

Apocrine Carcinoma of the Scalp with Aggressive Clinical Course – A Case Report and Review of the Literature

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ABSTRACT

Primary cutaneous apocrine carcinoma is a rare malignancy with about 50 cases reported in the literature. Axilla is the most common site of occurrence, but locations like scalp, anogenital region, ear canal, chest, wrist, finger and eyelid have been described. The neoplasm presents itself as an asymptomatic, slow-growing, solid or cystic mass that varies in color. Most patients have a history of a long-standing neoplasm before the diagnosis is made. The disease is considered to have an indolent clinical course with favorable outcome although more than half of reported patients had regional lymph node metastases at the time of diagnosis. Systemic dissemination to lung, bones, liver and brain is extremely rare with only 14 cases documented in the literature. Wide surgical excision with lymph node dissection upon confirmation of the lymph node metastases remains the only curable treatment. Care and management of the disseminated disease is still challenging. We report a case of a 65-year-old woman with a very aggressive apocrine carcinoma of the scalp prone to local recurrence and distant metastases to lung and bones.

Key words: apocrine carcinoma, scalp, lung and bone metastases

Introduction

Apocrine carcinoma of the skin is an extremely rare malignant sweat gland neoplasm with about 50 cases reported in the literature^{1,2} and no apparent preference toward gender, race or ethnicity. It is predominant in adults, age 50–70 years and affects body regions with high apocrine gland density. Axilla is the most common site, and other rare locations are the scalp, anogenital region, ear canal, chest, wrist, finger and eyelid^{3–6}.

Most patients usually present with an asymptomatic, slow growing, single or multiple, cutaneous or subcutaneous masses, which can be solid or cystic and vary in color from red to purple. It is often not diagnosed clinically since there are no distinguishable characteristics to raise suspicion. Time from the presentation of the skin lesion to the final diagnosis is prolonged, with most patients having a history of less than 1 year; still intervals of up to 30 years have been noted^{4,6,7}.

Pathohistologically, apocrine carcinoma has the appearance of adenocarcinoma with specific characteristics that include decapitation secretion, periodic acid-Schiff-positive diastase resistant material in the cells or in the lumen and positive immunostaining for gross cystic disease fluid protein^{1,3–6}. One report suggests tumor associated glycoprotein-72 (TAG-72) as a possible serum tumor marker for apocrine carcinoma, since its levels were elevated preoperatively and returned to normal levels after extirpation². These tumors display different architectural glandular patterns including papillary, tubular, solid or complex patterns. The female breast is developmentally and morphologically a modified apocrine gland. Breast carcinoma with apocrine features is pathohistologically very much alike cutaneous apocrine carcinoma and it must be excluded as a possible diagnosis with a clinical work-up^{2,4,6}.

Apocrine malignancies are initially only locally invasive but an early onset of regional lymph node metastases was also described. More than half of the reported patients with apocrine carcinoma had lymph node metastases at the time of diagnosis⁶. Systemic dissemination to the liver, lung, bones and brain is rare. Chamberlain *et al.* reported 10 cases, but additional reports that have been published since raise the number to only 14 cases of disseminated metastatic apocrine carcinoma in total^{1,6,8–10}. First treatment option is a wide, local surgical excision with clearance of affected lymph nodes. The use of adjuvant chemotherapy and radiotherapy has not been fully determined^{6,8–11}. Prognostic factors are difficult to establish due to low prevalence of the disease. Tumor size and site, lymphovascular and perineural invasion, histological type, degree of differentiation and resection margins are noted to have prognostic significance^{4,6}.

Most cases are reported to be indolent in their clinical course and rarely fatal.

Here, we report a case of a very aggressive apocrine carcinoma of the scalp prone to local recurrence with distant metastases to lung and bones.

Case Report

A 65-year-old woman presented with a 3 year history of a left scalp mass and enlarged nodes on the left side of the neck. Patient's past medical history included type 2 diabetes mellitus and arterial hypertension that were controlled by medication.

Physical examination showed a 4-cm-wide nummular, indurated, pink, painless skin mass of left parietal region with enlarged lymph nodes in II and V left cervical region. Excision biopsy and pathohistological examination reported carcinoma of apocrine origin. Ultrasound-guided fine-needle aspiration biopsy of the enlarged cervical lymph nodes confirmed metastasis from the same neoplasm. Other laboratory and radiographic findings were normal.

