-bloc” resection allows the surgeon to better control the eradication of the illness. In the present, case several reconstructive options could have been performed, nevertheless, due to the age of the patients, we opted for local flaps in order to achieve a functional and aesthetically acceptable restoration reducing the operative time; local flaps have been largely described for the reconstruction of small to medium defects of oral and extra-oral areas, especially for oro-nasal fistulas that can be observed following cleft surgery or implant surgery [17–19]. The prognosis of these tumors is poor with up to a 50% chance of local recurrence and 5-year survival drop to less than 50% [20]. Unfortunately, there are no uniform guidelines for the treatment of metastatic hydradenocarcinoma [21]. Results on the efficacy of radiotherapy and chemotherapy are controversial [11]. According to HC treatment, there is insufficient scientific evidence to establish the efficacy of valid treatments or accepted protocols but some authors suggest adjuvant radiation therapy for large tumors (>5 cm), positive margins following surgery (<1 cm), and moderately to poorly differentiated tumors with lymphovascular invasion [22]. In the present case, the patient was sent to us with a diagnosis of BCC relapse and indications for Mohs' surgery. However, since the evaluation of MRI imaging revealed a sort of full thickness involvement of the upper lip, we opted for an “en bloc” resection. Extemporaneous biopsies of all the margins were also performed which resulted free of cancer.

4. Conclusion

Although hydroadenocarcinoma is a rare tumor, it must always be kept in mind, especially in areas of previous BCC removal. From the present case we learned that biopsy examination is always recommended, even in case of supposed diagnosis performed by the dermatologist, because the therapeutic approach moves from a more conservative approach performed for BCC to a more aggressive eradication in case of HC.

Human and animal rights

All research procedures followed were in accordance with the Helsinki Declaration of 1964.

IRB approval

Exempt because retrospective case report.

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Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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