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Case report

Renal cell carcinoma with osteoclast-like giant cells

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Abstract. Primary extraskeletal epithelial neoplasms with osteoclast-like giant cells are rare. We describe a case of renal cell carcinoma with a sarcomatoid component and non-neoplastic osteoclast-like giant cells. The giant cells were noted in both the conventional and the sarcomatoid components of the neoplasm. Immunohistochemical studies indicate that these cells are monocyte/histiocyte in origin and most probably a host stromal reaction to the neoplasm.

Key words: Osteoclast-like giant cell – Renal cell carcinoma – Renal cell neoplasms – Multinucleated giant cell

Introduction

Extraskeletal neoplasms with multinucleated osteoclast-like giant cells have infrequently been described in a variety of organs and soft tissues. They are typically reported regardless of their location, under two main designations: "giant cell tumour-like" or osteoclastoma-like giant cell tumour (Andreef et al. 1964; Batsakis et al. 1988; Daroca et al. 1990; Eusebi et al. 1984; Ito et al. 1992; Kimura et al. 1983; Munoz et al. 1980; Rosai 1968; Schmaman et al. 1963; Silverberg and DiGiorgi 1973), and carcinoma with osteoclast-like giant cells (Agnantis and Rosen 1979; Alguacil-Garcia et al. 1984; Balogh et al. 1985; Esmaili et al. 1983; Fisher et al. 1983; Holz et al. 1972; Love and Daroca 1983; Oyasu et al. 1977; Prat and Scully 1979; Rosai 1968). This distinction, although in some instances ambiguous, serves the purpose of delineating malignant epithelial neoplasms with benign osteoclast-type cells from the hitherto uncharacterized giant cell (osteoclastoma)-like tumours. Both types, however, should be distinguished from giant cell carcinomas in which the giant cells are histologically malignant.

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In a search of the literature, we could only find a single report of two unusual sarcomatoid renal cell carcinomas with osteoclast-type cells surrounding osteoid-like material (Lee-Tsün and Willis 1963). We report a case of renal cell carcinoma with a sarcomatoid component and osteoclast-like giant cells, and discuss the histogenesis and clinical significance.

Case report

A 75-year-old female was referred to the King Faisal Specialist Hospital, Saudi Arabia, for painless haematuria. A CT scan confirmed the presence of a left renal mass for which she underwent a left radical nephrectomy. Her post-operative course has been uneventful.

Pathological examination

The neoplasm measured $9.5 \times 8.7 \times 6.0$ cm in diameter and occupied the upper half of the left kidney (Fig. 1). Although it appeared well-circumscribed, an extension into the perinephric adipose tissue was noted (Fig. 1). The tumour appeared tan, fleshy and soft with areas of haemorrhage and necrosis.

Thirty-five haematoxylin and eosin-stained slides representing different areas of the neoplasm were prepared for light microscopic examination. Immunohistochemical studies were performed using the avidin-biotin-peroxidase complex method on formalin-fixed, paraffin-embedded tissue sections. Sections were incubated with a "cocktail" of three anti-keratin mouse monoclonal antibodies (AE1 and AE3, Boehringer-Mannheim, Indianapolis, Ind., 1:200 dilution; and CAM 5.2, Becton Dickinson, Mountain View, Calif., 1:5) and with monoclonal antibodies to epithelial membrane antigen (E29, Dako, Santa Barbara, Calif., 1:40), vimentin (V9, Dako, 1:20), leukocyte common antigen (V9, Dako, 1:20), leukocyte common antigen (Dako, 1:40), and KP1 (Macrophage associated antigen) monoclonal antibody (Dako, 1:500) and *Ulex europaeus* (Vector, Burlingame, Calif.).

