Apocrine adenocarcinoma in the setting of apocrine hidrocystoma of the leg

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Abstract

Apocrine hidrocystoma is a benign, cystic lesion often presenting in the periorbital region. Apocrine adenocarcinoma is the rare, malignant counterpart occurring mainly in the axilla and anogenital region. There is a paucity of literature on both entities and co-occurrence has been reported in only 5 cases. We present the case of a 48-year-old man with a history of total body irradiation for chronic myelocytic leukemia, diabetes mellitus, and obesity who presented with a calf mass of two years' duration. Epidermal inclusion cyst was presumed and excisional biopsy was carried out. Pathologic analysis revealed apocrine adenocarcinoma in the setting of a precursor apocrine hidrocystoma. Our patient's unique altered immunity and the direct effects of irradiation on the local microenvironment may have resulted in his rare presentation of co-occurrence of apocrine adenocarcinoma within an existing apocrine hidrocystoma. To our knowledge, our patient is the first reported patient with this presentation in the lower extremity.

Keywords: plastic and reconstructive surgery, dermatopathology, apocrine adenocarcinoma, apocrine hidrocystoma

Introduction

Apocrine hidrocystoma is a rare, benign, cyst of proliferating apocrine glands often found in the periorbital area as a solitary, translucent, blue-appearing nodule [1]. Owing to its distinctive morphology and pathology, it rarely presents as a diagnostic conundrum. The malignant counterpart is apocrine adenocarcinoma, a rare entity found in areas of high apocrine gland density, mainly in the axilla and anogenital region. However, there have been cases in the eyelid arising from Moll's glands, scalp, nipple, lip, and others [2-5]. Co-occurrence of apocrine adenocarcinoma and hidrocystoma is extremely rare and has only been reported in 5 cases [6]. There is a paucity of literature on apocrine adenocarcinoma within a precursor apocrine hidrocystoma. Therefore, prognosis and treatment remain controversial. We present a patient with apocrine adenocarcinoma arising in a pre-existing apocrine hidrocystoma of the leg. To our knowledge, this is the first report of this unique pathology in the lower extremity.

Case Synopsis

A 48-year-old man presented with a right calf mass of two years' duration, with accelerated growth over the past year. Six months prior to presentation, sonography demonstrated a 3.7cm subcutaneous mass suggestive of an epidermal inclusion cyst. Incision and debridement expressed dark red fluid suggestive of an old hematoma. He was referred to the senior author for further evaluation. On exam, the calf lesion was cystic, non-tender, with a blue discoloration, and without erythema, drainage, or a palpable thrill. The patient presented concurrently with a right ankle mass of 4-5 years' initially

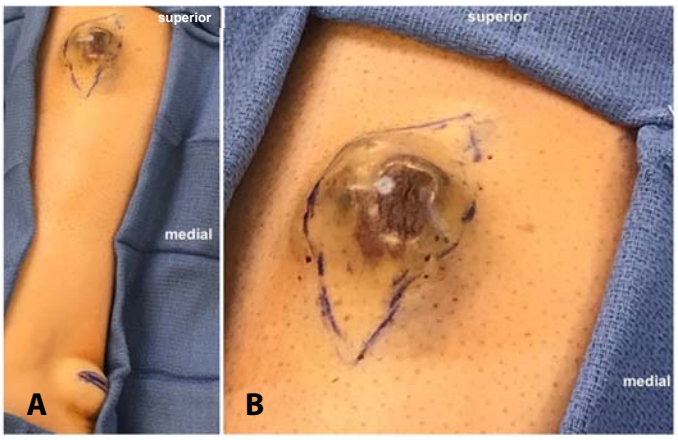

Figure 1. ***A)*** *Patient presented with a large, hemorrhagic mass in the right medial calf as well as a mass in the posteromedial right ankle overlying the Achilles tendon.* ***B)*** *The calf mass was soft, mobile, non-tender, with a blue/purple discoloration.*

diagnosed as a ganglion cyst. On exam, the ankle mass was firm, non-tender, and non-translucent (**Figure 1**).