Tumorous mass of the scalp was radically excised with approximately 2 cm free surgical margins, skin defect was covered by skin grafting and extended radical neck dissection left was performed. Histology findings of resected scalp specimen revealed a poorly differentiated apocrine carcinoma. Epidermis was intact and the neoplasm was centered in the dermis with papillary extensions invading subcutaneous tissue. The tumor had mixed solid-cystic pattern but predominantly solid architecture. Malignant cells had medium sized nuclei and abundant eosinophilic cytoplasm (Figure 1). Vascular invasion was present. Surgical margins were negative. Immunohistochemical staining showed tumorous cells positive for gross cystic disease fluid protein (GCDFP+), cytokeratin7 (CK7+) and epithelial membrane antigen (EMA+), and negative for S100 protein, cytokeratin20 (CK20) and carcinoembryonic antigen (CEA). The original scalp tumor specimen that had been obtained at the first excision biopsy was examined and compared. Findings were identical and the diagnosis was confirmed.

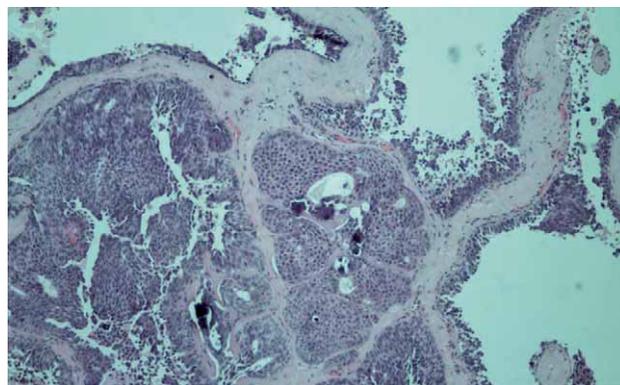


Fig. 1. Photomicrograph of the resected original scalp mass. Lesion is centered in the dermis with papillary extensions invading subcutaneous tissue and has predominantly solid architecture. Hematoxylin and eosin staining shows poorly differentiated apocrine carcinoma.

Eight out of 30 isolated nodes were metastatic. Patient was referred to an oncologist. An extensive work-up revealed no evidence of visceral malignancy and apocrine breast cancer was excluded with breast ultrasound, mammography and breast magnetic resonance imaging. The patient was given an adjuvant chemotherapy, 4 cycles of cisplatin and 5-fluorouracil preceded with external beam electron radiotherapy to the left scalp (total dose of 50 Gy) and cobalt radiotherapy to the neck (two opposing fields, total dose of 60 Gy).

The patient was well and asymptomatic for 10 months, when the local recurrence appeared in the left retroauricular region (Figure 2). The ultrasound examination of the neck with fine-needle aspiration biopsy revealed contralateral cervical lymph node metastases. The patient underwent tumor re-excision, reconstruction of the



Fig. 2. Local recurrence of the tumor in the left retroauricular region. Original site of tumor covered with skin grafting (black arrow).

defect with a rotational lobe and selective neck dissection in region I,II,III right. Histology was the same as before, with positive surgical margins and involvement of 8 out of 23 dissected lymph nodes with perinodal infiltration. After 2 months a recidive tumor appeared and anterior cervical nodes were positive. The patient was taken up for another tumor re-excision with selective neck dissection. Ultrasound examination also revealed an enlarged hypochoic node in the left axilla following its evacuation. Pathohistological examination confirmed a metastatic apocrine carcinoma. The patient had no evidence of visceral or pulmonal metastases. Second line of chemotherapy in form of paclitaxel and carboplatin every 21 days was admitted. The patient was without symptoms and local recurrence for 4 months. Positron emission tomography-computed tomography (PET-CT) scan revealed abnormal uptake at nodular lesion in the left parieto-occipital, retromandibular and parotid region. Abnormal uptake was also found in the intra-abdominal lymph nodes in the region of porta hepatis and hepatoduodenal ligament. Multiple lung metastases, osteolytic lesion of the left iliac bone, right shoulder and L5 vertebrae were also noted by the PET scan. This led to withdrawal of the chemotherapy treatment and administration of ibandronic acid. Locoregional cutaneous metastases were infiltrating the skin on the whole left side of the neck and upper pectoral region (Figure 3). The patient clinical condition was gradually deteriorating in a sense of shortness of breath and fatigue. Progression of the lung metastases to pulmonary carcinomatous lymphangiosis were revealed by chest X-ray examination. Three years after the initial diagnosis at the age of 68 the patient presented with confusion, disorientation and drowsiness. However, brain metastases were not observed by the computed tomography (CT) scan of the brain. The patient was treated with antiedematous and supportive



Fig. 3. Locoregional cutaneous metastases infiltrating the skin on the whole left side of the neck and upper pectoral region.

therapy but died due to respiratory failure caused by pulmonary lymphangiosis.

Discussion

We report a very rare case of a recurrent apocrine carcinoma of the scalp with a very aggressive clinical course. The tumor was undifferentiated and prone to local recurrence, lymphatic and hematogenous dissemination. According to the literature, disseminated metastatic apocrine carcinomas are extremely rare and only 14 cases have been reported to date^{1,6,8–10}.