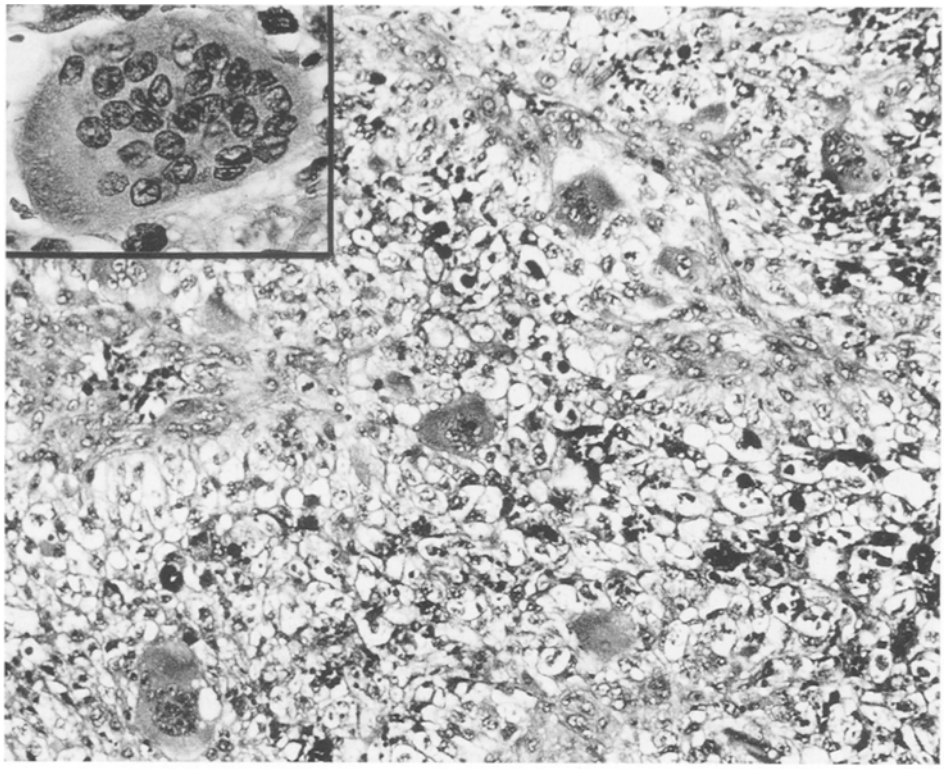

Fig. 1. Multinucleated giant cells in clear cell renal cell carcinoma component. The osteoclast-like giant cells (*inset*) are interspersed between mononuclear tumour cells

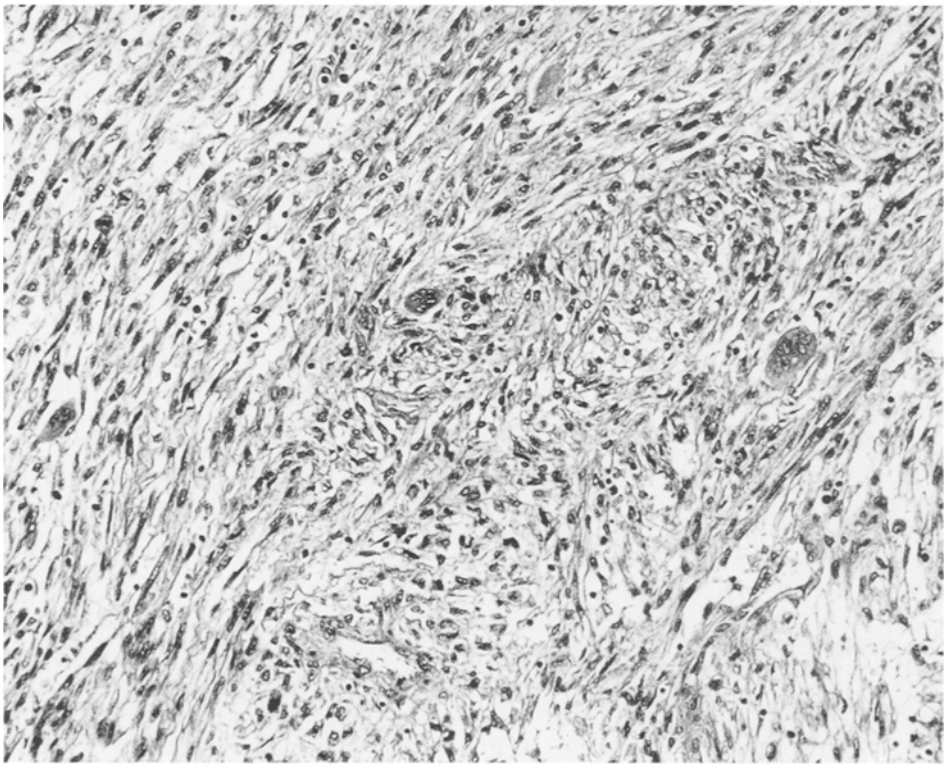

Fig. 2. Spindle cell sarcomatous renal cell carcinoma component with dispersed osteoclast-like giant cells

The neoplasm presented two histologically distinct components. The predominant components. The predominant component of the neoplasm displayed clear cell carcinoma, nuclear grade III (Fig. 2), while the smaller component consisted of spindle cells with sarcomatoid features (Fig. 3). The vast majority of the neoplastic cells were mononuclear. Dispersed among them, however, were osteoclast-like multinucleated giant cells, which appeared singly or in aggregates. In some areas, the giant cells were found to abut on dilated blood-filled