The patient had a distant history of chronic myelocytic leukemia treated with bone marrow transplant after total body irradiation complicated by graft versus host disease, class II obesity (BMI 36.82), type 2 diabetes mellitus, hypertension, hypertriglyceridemia, hypogonadism, obstructive sleep apnea, gout, trigeminal neuralgia, depression, and obsessive-compulsive disorder. His surgical history was notable for cholecystectomy and bilateral cataract surgery. Social history was noncontributory. Family history included type 2 diabetes in both parents and colorectal adenocarcinoma in his father.

Preoperative MRI revealed a non-enhancing mass in the medial calf subcutaneous soft tissues with intrinsic marked T1 hyperintensity suggestive of internal hemorrhage or keratinous products of an epidermal inclusion cyst. The patient was scheduled for excisional biopsy.

An elliptical excision circumscribing the calf mass, which measured 6×7cm, was performed (**Figure 1**). A liquified hematoma was identified. The capsule was thin, friable, and not adherent to the deep structures. The incision was closed primarily. The ankle mass was excised via an elliptical incision and closed primarily.

Light microscopy of the calf mass showed a well-circumscribed, large, cystic structure lined by bland-appearing epithelium with classic cytopathic changes of apocrine differentiation (**Figure 2A)**. In particular, the cells demonstrated abundant eosinophilic cytoplasm with decapitation secretion (**Figure 2B)**. In some areas, however, the epithelial lining was multilayered with supervening atypia (**Figure 2C)**. In such foci, irregular nests of glandular epithelium assumed an infiltrative growth pattern into the surrounding stroma (**Figure 2D)**. There was marked cellular atypia, cell necrosis, and scattered atypical mitotic figures.

Subsequent to diagnosis, wide local excision of the tumor cavity site with 2cm margins was performed with negative margins. The lesion was closed with a rotational flap (**Figure 3**). He has since been evaluated by the hematology-oncology and

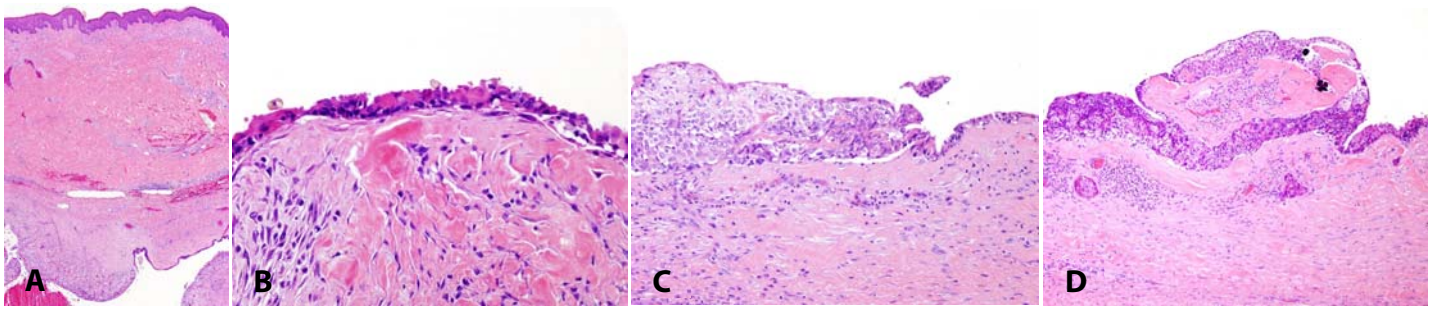

Figure 2. *Pathology.* ***A)*** *Low power magnification demonstrated a large epithelial lined cyst within the dermis; there was evidence of trauma characterized by fibrosis and neovascularization. Higher power magnification demonstrated an apocrine cytomorphology. H&E, 20×.* ***B)*** *The cells lining the cyst wall exhibited abundant eosinophilic cytoplasm with a decapitation pattern of secretion. H&E, 400×.* ***C)*** *In areas, however, the cyst wall showed significant epithelial hyperplasia with supervening atypia including such foci juxtaposed to blander areas of conventional apocrine hidrocystoma. H&E, 200×.* ***D)*** *Areas of infiltrative growth were identified in the surrounding fibrous stroma. H&E, 100×.*

