Giant Pendulous Carcinosarcoma – Squamous Cell Carcinoma-Type – of the Leg – A Case Report and Review of the Literature

Uwe Wollina1, Ina Riedel2, Mohammad R. Abushika1, Torello Lotti3, Georgi Tchernev4,5

1Städtisches Klinikum Dresden - Department of Dermatology and Allergology, Dresden, Sachsen, Germany; 2Städtisches Klinikum Dresden - Institute of Pathology "Georg Schmor" Dresden, Sachsen, Germany; 3University G. Marconi of Rome - Dermatology and Venereology, Rome, Italy; 4Department of Dermatology, Venereology and Dermatologic Surgery, Medical Institute of Ministry of Interior, Sofia, Bulgaria; 5Onkoderma, Policlinic for Dermatology and Dermatologic Surgery, Sofia, Bulgaria

Abstract

Cutaneous carcinosarcoma (CCS) is a rare non-melanoma skin cancer with a biphasic growth pattern. A tumour is composed of epithelial and mesenchymal cells that show clonality. In most cases, CCS develops in the head-and-neck region on the chronic sun-exposed skin of males. Here, we describe an 80-year-old female patient who developed a giant, pendulous CCS on the leg. A tumour was surgically removed. We found no evidence of metastatic spread.

Introduction

Cutaneous carcinosarcoma (CCS) also known as sarcomatoid carcinoma is a rare non-melanoma skin cancer occurring mainly on sun-exposed skin of elderly males. The tumour is biphasic, i.e., composed of epithelial and mesenchymal elements. Various subtypes have been described such as a basal cell, pilomatrical, squamous cell, and trichoblastic [1][2].

The neoplastic cells show coexpression of keratins and vimentin – in particular, the spindle cells. Also, coexpression of p53, p16 and p63 has been reported in epithelial and spindle cells [3]. CCS display multiple copy number variations (CNVs) and copy-neutral loss of heterozygosity (CN-LOH). Furthermore, epithelial and spindle cells share the same clonality [4][5].

Here we report a case of CSS – squamous cell type – of the leg.

Case report

An 80-year-old female patient was referred to our department. The primary reason for hospital admission was an edematous swelling of the right leg and slight increase of fibrinogen to 4.96 g/L (normal range: 1.8-4.5). Duplex sonography revealed a 3-storey deep venous thrombosis of the right leg. Since the bandages had to be removed for diagnostics, a giant exophytic, pendulous, malodorous tumour became apparent. Therefore, she was referred to our department.
Her medical history was remarkable for breast cancer 1995, renal cell carcinoma 2015, and chronic lymphatic leukaemia. She suffered from type II diabetes mellitus and arterial hypertension. She had secondary lymphedema of the arm after axillary dissection 1995.

On examination, we observed a 9 cm x 7 cm large, partially ulcerated, pendulous tumour on her upper right leg (Fig. 1).

Laboratory findings: Leucocytes 11.71 Gpt/L (normal range: 3.8-11), erythrocytes 3.86 Tpt/L (4.2-5.4), hypochromic erythrocytes 14.6% (< 2.5%), microcytic erythrocytes 2.4% (< 1.5%), hemoglobin 6.4 mmol/L (7.4-10.7), hematocrit 0.336 (0.37-0.47), C-reactive protein 69.6 mg/L (< 5).

Imaging techniques did not reveal any metastatic spread.

Treatment was surgically excised with wide excision (2 cm safety margin) and primary closure by tissue expansion. Healing was uneventful.

Histopathologic examination of the specimen was performed. Histological examination showed a polypoid ulcerated tumour with structures of squamous cell carcinoma associated with the overlying epidermis, and beneath structures of a malignant spindle cell component in parts seeming one component transit into the other. The interlacing cords of epithelial cells extended from the epidermis and the ulcerated tumour surface to the intermediate dermis (Fig. 2a). Some of the deeper situated cords developed bulbar formations resembling glandular structures (Fig. 2b). However, ductal formations were completely missing.

In both cellular components, immunohistochemistry demonstrated expression of cytokeratins (CK 5/6 and PanCK). In particular, in the spindle cell component, there was coexpression with vimentin, which was interpreted as clues to sarcomatoid dedifferentiated squamous cell carcinoma (CCS) (Fig. 2).

The patient also received low-molecular-weight heparin certoparin–sodium 8,000 U subcutaneously per day to treat the deep vein thrombosis.

Discussion

CCS is a rare tumour entity initially described by Dawson in 1972 [6]. We report a case of squamous cell type CCS on the leg of an elderly woman. The localisation on the leg is a rarely reported clinical feature since most of these tumours develop on the chronic sun-damaged skin of the head and neck region [1][2][3].