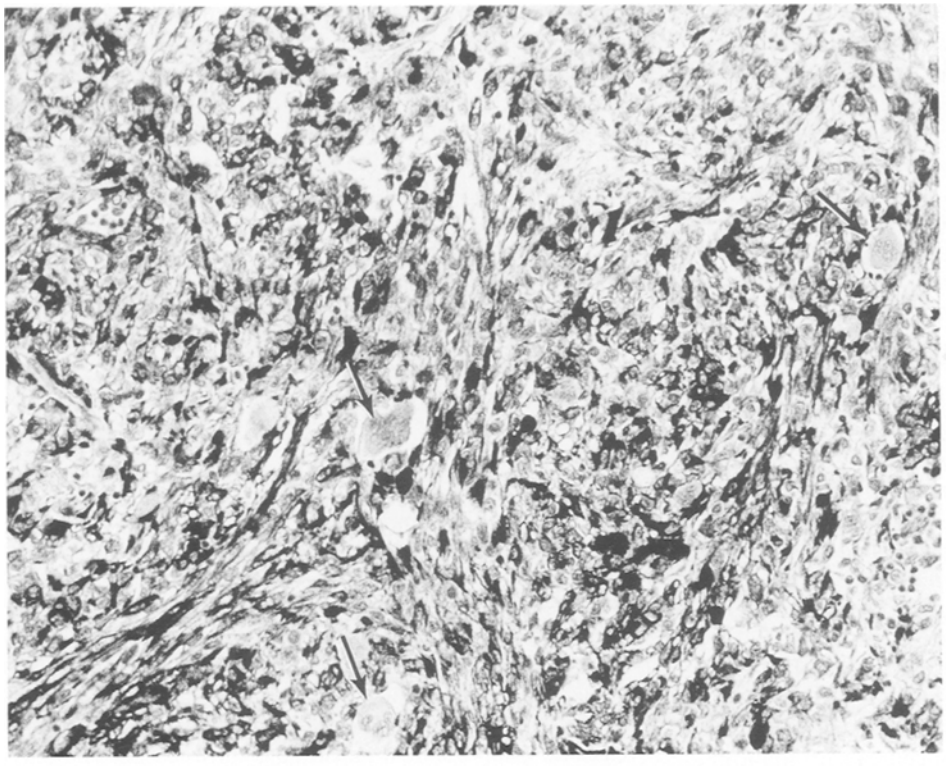

Fig. 3. Keratin immunostaining of the sarcomatous component of the neoplasm showing strong positivity in mononuclear tumour cells. Note that giant cells (*arrows*) are non-reactive to such staining

