Primary cutaneous carcinosarcoma: report of a case with poroid and fibrohistiocytic differentiation

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Carcinosarcoma is a biphasic neoplasm composed of malignant epithelial and mesenchymal elements that are intimately admixed. It has been described in many different organs such as the uterus, bladder, lung, kidney, breast, oropharynx, and the gastrointestinal tract, but it very rarely develops in the skin. The prognosis is uncertain and depends on the epithelial component, but local recurrence and metastasis rates are lower when compared to similar tumors located elsewhere in the body.

Case report
An 89-year-old man presented with an ulcerated solitary exophytic nodule located on the back of the left leg that had steadily grown over the past year to a diameter of 2.6 cm. It was ulcerated and bled occasionally but lymph nodes were unaffected. An excisional biopsy and skin graft were performed, and no residual tumor was detected (figure 1).

The pathologic findings showed an ulcerated invasive biphasic mass with a mesenchymal component...
formed by large irregular dyscohesive pleomorphic mono and multinucleated cells with wide eosinophilic cytoplasm, and some cells with eosinophilic intracytoplasmic globules. They also had irregular nuclei with vesicular and granular chromatin, and prominent nucleoli. Three atypical mitoses per high power field were identified. The epithelial component was circling its mesenchymal counterpart, and consisted of atypical cohesive cells with clear cytoplasm, round and oval-shaped nuclei with vesicular chromatin and prominent nucleoli, forming a trabecular pattern, nests, and some tubular structures (figure 2A-2D).

Immunohistochemical staining showed a positive reaction for EMA and it was negative for CD10, CD31 and MyoD1 in the epithelial component. In the mesenchymal component, there was a positive reaction for CD10, and negative for EMA, CD31 and MyoD1 (figure 3A-3D).

The histopathological findings were consistent with a cutaneous carcinosarcoma with adnexal differentiation (porocarcinoma), and pleomorphic sarcoma with fibrohistiocytic differentiation.

Figure 1
Exophytic ulcerated nodular lesion located on the back of the left leg.

Figure 2
2A: Ulcerated malignant tumor with a predominant epithelial component. The sarcomatous component is superficial and ulcerated (arrow). HE2.5x.
2B: The epithelial component is formed by a nest of cells with tubular structures.
2C: The mesenchymal component is formed by large pleomorphic cells with enlarged and hyperchromatic nuclei in addition to some binucleated cells. HE20x.
2D: Several mitosis can be seen.
Discussion

Carcinosarcoma is a malignant biphasic tumor described in different anatomical sites but infrequently develops in the skin. The first description of carcinosarcoma was made by Virchow in 1864 but a primary cutaneous carcinosarcoma was first described by Grime in 1948 in a biopsy showing squamous cell carcinoma with fibrosarcoma that had developed in a post-burn scar. Since then, we found 80 cases of cutaneous carcinosarcoma reported in the English literature (Table 1). According to these case reviews, the average age of clinic presentation is 76 years old, and ranges from 48 to 92 years old. It is more frequent in men (n: 57) than in women (n: 23), 71.2% compared to 28.7%. In the skin the most frequent locations are photoexposed areas, mainly in the face and ears although they have been described in places like the armpit and gluteus.

The prognosis is variable and depends directly on the epithelial carcinoma component differentiation. If it comes from the epidermis (basaloid or squamous), the disease-free survival rate at 5 years is 70%. However, if the epithelial component has adnexal differentiation (poroid or trichoblastic), the disease-free survival rate at 5 years is 25%. The suggested treatment consists of a surgical resection through Mohs surgery.

The epithelial component can arise from the epidermis (basaloid or squamous) or derived from eccrine, apocrine, follicular, matrical, or trichilemmal skin appendages. The sarcomatous component can be homologous, meaning it is made of the same tissue where the lesion develops, or heterologous and formed from a tissue elsewhere on the body. This component can have, but is not limited to, osteoblastic, chondroblastic, smooth muscle, skeletal muscle, or fibrohistiocytic differentiations.