We could identify only three case reports with CCS of the leg – one in a 32-year-old female with a burn scar [7], another case of a 52-year-old female with a very rare myofibroblastic sarcomatous variant [8], and a last one of a 54-year-old male [9].

In the present case, we observed an ulcerated malodorous tumour that raised several differential diagnoses in a patient with multiple neoplastic disorders, including metastasis of breast or renal cancer, SCC, Merkel cell carcinoma, amelanotic melanoma, osteosarcoma, and rhabdomyosarcoma [10][11][12][13]. By histologic examination, a CCS of squamous cell subtype could be confirmed.

Cutaneous SCC can be associated with reactive fibroblastic proliferation. These spindle cells, however, do not co-express vimentin and keratin as seen in our case (Fig. 2c). In SCC epithelial-mesenchymal transition (EMT) is required for tumour invasion and dissemination. This is accompanied by overexpression of transcriptional factors Twist and ZEB1 [14].

Basosquamous carcinoma, also known as metatypical basal cell carcinoma (BCC), is a rare subtype of SCC. It occurs in two subtypes – mixed and intermediari. The mixed type shows focal keratinisation with a parakeratotic centre. The intermediari type is characterised by a network of narrow strands composed of an outer row of darkstaining basaloid cells and an inner layer of larger cells appearing lighter. Some of these tumours may express smooth muscle actin or myosin [15].

Cutaneous adenosquamous carcinoma is extremely rare neoplasia composed of malignant squamous and glandular cells without co-expression of keratin and vimentin. Luminal cells express cytokeratin 7. All tumour cells express cytokeratin 5/6.
and p63. Cutaneous adenosquamous carcinoma is considered as a locally aggressive high-risk subtype of SCC [16].

BCC with ductal and glandular differentiation is very uncommon. The preferred tumour localisation is the eyelids. The glandular structures demonstrate an apocrine differentiation [17]. In contrast to our case, no co-expression of keratin and vimentin was reported. The present tumour had some glandular-like bulbar formations but no ductal parts.

The tumour was ulcerated, and ulcerated CCS of the hand had been described previously [18].

Our patient presented initially because of leg swelling caused by deep vein thrombosis. Tumors can alter the clotting system by various events including circulating tumour cells. Both ovarian and uterine carcinosarcoma-induced deep venous thrombosis have been reported [19][20].

The treatment of choice is surgery. Despite R0-resection, in one study, 27% of cases developed metastatic disease [21]. Negative prognostic factors are histologic subtype, age, tumour size > 2 cm, and nodal status. Patients with basal or squamous cell carcinoma-type CCS have a mean age of 72 years with clear male dominance. The 5-year disease-free survival is 70%. In contrast, adnexal CCS occurs in younger patients (mean age 58 years) and those have only a 25% 5-year disease-free survival [22].

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References

1. Clark JJ, Bowen AR, Bowen GM, Hyngstrom JR, Hadley ML, Duffy K, Florell SR, Wada DA. Cutaneous carcinosarcoma: a series of six cases and a review of the literature. J Cutan Pathol. 2017; 44(1):34-44. https://doi.org/10.1111/jcp.12843 PMid:27730657

2. Wollina U, Koch A, Schönlebe J, Tchernev G. Carcinosarcoma of skin (sarcomatoid carcinoma) — a rare non-melanoma skin cancer (Case review). Georgian Med News. 2017; 263:7-10.

3. Zbaczik AP, Rawal A, Lee B, Werling R, Knapp D, Mesa H. Cutaneous basal cell carcinosarcoma: case report and literature review. J Cutan Pathol. 2015; 42(11):903-10. https://doi.org/10.1111/jcp.12578 PMid:26268472

4. Paniz-Mondolfi A, Singh R, Jour G, Mahmoodi M, Diwan AH, Barkoh BA, Cason R, Huttonbach Y, Benaim G, Galbincea J, Luthra R. Cutaneous carcinosarcoma: further insights into its mutational landscape through massive parallel genome sequencing. Virchows Arch. 2014; 465(3):339-50. https://doi.org/10.1007/s00428-014-1628-0 PMid:25031014

5. Hamrs PW, Fullen DR, Patel RM, Chang D, Shalin SC, Ma L, Wood B, Beer TW, Siddiqui J, Carskadon S, Wang M, Palanisamy N, Fisher GJ, Andea A. Cutaneous basal cell carcinosarcomas: evidence of clonality and recurrent chromosomal losses. Hum Pathol. 2015; 46(5):690-7. https://doi.org/10.1016/j.humpath.2015.01.006 PMid:25704628

