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Case Report

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Metastatic apocrine adenocarcinoma of the axillary area

Authors' Contribution:
A Study Design
B Data Collection
C Statistical Analysis
D Data Interpretation
E Manuscript Preparation
F Literature Search
G Funds Collection

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Summary

Background Apocrine adenocarcinoma of the skin is a rare entity. It is characterized by slowly enlarging, painless, indurate nodules or plaques and often misdiagnosed as benign skin tumours. Although these tumours show characteristic tubular structures mixed with cellular cords and have some pattern of cytokeratins, primary apocrine carcinoma is indistinguishable from metastatic mammary ductal carcinomas. Like other apocrine carcinomas it is radioresistant and therefore surgical resection is the method of choice in treatment of patients. Distant metastases have been reported in a limited number of published cases.

Aim We present the case of a 66-year-old woman with apocrine adenocarcinoma of the left axillary area with local lymph node and distant metastases.

Case Report A 66-year-old woman was admitted to hospital because of a tumour located in the skin of the axillary area. After incision biopsy lobular breast carcinoma was initially suspected. Correlation of clinical, histological and immunohistochemical data allowed the rare apocrine adenocarcinoma to be diagnosed. The tumour was excised with axillary lymph nodes. Next chemotherapy was applied as palliative treatment.

Conclusions Our observations lead us to following conclusions: (I) apocrine adenocarcinoma is a rare and difficult to diagnose tumour requiring special examination; (II) metastases to lung, liver and bones cause worse prognoses; (III) a wide surgical excision is the treatment of choice.

Key words **apocrine adenocarcinoma • apocrine carcinomas • breast ductal carcinoma • case report**

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Background

Apocrine adenocarcinoma is a rare entity and most documented cases have been located in the axilla area [1,2]. Clinically, apocrine adenocarcinoma is recognized by the presence of slowly enlarging, painless, indurate nodules or plaques. Therefore it is frequently confused with benign skin tumours [1,2]. The scalp, eyelid (Moll's gland carcinoma), ear, anogenital region, chest, lip and nipple areas are occasionally affected [1–4]. Confusion with benign tumours and less aggressive malignancies, such as dermatofibroma, can lead to inadequate initial treatment and extensive recurrences [1–4]. Histologically, these tumours are characterized by the presence of tubular structures mixed with variable amounts of cellular cords. The dermis is infiltrated and the subcutaneous fat and the perineural spaces are in most cases involved. The stroma is nearly always desmoplastic and hyalinized. Epidermal contraction and ulceration sometimes occur. Expression of cytokeratins reveals the following pattern: AE1/AE3, CAM 5.2, EMA, CEA, CK15 and GCDFP-15. Lysozyme, α_1-antichymotrypsin and S-100 protein are also present in some tumours. Primary cutaneous apocrine adenocarcinoma is indistinguishable in terms of histology from metastatic mammary ductal carcinoma, especially with apocrine differentiation. Since most apocrine carcinomas are radioresistant, local wide surgical excision is recommended. Chemotherapy and radiotherapy have a limited role in advanced cancers. Lymph node metastases have been documented in some cases. According to the literature, distant metastases are encountered in the minority of published cases [1,2].

Aim

In the following report we present the case of a 66-year-old woman with apocrine adenocarcinoma of the left axillary area with local lymph and distant metastases.

Case Description

In December 2004, a 66-year-old Polish woman was examined in an ambulatory of Great Poland Cancer Centre by a surgeon because of a slow-growing skin tumour. Physical examination showed that the tumour was located in the skin of the axillary area. The tumour appeared as a painless, indurate, irregular nodule measuring 6×8cm. The tumour seemed to have invaded the surrounding subcutaneous tissue and underlying axillary lymph nodes. The overlying skin was smooth like the skin of a scar.