Of all the cases we found in the literature, 67.9% had a basaloid epithelial differentiation, 32% had squamous differentiation, and only 8.6% showed adnexal differentiation. Among the mesenchymal components 16.25% had atypical fibroxanthoma (undifferentiated pleomorphic sarcoma), and 37.5% had a heterologous component with osseous being the most frequent (Table 1).
| Case number | Reference | Age/ Years | Gender | Location         | Clinical diagnosis | Epithelial component differentiation | Mesenchymal component differentiation |
|-------------|-----------|------------|--------|------------------|--------------------|--------------------------------------|--------------------------------------|
| 1           | (17) 1948 | 48 M      | Arm    | NR               | SCC                | Fibrosarcoma                        |
| 2           | (3) 1972  | 75 M      | Thorax | NR               | Squamous/basal     | Osteoid - chondroid                  |
| 3           | (21) 1981 | 74 M      | Armpit | NR               | BCC                | Chondroid – osteoid-fibrosarcoma - synovial |
| 4           | (22) 1988 | 91 F      | Forehead | NR               | BCC                | Osteosarcoma                        |
| 5           | (23) 1993 | 44 M      | Back   | NR               | BCC                | Cell fused sarcoma                   |
| 6           | (24) 1995 | 86 M      | Tragus (Ear) | SCC               | BCC                | Osteosarcoma                        |
| 7           | (14) 1996 | 69 F      | Arm    | NR               | Squamous           | Pleomorphic sarcoma                  |
| 8           | (12) 1997 | 71 M      | Eyelid | NR               | Squamous           | Osteoid                             |
| 9           |           | 74 M      | Scalp  | Dermatofibrosarcoma protuberans | Squamous           | Smooth and skeletal muscle |
| 10          |           | 83 M      | Scalp  | NR               | Squamous           | Osteoid and chondroid                |
| 11          |           | 67 M      | Nose   | Pyogenic granuloma | Eccrine porocarcinoma | Osteoelast-like and osteoid-like giant cells |
| 12          | (25) 1998 | 82 M      | Supraclavicular region | NR               | BCC                | Malignant fibrous histiocytoma (Undifferentiated pleomorphic sarcoma) |
| 13          | (1) 1999  | 72 M      | Arm    | Swollen epidermal cyst | BCC                | Fibrosarcoma                        |
| 14          | (26) 2003 | 64 M      | Ear    | NR               | BCC                | Myxoid fibrous histiocytoma          |
| 15          | (13) 2003 | 73 F      | Arm    | SCC              | BCC                | Atypical fibroxanthoma               |
| 16          | (7) 2005  | 77 F      | Forehead | NR               | BCC                | Pleomorphic sarcoma                  |
| 17          |           | 70 M      | Chin   | NR               | BCC                | Pleomorphic sarcoma                  |
| 18          |           | 83 M      | Ear    | NR               | BCC                | Pleomorphic sarcoma – osteoid – myofibroblast |
| 19          |           | 86 M      | Back   | NR               | BCC                | Pleomorphic sarcoma - leiomyosarcoma |
| 20          | (4) 2005  | 78 M      | Temporal bone | NR               | BCC                | Atypical fibroxanthoma               |
| 21          |           | 81 F      | Chin   | NR               | BCC                | Atypical fibroxanthoma with heterologous component - chondrosarcoma |