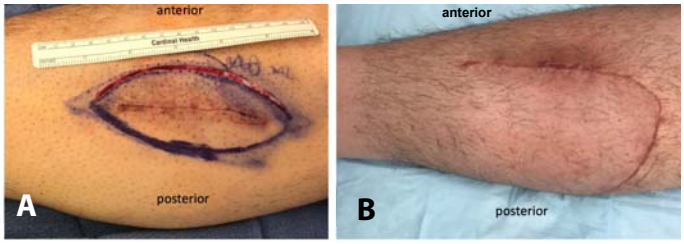

Figure 3. ***A)*** *The previously created tumor cavity site was excised in an elliptical fashion measuring approximately 12×4cm.* ***B)*** *On postoperative day 71/43, the fasciocutaneous advancement flap healed well without any recurrence of calf mass appreciated on clinical examination.*

radiation-oncology departments for PET-CT scan and stringent screening, though no systemic therapy will be undertaken as he has no evidence of metastatic disease.

Case Discussion

Apocrine hidrocystoma is a rare, benign, cysts of the secretory portion of the apocrine coil. They are most frequent along the eyelid margin, presumably arising from the glands of Moll, but also found in the scalp, trunk, and extremities [1, 7]. These lesions are typically solitary and found in adults 30-70 years-old. These benign masses are treated by simple needle puncture, although other methods including electrodessication have been described [1, 8].

The reported incidence of apocrine adenocarcinoma is approximately one in 6-20million patients per year [4]. The median patient age is 67 without racial or gender preference [4, 5]. They are found in areas of high apocrine sweat gland density, mainly in the axilla and anogenital region, but also reported in the eyelid, scalp, nipple, lip, and others [4, 5, 9-12]. They may be solid or cystic masses and grow slowly with median preoperative duration of 12 months [13]. Current therapy recommends wide local excision with 1-2cm margins and lymph node exploration if clinically positive [4]. In cases without lymph node disease, use of adjuvant chemoradiation is controversial [4]. Local recurrence and metastatic disease can occur [4].

Co-occurrence of apocrine adenocarcinoma and hidrocystoma is extremely rare and has only been reported in 5 cases, all in the axilla of elderly Japanese men [6]. The morphologic hallmark of these neoplasms were areas of infiltrating carcinoma arising in a background of apocrine hidrocystoma. Two cases demonstrated regional lymph node metastasis and one patient had cutaneous recurrence of the tumor 38 months after the initial surgery and expired from respiratory insufficiency. All other patients were alive at 22-46 months follow up [6].

To our knowledge, our patient is the first reported case of an apocrine adenocarcinoma in a precursor apocrine hidrocystoma in the lower extremity. The patient's history of CML and TBI were risk factors for the development of this rare malignancy, especially since he had experienced other side effects of TBI treatment, including cataract, hypogonadism, and dyslipidemia [14]. Secondary cancer is a known complication of TBI, though there have been no reports of apocrine adenocarcinoma [14, 15]. Given the previous irradiation, chronic inflammatory conditions including diabetes and obesity, personal and family history of carcinomas, we surmise that our patient is at risk for recurrent and distant metastatic disease. He will continue to undergo frequent monitoring with regular ^{18}F-FDG PET/CT [16].

The interplay between the patient's altered immunity from both iatrogenic and endogenous immune dysregulation along with the effects of TBI on the local microenvironment are likely oncogenic factors that facilitated malignant transformation. However, the exact oncogenic events remain elusive. This case underscores the importance in recognizing that all forms of neoplasia have the potential for malignant transformation, especially when the natural tumor surveillance mechanisms become impaired.

Potential conflicts of interest

The authors declare no conflicts of interests/[the following potential conflicts].

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