Case Report

Adrenal Sarcomatoid Carcinoma: A case report and review of the literature

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ABSTRACT
Adrenocortical sarcomatoid carcinoma (ASC) is an extremely rare variant of adrenocortical carcinoma (ACC). Its relative rarity and its characteristic histological pattern of both epithelioid and sarcomatoid components may pose diagnostic challenges which influence treatment. Here, we report a case of ASC in a 58 year-old man presenting with increasing abdominal pain and associated abdominal bloating with a large right adrenal mass detected by computed tomographic scan (CT). To our knowledge, only eleven prior cases of ASC have been reported in the literature. Here, we discuss the clinical, radiological and histopathological findings in our case, review the literature on ASCs and offer opinion on best management.

INTRODUCTION
Sarcomatoid carcinomas are tumours which contain both carcinomatous and sarcomatous differentiation. They have been identified in a variety of organ and tissue sites, including kidney, bladder, lung, breast and oesophagus.¹⁻³ Adrenocortical carcinoma (ACC) is an uncommon, aggressive malignancy with an estimated incidence of 1-2 per million population per year and, when untreated, a mean survival of 2.9 months.⁴⁻⁷ Adrenocortical sarcomatoid carcinoma or carcinosarcoma (ASC) is a rare subgroup of ACC. To our knowledge, only eleven cases have been previously reported in the literature.⁸⁻¹⁷ We present the twelfth case and review the previous published literature to identify management strategies for the treatment of this rare tumour subtype.

CASE REPORT
A 58-year-old caucasian male presented with a gradual onset of right sided loin pain over a number of months. A sudden increase in his pain prompted admission to a District General Hospital. The patient described a constant right loin pain with radiation to his groin. Initial urinalysis showed haematuria and a CT of his urinary system was arranged to investigate possible renal calculi. This identified an underlying adrenal mass. A further CT scan of the chest abdomen and pelvis confirmed a 9 x 7cm right sided adrenal mass.

The patient was transferred to a Regional Specialty Endocrine Surgery centre where hormone studies were performed.
to determine the potential functionality of the tumour. 24 hour urinary catecholamines, a dexamethasone suppression test, the Cortisol/Creatinine ratio and testosterone, dihydroxyepiandrosterone sulphate (DHEAS) and aldosterone levels were all within normal limits confirming the presence of a non-functioning adrenal mass. The patient went on to have an adrenalectomy and nephrectomy for the underlying lesion. The initial laparoscopic procedure was converted to open due to adherence of the mass to surrounding structures making for a difficult dissection from the inferior vena cava, inferior surface of the liver and the posterior abdominal wall musculature to which it was attached. Despite these difficulties a complete macroscopic excision was achieved. Post operatively the patient made an uneventful recovery. Given the extent of the primary tumour, and despite evidence of macroscopic excision, it was felt that the patient’s greatest risk of relapse was at the site of surgery from a local recurrence. The patient went on to have 25 fractions of external beam radiotherapy at a dosage of 45 Gray (Gy). The benefits of chemotherapeutic agents were discussed with the patient and he and the oncology team felt that, given the absence of metastatic disease, any potential benefit was outweighed by potential morbidities of the treatment. At 16 months from initial diagnosis and treatment the patient was found to have evidence of metastatic disease to lung and brain. However a tissue diagnosis confirmed this to represent disease load from a second primary malignancy of lung origin. To date there is no evidence of local recurrence on CT PET or MRI of the previous adrenal malignancy.

MICROSCOPIC EXAMINATION

Histology of multiple representative sections showed a malignant tumour composed of diffuse sheets of epithelioid and spindle cells. There was marked nuclear atypia. No clear cell component was identified. Mitotic activity was brisk, at approximately 70 mitoses per ten high-power fields. The epithelioid and spindled areas were equally mitotically active. Numerous atypical mitoses were present. There was extensive necrosis. Tumour giant cells were present as well as a prominent lymphohistiocytic infiltrate (Figures 3a and 3b). No venous invasion was identified, and no evidence of extension into the surrounding soft tissues was seen. No normal adrenal gland tissue was identified. The kidney, which was removed en bloc, was histologically unremarkable. The area of kidney adjacent to the tumour was sampled in its entirety for histology. This showed no involvement by tumour.