Our patient was treated with repeated local excisions and dissections of involved lymph node regions at the beginning of the disease. The only recommended and curable treatment for localized apocrine carcinoma is wide surgical excision with dissection of the lymph nodes, if lymphatic spread has been proven. Some authors advise prophylactic regional lymph node dissection particularly in cases of recurrent local lesions after wide excision or with poorly differentiated tumors while others state that prophylactic lymph node dissection does not enhance survival rate^{8,9}.

Care and management of the disseminated disease remains challenge. Each following case report outlines diverse responses to multiple applied chemotherapy drugs. Tlemcani et al. report response to chemotherapy durable for 16 months in the case of a metastatic apocrine carcinoma of the scalp with multiple lung and bone metastases treated with paclitaxel and carboplatin every 21 days combined with palliative radiotherapy to the bone lesions⁶. Another report depicts a patient with a metastatic apocrine carcinoma of the scalp who received several regimens of chemotherapy that included 4 courses of adriamycin, etoposide and docetaxel periodically which stabilized the disease for approximately 2 years when it finally progressed to the brain¹. Gallerani et al. report a case of a metastatic axillary apocrine carcinoma that evolved during treatment with cisplatin and cetuximab¹⁰. Kumar et al. portray a case of an apocrine carcinoma of the eyelid with an optimal response to cisplatin, adriamycin and cyclophosphamide that controlled the disease for about 2 years⁵. Adjuvant chemotherapy in form of 5-fluorouracil and cisplatin combined with adjuvant radiation controlled the apocrine carcinoma of the arm for 6 months until it worsened with lung metastases⁹. Evidently, metastatic apocrine carcinoma generally has a weak response to chemotherapy. Nonetheless, patients with disseminated disease should be treated with any applicable chemotherapy regime reported in the literature by now.

Reports on the efficiency of radiotherapy vary: some impose radioresistance and others recommend adjuvant radiation in cases with advanced local and regional metastases. Chamberlain et al. suggested local adjuvant radiation for large tumors (> 5 cm), positive surgical margins or poorly differentiated lesions with lymphovascular invasion and adjuvant radiation to the affected regional lymph nodes in the case of extranodal extension or involvement of more than 4 lymph nodes⁶. Deficient literature offers no appropriate radiation treatment plan containing schedule or dose.

Our patient received adjuvant radiotherapy to the left scalp and neck, followed by adjuvant chemotherapy in form of 4 cycles of cisplatin and 5-fluorouracil. Regardless of both surgical and non-surgical therapeutic measures, the disease was controlled only for 10 months when local recurrence appeared. According to the literature, a long term remission is achievable by surgery alone despite the local recurrences and regional lymph node metastases that may occur years after the first operation. Some authors reported a 28% 5-year recurrence rate^{5,6}. As stated in the literature, prolonged remission of the disseminated disease is achievable, however, the dis-

ease is without exception fatal at this stage. We believe that repeated local excisions and dissections of affected lymph node regions, accompanied by second line of chemotherapy (paclitaxel and carboplatin) delayed the progression of the disease briefly before it disseminated to distant lymph nodes, lung, bones and probably brain. Pulmonary metastases showed considerably rapid progression and finally were the cause of our patient demise.

Clinical trials and investigations in order to attain specific guidelines regarding adjuvant radiotherapy and chemotherapy are almost impossible to conduct due to the rareness of the disease and may never be available.

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APOKRINI KARCINOM KOŽE GLAVE AGRESIVNOG KLINIČKOG TIJEKA – PRIKAZ SLUČAJA I PREGLED LITERATURE

SAŽETAK

Primarni kožni karcinom podrijetla apokrinih žlijezda je rijetka maligna bolest sa oko 50 slučajeva prikazanih u literaturi. Najčešće zahvaća područje aksile ali opisani su i na koži glave, anogenitalne regije, vanjskog zvukovoda, prsišta, šake, prstiju te vijeđa. Neoplazma se prezentira kao asimptomatska, spororastuća, čvrsta ili cistična tumorska masa s varijacijama u boji. Većina pacijenata ima anamnezu o dugotrajnom postojanju neoplazme prije postavljanja dijagnoze. Smatra se bolešću indolentnog kliničkog tijeka sa očekivanim povoljnim ishodom iako više od polovice pacijenata u trenutku postavljanja dijagnoze ima zahvaćene regionalne limfne čvorove. Dokumentirano je samo 14 slučajeva sistemske diseminacije bolesti s metastazama u pluća, kosti, jetru i mozak. Široka resekcija tumora sa disekcijom zahvaćenih limfnih čvorova je jedina djelotvorna metoda liječenja. Liječenje metastatske bolesti i dalje predstavlja izazov. Prikazujemo slučaj 65-godišnje žene sa izrazito agresivnim apokrinim karcinomom kože glave, sklonim lokalnim recidivima, udaljenim metastazama u pluća i kosti.