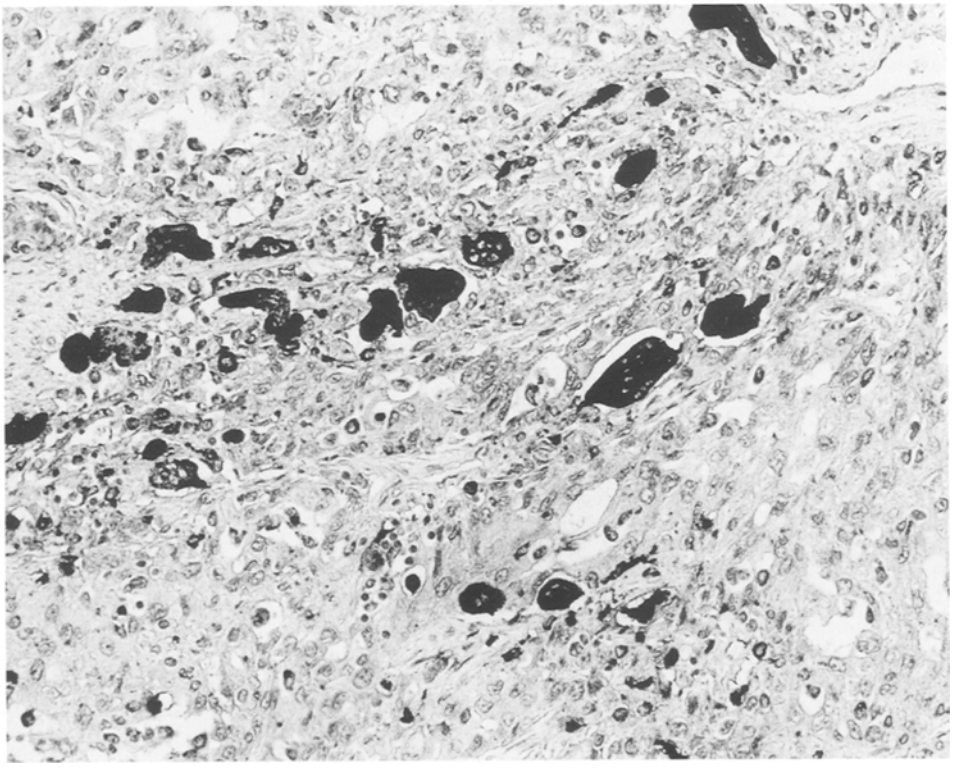

Fig. 4. CD68 immunostaining showing intense reaction in multinucleated giant cells and negative staining of tumour cells

vessels. Although conspicuous areas of haemorrhage and necrosis were present, there was no significant presence of multinucleated giant cells in these areas.

The multinucleated giant cells had centrally aggregated nuclei that varied in number from 4–30 nuclei (Figs, 2, 3). The nuclei were small, monotonous, with small central nucleoli, and appeared more vesicular than the mononuclear neoplastic cells. The cytoplasm of the multinucleated giant cells was generally amphophilic.

Immunohistochemically, epithelial membrane anti-

gen and cytokeratins were demonstrated in the mononuclear tumour cells of the sarcomatoid and non-sarcomatid areas (Fig. 4). The multinucleated giant cells, however, did not react with either of these two markers. Strong staining with KP1 (CD68) antibody and weak reactivity for vimentin was seen in the multinucleated giant cells, but not in the carcinoma cells. A strong reactivity to vimentin, however, was noted in vessels within tumour. Both the multinucleated giant cells and the carcinoma component were negative for *U. europaeus* agglutinin I and leukocyte common antigen.

Discussion

Renal cell carcinomas with osteoclast-like giant cells are very rare. A single report, in which two sarcomatoid renal cell carcinomas with osteoid-like formation and osteoclast-like giant cells has been published (Lee-Tsün and Willis 1963). In both cases, the giant cells were present only in the sarcomatoid component and were abutting on osteoid-like material. The nature and subcellular characteristics of the tumour and the osteoclast-like giant cells were not discussed.

In the present case, the osteoclast-like giant cells occurred in both the conventional renal cell carcinoma and in the sarcomatoid components of the neoplasm and were also noted in close proximity of blood vessels. This is rather different from previous report indicating that such cells were only observed in sarcomatoid areas (Alguacil-Garcia et al. 1984; Esmaili et al. 1983; Fisher et al. 1983; Holz et al. 1972; Lee-Tsün and Willis 1963; Love and Daroca 1983; Oyasu et al. 1977; Prat and Scully 1979). Immunohistochemical staining of the giant and neoplastic cells were diametrically different. While tumour cells, both in the conventional and the sarcomatous parts of the neoplasm, strongly expressed epithelial membrane antigen and keratin, the giant cells were nonreactive. However, KP1 (CD68) monoclonal antibody, which is a highly specific marker for monocyte/macrophage lineage (Micklem et al. 1989) stained the osteoclast-like giant cells strongly but did not react with the carcinoma or sarcomatoid tumour cells.

These findings corroborate earlier studies and indicate a separate histogenetic derivation for multinucleated giant cells and tumour cells (Athanasou et al. 1989; Athanasou and Quinn 1990; Brecher et al. 1986). Our findings and those of others suggest a monocyte/histiocyte for the osteoclast-like giant cells (Athanasou et al. 1989; Athanasou and Quinn 1990; Brecher et al. 1986; Sutton and Weiss 1966). Moreover, the findings also suggest that the giant cells are a form of host reaction to the epithelial neoplasm.

The mechanism by which giant cells form in these neoplasms is unknown. It is possible that malignant neoplasms may elaborate certain chemotactic factors or angiogenic substances that attract monocyte/macrophage cells, promote tumour vascularization, and thereby facilitate the migration of these cells into tumours (Athanasou et al. 1989; Love and Daroca 1983; Tavassoli and Norris 1986). It has also been suggested that tumours with osteoclast-like giant cells may produce parathormone (PTH) like substances which promote their formation (Athanasou et al. 1989). In this regard, PTH is known to induce giant cell formation from precursors in bone (Athanasou et al. 1989). The identification and isolation of these putative substances may unravel the mechanism for this unique finding and its prognostic significance, if any.

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