Tabla 1
Guímera-Martín and Paniz-Mondolfi. Modified from3,10
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| Case number | Reference   | Age/Years | Gender | Location     | Clinical diagnosis | Epithelial component differentiation | Mesenchymal component differentiation |
|-------------|-------------|-----------|--------|--------------|--------------------|--------------------------------------|---------------------------------------|
| 22          |             | 75        | F      | Hand         | NR                 | BCC and SCC                          | Atypical fibroxanthoma                |
| 23          |             | 90        | M      | Ear          | NR                 | BCC                                  | Atypical fibroxanthoma                |
| 24 (27) 2005|             | 61        | M      | Leg          | NR                 | BCC                                  | Cell fused sarcoma                    |
| 25 (3) 2005 |             | 70        | F      | Scalp        | NR                 | Adenocarcinoma                       | Rhabdomyosarcoma                       |
| 26 (28) 2006|             | 62        | M      | Leg          | NR                 | BCC                                  | Osteosarcoma                          |
| 27          |             | 83        | F      | Leg          | NR                 | BCC                                  | Osteosarcoma                          |
| 28          |             | 92        | F      | Forehead     | NR                 | BCC                                  | Osteosarcoma/ giant cell-rich         |
| 29          |             | 87        | M      | Preauricular | NR                 | BCC                                  | Osteosarcoma                          |
| 30          |             | 75        | M      | Olecranon    | NR                 | BCC                                  | Osteosarcoma                          |
| 31          |             | 77        | F      | Periocular   | Pyogenic granuloma/ BCC | BCC                              | Osteosarcoma                          |
| 32          |             | 61        | M      | Arm          | Pyogenic granuloma  | BCC                                  | Osteosarcoma/ giant cell-rich         |
| 33          |             | 68        | M      | Scalp        | NR                 | BCC                                  | Osteosarcoma                          |
| 34          |             | 89        | M      | Forehead     | NR                 | BCC                                  | Osteosarcoma                          |
| 35          |             | 75        | F      | Ear          | NR                 | BCC                                  | Osteosarcoma                          |
| 36          |             | 65        | F      | Periocular   | NR                 | BCC                                  | Giant cell-rich estroma               |
| 37 (29) 2006|             | 53        | M      | Abdominal    | NR                 | BCC                                  | Osteosarcoma                          |
| 38 (15) 2006|             | 93        | M      | Vertex       | SCC                | BCC                                  | Cell fused sarcoma                    |
| 39          |             | 80        | F      | Shin         | SCC                | BCC                                  | Cell fused sarcoma                    |
| 40          |             | 86        | M      | Forehead     | NR                 | SCC                                  | Cell fused sarcoma                    |
| 42          |             | 90        | M      | Auricular pavilion | NR                 | SCC                                  | Cell fused sarcoma                    |
| 43 (18) 2007|             | 62        | M      | Thorax       | NR                 | BCC                                  | Cell fused sarcoma                    |
| 44          |             | 83        | M      | Ear          | NR                 | BCC                                  | Cell fused sarcoma                    |
| 45          |             | 70        | M      | Ear          | NR                 | Poorly differentiated SCC             | Cell fused sarcoma/ Atypical fibroxanthoma |
| 46 (30) 2007|             | 78        | M      | Chin         | NR                 | BCC                                  | Fibrosarcoma/DFSP                     |
| 47 (31) 2008|             | 84        | M      | Temple       | NR                 | BCC                                  | Giant cells/ Atypical fibrous histiocytoma |
| Case number | Reference Age/ Years | Gender | Location     | Clinical diagnosis | Epithelial component differentiation | Mesenchymal component |
|------------|----------------------|--------|--------------|-------------------|--------------------------------------|----------------------|
| 48         | 58                   | M      | Chin         | NR                | BCC                                  | Atypical fibrous histiocytoma |
| 49         | 77                   | M      | Shoulder     | BCC               | BCC                                  | Osteosarcoma           |
| 50         | 79                   | M      | Chin         | NR                | BCC                                  | Osteosarcoma           |
| 51         | 69                   | M      | Inner canthus| BCC               | BCC histiocytoma                     | Giant cells/ Atypical fibrous |
| 52         | (20) 2008 83 F Face  | NR    | BCC          |                   |                                      | Myofibroblastic        |
| 53         | (16) 2009 87 F Helix | NR    | BCC and SCC  |                   |                                      | Osteosarcoma           |
| 54         | (32) 2009 85 F Scalp | NR    | BCC          |                   |                                      | Fibrosarcoma/ osteosarcoma |
| 55         | (33) 2009 87 M Gluteal | NR | Myoepithelial (basaloid and Squamoid) with duct formation | Fused and giant cells with myxochondroid stroma |
| 56         | (2) 2010 58 F Hand   | NR    | Squamous     |                   | Liposarcoma                          |
| 57         | (19) 2010 73 M Temple| NR    | BCC          |                   | Atypical fibrous histiocytoma with osteoclast-like giant cells |
| 58         | (5) 2013 84 M Shoulder| Dermatofibrosarcoma Protuberans/ liposarcoma | Squamous | Undifferentiated cell fused sarcoma |
| 59         | (9) 2013 86 M Forehead| NR    | Poorly differentiated SCC | Myogenic sarcoma |
| 60         | 76                   | M      | Back         | NR                | Dedifferentiated SCC                 | Neurogenic sarcoma     |
| 61         | 53                   | M      | Ear          | NR                | Dedifferentiated SCC                 | Rhabdomyosarcoma       |
| 62         | 84                   | M      | Eyelid       | NR                | Poorly differentiated SCC             | Malignant fibrous histiocytoma |
| 63         | 86                   | M      | Forehead     | NR                | Poorly differentiated SCC             | Myogenic sarcoma       |
| 64         | 74                   | F      | Temple       | NR                | Poorly differentiated SCC             | Myofibroblastic sarcoma |
| 65         | (10) 2014 92 F Armpit| BCC   | SCC          |                   | Sarcomatous - fused cells – Rhabdomyomatous |
| 66         | 90                   | M      | Scalp        | SCC               | SCC                                  | Sarcomatous - fused cells |