MACROSCOPIC EXAMINATION

The specimen weighed 573 g. The right kidney measured 12 x 7 x 5 cm and was compressed superiorly by a 12 x 5 x 6 cm adrenal mass. On sectioning of the specimen, the mass was found to be well-circumscribed with no macroscopic evidence of extracapsular extension. There was extensive haemorrhage and necrosis within the mass (Figure 2). The interface between the kidney and the mass was examined carefully by close serial sectioning. No communication between the two was identified

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The tumour cells showed strong, diffuse positivity with cytokeratins AE1/3 and Cam5.2. Cytokeratin 7 and epithelial membrane antigen showed patchy positivity. Weak positivity with synaptophysin was also present. The only other positive
immunohistochemical markers were CD10, vimentin (strong), desmin and S100 (weak). RCC marker antigen was negative. All other epithelial (including neuroendocrine) and mesenchymal markers were negative, as were melanocytic markers. MIB1 proliferative index was approximately 40%.

Due to these morphological and immunohistochemical findings, it was important to consider the possibility of sarcomatoid renal cell carcinoma. There was, however, no communication between the ipsilateral kidney and the adrenal mass. The contralateral kidney was radiologically normal. The most likely diagnosis on the basis of the clinical, radiological and pathological findings was therefore felt to be adrenocortical sarcomatoid carcinoma.

**DISCUSSION**

We present the twelfth documented case of Adrenocortical sarcomatoid carcinoma and a comprehensive summary of the previous literature. The age of presentation of ASC ranges from 29 - 79 years (mean 54.3 years). Although the number of cases reported is small, there is a female to male ratio of 1.4. Despite aggressive treatment, this variant of ACC has a poor prognosis, with the majority of patients succumbing to the disease within 3 - 12 months (mean 7 months) following surgical intervention. The greatest determinants of early demise appear to be limited surgical resection and presence of distant metastatic spread at time of presentation.

All twelve cases can be defined as being carcinosarcoma or sarcomatoid carcinoma as suggested by Strum et al.\(^{14}\) Carinosarcoma combines features of conventional ACC and areas of sarcoma which include heterologous elements such as rhabdomyosarcoma (skeletal muscle differentiation), chondrosarcoma and osteosarcoma. Sarcomatoid carcinoma, also referred to as carcinoma with sarcoma-like component, is mostly composed of malignant spindle cells without any identifiable heterologous differentiation.\(^{14}\) Our case represents a sarcomatoid carcinoma since there was a prominent population of malignant spindle cells which did not show any recognizable differentiation. These findings were similar to six of the previous eleven reported cases.\(^{8,9,13,14,15,16}\) The other five previously reported cases were more appropriately classified as carcinosarcoma, with rhabdomyosarcoma identified as the sarcomatous component in three,\(^{10,11,17}\) pleomorphic rhabdomyosarcoma in one\(^{18}\) and the final case showing elements of both osteosarcoma and chondrosarcoma.\(^{12}\)