Material obtained in fine needle aspiration biopsy of the mass was insufficient for diagnosis. Therefore, the patient had an incision biopsy in the surgical ambulatory. Histological study found proliferated ducts infiltrating the dermis and subcutaneous fat tissue, which suggested a lobular breast carcinoma or sclerosing sweat duct carcinoma. Immunohistochemical study performed on paraffin-embedded tissue sections showed positive staining for cytokeratins AE1/AE3, CAM5.2, GCDFP-15 (gross cystic disease fluid protein-15) and negative reactivity with antibodies against S-100 protein, oestrogen receptor (ER) and progesterone receptor (PgR). Clinical data (axillary area involvement, no breast tumours, slow growing) correlated with histological and immunohistochemical findings suggested a rare malignant skin tumour arising from the apocrine glands.

In February 2005 the patient was admitted to the 2nd Department of Oncological Surgery of Great Poland Cancer Centre, Poznań. Presurgical examinations were ordered. Abdominal ultrasound showed a tumour in the 4th segment of the liver measuring 11mm, which was suspected of metastasis. Haematological and biochemical tests and x-ray chest examination were normal. We recommended wide tumour excision with axillary lymph node dissection. Consequently, after she had agreed, she underwent the operation. The postoperative course was uneventful and the patient was discharged on the 5th day after the operation. Histological examination of the excised tumour revealed proliferating ducts situated by two layers of epithelium infiltrating the dermis and subcutaneous tissue. There was a diffuse growth pattern in the deeper parts of dermis and involvement of subcutaneous fat. The stroma was desmoplastic and hyalinized infiltrated by pleomorphic cells similar to those observed in breast lobular carcinoma. Hyperplastic apocrine glands were found in close proximity to the tumour. Cancer cells contained abundant eosinophilic cytoplasm. Nuclei were large and vesicular with conspicuous nucleoli. The carcinoma cells were characterized by a tubular growth pattern and formed solid foci. Lipid tissue was infiltrating. All examined lymph nodes were metastatic with infiltration of perinodal fat tissue. Histological examination correlated with clinical and immunohistochemical data established the diagnosis of apocrine adenocarcinoma.

The patient was further observed as an ambulatory treated outpatient. She underwent a metastatic work-up. CT imaging showed a hypodensic metastatic lesion measuring 11mm in diameter in the right lobe of the liver. There were bone metastases in the lumbar and thoracic part of the spine and osteolytic multifocal metastasis in the hip bone.

We recommended chemotherapy and palliative treatment. The patient underwent an AC chemotherapy course with Adriablastin and Endoxan in standard doses (Endoxan 905mg, Adriablastin 90mg in 3-week cycle). The patient was under symptomatic and palliative treatment and is still being treated at the Great Poland Cancer Centre as an outpatient.

Discussion

Apocrine adenocarcinoma of the skin is a rare and usually misdiagnosed malignant entity. The lesion was suspected to be a benign skin tumour at first clinical examination. It is recognized by the presence of slowly enlarging, painless, indurate nodule. Confusion with benign tumours led to inadequate initial treatment and extensive recurrences [1–3]. In the presented case there was no CT imaging in presurgical examinations. Clinical experience suggested a favourable prognosis with no distant metastases; hence local wide excision was proposed. After incision biopsy lobular breast carcinoma was initially suspected. Apocrinal tumours and ductal breast carcinoma form ductal structures, although similar cellular atypia, sclerotic stroma, subcutaneous and musucular invasion are observed in both types of neoplasm [5–9]. Differentiation between benign and other malignant variants of apocrine lesions is difficult [7,10,11]. Our experience allowed us to conclude that only wide excision biopsy and subsequent careful microscopic examination lead to appropriate diagnosis of an apocrine adenocarcinoma. Cytoplasm labelling for cytokeratin 7 (CK7) and EMA, known as distal tubule marker, and cytokeratins AE1/AE2 and CAM 5.2 supports an eccrine origin [12]. The presence of S-100 and CEA immunoreactivity also suggests eccrine differentiation [2] (S-100 protein in our cases was negative, CEA not used). The eccrine ductal structures additionally expressed gross cystic disease fluid protein – 15 (GCDFP-15) [13]. Clinical data, microscopic examination, immunohistochemical studies (positive staining for cytokeratin AE1/AE3, CK7, CAM5.2, GCDFP-15 and negative reactivity with antibodies against S-100 protein, oestrogen and progesterone receptor) allowed apocrine adenocarcinoma to be finally distinguished from ductal breast carcinoma or benign syringoma in the presented case.