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| Case number | Reference | Age/Years | Gender | Location      | Clinical diagnosis | Epithelial component differentiation | Clinical differentiation | Mesenchymal component            |
|-------------|-----------|-----------|--------|---------------|--------------------|---------------------------------------|--------------------------|----------------------------------|
| 67          |           | 83        | M      | Forehead      | SCC                | SCC                                   | Sarcomatous - fused cells |                                  |
| 68          |           | 54        | M      | Back          | BCC                | BCC                                   | Sarcomatous - fused cells – Osteoid |                                  |
| 69          |           | 73        | M      | Back          | BCC                | BCC                                   | Sarcomatous - fused cells – Osteoid |                                  |
| 70          |           | 59        | M      | Scalp         | BCC                | BCC                                   | Sarcomatous - fused cells – Leiomyomatous |                                  |
| 71          | (34) 2015 | 71        | M      | Arm           | Pyogenic granuloma or vascular neoplasm | BCC                                   | Sarcomatous - fused cells |                                  |
| 72          | (8) 2016  | 77        | M      | Chin          | NR                 | BCC/pilomatrical                       | Undifferentiated cell fused sarcoma |                                  |
| 73          |           | 82        | M      | Scalp         | NR                 | Basaloid SCC                          | Undifferentiated cell fused sarcoma |                                  |
| 74          |           | 81        | M      | Forehead      | NR                 | Tricoblastic                          | Undifferentiated cell fused sarcoma |                                  |
| 75          |           | 85        | M      | Finger        | NR                 | Tricoblastic                          | Undifferentiated cell fused sarcoma |                                  |
| 76          |           | 73        | M      | Ear           | NR                 | BCC                                   | Undifferentiated cell fused sarcoma |                                  |
| 77          |           | 90        | M      | Ear           | NR                 | BCC                                   | Undifferentiated cell fused sarcoma |                                  |
| 78          | (6) 2017  | 88        | F      | Supraclavicular | SCC/keratoacanthoma | BCC                                   | Sarcomatous–fused cells with chondroid component |                                  |
| 79          | (11) 2018 | 85        | F      | Forehead      | NR                 | BCC                                   | Sarcomatous–pleomorphic fused cells |                                  |
| 80          | (35) 2018 | 80        | F      | Leg           | Metastasis/ Merkel cell carcinoma/ melanoma | Squamous                            | Sarcomatous – fused cells |                                  |
| 81          | Current   | 89        | M      | Leg           | Melanoma/SCC       | Poroid                                | Atypical fibroxanthoma |                                  |

NR: not referred; BCC: Basal cell carcinoma; SCC: Squamous cell carcinoma; DFSP: dermatofibrosarcoma protuberans; M: Male; F: Female
Clinically the presentation is variable and often presents as an exophytic nodular lesion that can mimic a basal cell carcinoma, squamous cell carcinoma, keratoacanthoma, or Merkel-cell carcinoma.6

There are several morphological criteria that define a carcinosarcoma. First, dual neoplasia with epithelial and mesenchymal components must be confirmed by histology and immunohistochemical reactions. Second, a collision tumor or metastasis must be excluded. Lastly, cells must be coherent and show solid pattern proliferation without stromal sarcomatous changes in the surrounding tissue.7,8

The histogenesis of carcinosarcoma remains unknown, although four theories have been proposed.9–11 First among them is the theory of collision or convergence, which posits that the tumor is composed of two different synchronic neoplasms originating from two or more undifferentiated progenitor cells. Second is the theory of conversion, in which a part of the carcinoma shows a metaplastic transformation into a sarcomatous component. Third is the theory of composition that hypothesizes that the mesenchymal component is not a tumor but reactive stroma with “pseudosarcomatous” changes. Finally, there is the divergent or combination theory that both the epithelial and the mesenchymal components are originated from a common pluripotential progenitor cell.4

Biernat et al10 demonstrated the similar expression of p53 in both the epithelial and sarcomatous components which supports the theory that they have a common origin, favoring the divergence or conversion theories.

The diagnosis can be made by biopsy analysis, using Hematoxylin and Eosin staining in addition to complementary immunohistochemical analyses that allows the origin of the cell line to be more accurately classified. The treatment is surgical resection by Mohs surgery with strict clinical follow up.

The differential diagnosis includes cutaneous metastasis from sarcoma, squamous cell carcinoma, melanoma, or atypical fibroxanthoma.

Conclusion

We have presented the case of an 89-year-old man with an exophytic tumor histopathologically diagnosed as cutaneous carcinosarcoma with adnexal differentiation (porocarcinoma) and pleomorphic sarcoma with fibrohistiocytic differentiation. Primary cutaneous carcinosarcoma is an infrequent neoplasm of uncertain etiology, potentially locally recurrent and metastatic. The prognosis is primarily determined by the epithelial component (adnexal or epidermic), and the elected treatment is surgical excision by Mohs surgery with strict clinical follow up.

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