| Case No. | Reference | Age | Sex | Clinical Presentation | Metastatic Disease at Presentation | Size +/- Weight | Sarcomatous Component | Postoperative Survival |
|----------|-----------|-----|-----|-----------------------|-----------------------------------|----------------|----------------------|-----------------------|
| 1        | Okazumi et al. (1987) | 46  | M   | Abdominal distention   | No                                | 14cm, 880g     | Spindle cell          | 6 months              |
| 2        | Collina et al. (1989) | 69  | F   | Abdominal pain         | No                                | 11cm           | Spindle cell          | 6 months              |
| 3        | Decorato et al. (1990) | 42  | F   | Abdominal pain         | No                                | 19cm, 1400g    | Rhabdomyosarcoma      | 7 months              |
| 4        | Fischler et al. (1992) | 29  | F   | Weight loss, virilization | No                                | 12.5cm, 610g   | Rhabdomyosarcoma      | 8 months              |
| 5        | Barksdale et al. (1993) | 79  | F   | Hypertension            | Invasion of Inferior Vena Cava    | 5cm, 199g      | Osteosarcoma, chondrosarcoma | Not recorded |
| 6        | Lee et al. (1997)      | 61  | M   | Flank pain              | Liver                             | 12cm           | Spindle cell          | 2 days                |
| 7        | Strum et al. (2008)    | 31  | M   | Abdominal pain          | No                                | 12cm, 620g     | Spindle cell          | 3 months              |
| 8        | Coli et al. (2010)     | 75  | F   | Abdominal pain          | No                                | 15cm           | Spindle cell          | 12 months             |
| 9        | Sasaki et al. (2010)   | 45  | M   | Abdominal pain          | Retroperitoneum, pancreas and duodenum | 17cm, 2974g    | Rhabdomyosarcoma      | 3 months              |
| 10       | Feng et al. (2010)     | 72  | M   | Flank pain              | No                                | No record      | Spindle Cell          | Not recorded |
| 11       | Thway et al. (2012)    | 45  | M   | Abdominal pain          | Retroperitoneal nodes and pulmonary deposits | 24cm, 6500g    | Pleomorphic rhabdomyosarcoma | 11 months            |
| 12       | Current Study (2013)   | 58  | M   | Flank pain              | No                                | 12cm, 573g     | Spindle cell          | No evidence of metastatic adrenal disease at 17 months |

**TABLE 1:** Summary of ASC reported in the literature to date
The rarity of these subgroups of ACC presents a histopathological challenge, particularly when applying the Weiss scoring system which has remained the most widely used means of assessing the potential for malignancy in adrenocortical neoplasms.20,21 The presence within a tumour of a sarcomatous or sarcomatoid component seems to be a predictor of shorter survival in ACC. Sarcomatoid histology is not accounted for in the Weiss system, which may lead to confusion when dealing with these tumours, particularly with regards to the proportion of diffuse architecture required.22 In this setting, Sturm and colleagues have proposed that a sarcomatoid component should be well circumscribed and represent at least 10% of the tumour bulk in order to establish this unusual diagnosis.14,22 Whilst this rare tumour subtype represents a significant clinical, radiological and histopathological diagnostic challenge, its prompt identification will ensure the best long term prognosis in a cancer that requires a maximally aggressive management approach.

Given the rarity of this tumour subtype an evidence-based consensus regarding best oncological treatment is difficult. The use, or documented use, of adjuvant treatments in the previous cases was variable. In eight cases no additional treatments were reported8,10,12,13,15,16,17,18 the remaining three cases opted mainly for chemotherapy with a combination of Cisplatinum and Etoposide reported by Collina9 and Fischler et al14 and Cisplatinum used in isolation by Strum et al.14 Fischler also reported additional adjuvants with Mitotane in combination with chemotherapeutics. Only one of the previous cases used radiotherapy but it is assumed, given the radiation doses described and the context of bony metastatic disease, that this was for symptomatic palliation only.9 Our patient was clinically well 14 months following surgical intervention with follow up CT imaging showing no evidence of local recurrence. Our patient has been the longest survivor when compared to previous cases however he has unfortunately gone on to develop evidence of malignant spread from a second primary lung malignancy. We maintain that the greatest chance of long term survival from adrenal sarcomatoid carcinoma to be early detection prior to metastatic spread, radical complete excision and adjuvant external beam radiotherapy in an attempt to prevent local disease recurrence. Despite these findings our patient has been the longest survivor when compared to previous cases and we therefore surmise that the greatest chance of long term survival to be early detection prior to metastatic spread, radical complete excision and adjuvant external beam radiotherapy in an attempt to prevent local disease recurrence.

All authors have no conflict of interest

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