6. Dawson EK. Carcin-sarcoma of the skin. J R Coll Surg Edinb. 1972; 17(4):243-6. PMid:5079312

7. Rouas L, Amrani M, Regrayi A, Gama L, Bellabas MA. Carcinosarcomas of the skin. Ann Dermatol Venereol. 2006; 133(4):362-4. https://doi.org/10.1016/j.s1511-9638(06)70916-4

8. Agostini T, Mori A, Leporatti G, Dini M, Franchi A. Cutaneous carcinosarcoma: report of a case with myofibroblastic sarcomatous component. Dermatol Surg. 2008; 34(3):418-22. https://doi.org/10.1097/SDS.0b013e3182385afa PMid:19622364

9. Iakovides J, Delides GS. Carcinosarcomas of the skin—report of two cases. Arch Geschwulstforsch. 1988; 59(6):461-4. PMid:3223796

10. Terada T. Sarcomatoid carcinoma of the lung presenting as a cutaneous metastasis. J Cutan Pathol. 2010; 37(4):482-5. https://doi.org/10.1111/j.1600-0650.2009.01292.x PMid:19602061

11. Scatena C, Massi D, Franchi A, De Paoli A, Canzonieri V. Rhabdomyosarcoma of the skin resembling carcinosarcoma: report of a case and literature review. Am J Dermatopathol. 2012; 34(1):1-6.

12. Ram R, Saadat P, Peng D, Vadamal M. Case report and literature review: primary cutaneous carcinosarcoma. Ann Clin Lab Sci. 2005; 35(2):189-94. PMid:15943184

13. Wollina U, Langner D, Tchernev G. Mushroom-like skin tumors: report of three cases. Open Access Maced J Med Sci. 2017; 5(4):515-7. https://doi.org/10.3889/oamjms.2017.109 PMid:28785347 PMCiG:PMCi535672

14. Toll A, Masferrer E, Hernández-Ruiz ME, Fernández-Pulido C, Yélamos M, Jaka A, Tumeu A, Jucigla A, Gimeno J, Báró T, Casado B, Gandadillas A, Costa I, Mojal S, Pe-a R, de Herreros AG, García-Patos V, Pujol RM, Hernández-Muoz I. Epithelial to mesenchymal transition markers are associated with an increased metastatic risk in primary cutaneous squamous cell carcinomas but are attenuated in lymph node metastases. J Dermatol Sci. 2013; 72(2):93-102. https://doi.org/10.1016/j.jdermsci.2013.07.001 PMid:23928229

15. Kazantseva IA, Khlebnikova AN, Babaev VR. Immunohistochemical study of primary and recurrent basal cell and metatypical carcinomas of the skin. Am J Dermatopathol. 1996; 18(1):35-42. https://doi.org/10.1097/00000372-199602000-00006 PMid:8721589

16. Ko CJ, Leffell DJ, McNiff JM. Adenosquamous carcinoma: a report of nine cases with p63 and cytokeratin 5/6 staining. J Cutan Pathol. 2009; 36(4):448-52. https://doi.org/10.1111/j.1600-0560.2008.01083.x PMid:19278431

17. Misago N, Sato T, Narisawa Y. Basal cell carcinoma with ductal and glandular differentiation: a clinicopathological and immunohistochemical study of 10 cases. Eur J Dermatol. 2004; 14(6):383-7. PMid:15564201

18. El Harroudi T, Ech-Charif S, Amrani M, Jallal A. Primary carcinosarcoma of the skin. J Hand Microsurg. 2010; 22(7):79-81. https://doi.org/10.1016/j.jcsm.2010.01.003 PMid:2282673 PMCiG:PMCi3122707

19. Dittus C, Fountzilas C, Saha D, Magee A. A rare case of ovarian carcinosarcoma with neuroendocrine differentiation. J Community Support Oncol. 2014; 10(2):71-4. https://doi.org/10.12788/jcso.0018 PMid:24971408

20. Kimura T, Chino M, Ogasawara N, Nakano T, Izumi S, Takeuchi H. Trousseau's syndrome with brachiocephalic vein thrombosis in a patient with uterine carcinosarcoma. A case report. Angiology. 1999; 50(6):515. PMid:10378629

21. Syme-Grant J, Syme-Grant NJ, Motta L, Stevenson JH, Evans AT. Are primary cutaneous carcinosarcomas underdiagnosed? Five cases and a review of the literature. J Plast Reconstr Aesthet Surg. 2006; 59(12):1402. https://doi.org/10.1016/j.bjps.2005.12.057 PMid:17115307

22. Tran TA, Moller S, Choudhri PJ, Carlson JA. Cutaneous carcinosarcoma: adnexal vs. epidermal types define high- and low-risk tumors. Results of a meta-analysis. J Cutan Pathol. 2005; 32(1):2-11. https://doi.org/10.1034/j.1600-0649