Normal apocrine glands are often found in close proximity to the tumour and occasionally longstanding pre-existent benign apocrinal lesions may be evident, raising the possibility of malignant transformation [1,2]. The problem for immunohistochemical investigations is whether apocrine hyperplasia is a precursor of cancer or whether apocrine hyperplasia and adenoma may be successive steps in the linear progression to apocrine adenocarcinoma [2]. Apocrine adenocarcinomas have to be distinguished from metastases, especially from breast cancer. Apocrine cells may be present in up to 50% of cases of DCIS, although Eusebi et al. [6,14] consider it as an infrequently recognized phenomenon. The most useful discrimination for making such a distinction is a detailed clinical history and careful examination of the patient. Immunohistochemistry is not very useful in making the differential diagnosis because the immunophenotype of apocrine adenocarcinoma (positive staining for cytokeratins AE1/AE3, CAM 5.2, GCDFP 15 and negativity for ER and PR) is not specific and all of the studied antigens can be observed, to varying extent, in metastases of visceral tumours.

The histological analysis suggested that the wide spectrum of morphologic appearances may be due to the variable grade of differentiation of tumours. Apocrine adenocarcimoma appears as a tumour that frequently recurs and is capable of metastasizing [1,2]. Lymph node involvement has been documented in some cases of this tumour. Our case showed regional lymph node invasion. Presurgical exams showed no symptoms of distant metastases. The patient underwent wide excision with axillary lymphadenectomy. The histological findings revealed massive lymph node metastases with infiltration of perinodal fat tissue.

The patient was further observed as an ambulatory treated outpatient. When seen 2 months after the operation she suffered from spine, hip and thoracic pain. Metastatic work-up showed a hypodensic, metastatic lesion 11mm in diameter in the right lobe of the liver; there were bone metastases in the lumbar and thoracic part of the spine and hip bone osteolytic multifocal metastasis in CT imaging. According to the literature data sites of apocrine adenocarcinoma metastases include nodes, lungs, liver and bone [15,16]. In the majority of cases deposits from undiagnosed

visceral and breast adenocarcinomas are virtually indistinguishable microscopically from apocrine tumours and must be ruled out before a diagnosis of apocrine cancer is made [7].

The recommended treatment of apocrine adenocarcinoma is wide surgical excision along with regional lymph node dissection in the presence of clinically positive nodes. This kind of tumour is rather chemoresistant and chemotherapy has been infrequently employed [17]. In this case, palliative chemotherapy was applied but there was no evidence of benefits of this treatment.

Conclusions

I. Apocrine adenocarcinoma is a rare malignancy with high metastatic and recurrence potential. The region of the axilla is the most common site of occurrence and it usually spreads to lymph nodes. It is recognized by the presence of slowly enlarging, painless, indurated nodule. Confusion with benign tumours led to inadequate initial treatment and extensive recurrences.

Differentiation diagnosis is often difficult. The most useful discrimination for making such a distinction is a detailed clinical history and careful examination of the patient. Findings that distinguish apocrine adenocarcinoma from breast carcinomas or other tumours are: clinical data and microscopic examination. Immunohistochemical studies are, in this case, of lesser value.

II. Lungs, liver and bones are the distant sites of metastases that result in fatal course of the disease.

III. A wide surgical excision is the treatment of choice with clearance of draining lymph nodes. The role of adjuvant chemo- and radiotherapy is not established.

IV. The reported case demonstrates the difficulties in diagnosing apocrine adenocarcinomas and indicates that this entity should be considered in the differential diagnosis of slowly growing skin tumours with clinically benign features in the region of the axilla.

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