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casereports

TITLE OF CASE

Metastatic extraskeletal myxoid chondrosarcoma in a greater kudu (*Tragelaphus strepsiceros*)

AUTHORS

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SUMMARY

Extraskeletal myxoid chondrosarcoma was diagnosed on the ventral abdomen of a kudu with metastasis to the omentum and lungs. Histopathological examination of the large (20cm x 10cm) primary, multinodular, moderately cellular neoplastic mass was characterised by neoplastic mesenchymal cells arranged in strands and bundles, interspersed by multiple foci of cartilage immersed in a myxoid matrix. The neoplastic cells revealed diffuse vimentin and S100 positivity and the myxoid matrix was positive with Alcian blue. The microscopic examination in addition to the Alcian blue and immunohistochemistry findings confirmed the diagnosis.

BACKGROUND

Exstraskeletal chondrosarcoma is a malignant mesenchymal neoplasm that occurs in tissues and/or organs other than the skeletal system (1). It is a rare neoplasm that has been documented in humans and animals (1). The majority of extraskeletal chondrosarcomas resemble either the conventional or mesenchymal subtypes but a myxoid variant has been reported in humans, a dog and two separate cases in cows (2-5). In humans, extraskeletal chondrosarcomas are considered indolent with a favourable prognosis and low metastatic rate. Extraskeletal chondrosarcoma has not been reported in wild antelope. This report describes a case of extraskeletal myxoid chondrosarcoma on the ventral abdomen of a kudu with metastasis

to the omentum and lungs.

CASE PRESENTATION

An adult, female kudu presented for post mortem examination in the month of May (late autumn/early winter in the southern hemisphere) after she was found dead in a camp where she was extensively kept. The owners of the kudu did not report any clinical signs prior to death. External examination revealed poor body condition (1/5 body condition score) and a large 20cm x 10cm, well circumscribed, multilobulated, tan-grey, retroperitoneal, ventral abdominal mass (Figure 1). She had a full lactating udder. The animal was cachectic as supported by the serous atrophy of bone marrow fat, cardiac coronary groove fat as well as renal pelvic fat. She had three fractured premolar teeth. The fractured teeth, the fact that she was lactating and the chronic neoplastic disease perpetuated the negative energy balance. The post mortem examination revealed multiple, variably sized metastasis to the omentum and lungs (Figure 2).

Tissue impression smears of the primary neoplastic mass were made using the scrape cytology technique, since the routine imprint cytology technique did not yield diagnostic smears. All smears were stained using the Diff-Quick staining protocol. The cytology smears revealed spindle-shaped to polygonal neoplastic cells characterised by a moderate degree of pleomorphism, moderate anisokaryosis, normo- to hyperchromatic nuclei, inconspicuous nucleoli and the presence of mitotic figures. Neoplastic cells were interspersed by ample eosinophilic matrix and multinucleated giant cells were common (Figure 3).

Tissue samples from the primary neoplastic mass, metastatic masses as well as all the major organs were fixed in 10% buffered formalin, and routinely processed, embedded and sectioned for histopathological evaluation. All the sections were stained with haematoxylin and eosin (HE). Sections of the primary neoplastic mass and metastatic masses were prepared for Alcian blue staining and immunohistochemistry. Immunohistochemical labelling was performed by the avidin-biotin complex technique using the listed antibodies after antigen retrieval at pH6 and

using the Dako Real En Vision Detection System. The antibodies used were vimentin, cytokeratin, S100 and desmin; primarily to exclude neoplasia of epithelial origin as well as the possibility of other mesenchymal tumours.

Microscopic examination of the primary neoplastic mass revealed a multinodular, moderately cellular neoplastic mass with neoplastic mesenchymal cells arranged in strands and bundles immersed in a myxoid matrix. Neoplastic cells were spindle-shaped to oval to round, with a scant amount of pale eosinophilic, occasionally vacuolated cytoplasm. Nuclei were round to oval, hyperchromatic with an average mitotic rate of eight mitotic figures per high power field. Multiple foci of poorly formed cartilage/chondroid matrix could be observed interspersed between the neoplastic cells (Figure 4). Throughout the mass, multiple large atypical cells with prominent nucleoli as well as multinucleated cells could be seen. The mass also revealed large areas of necrosis as well as multifocal, variably sized areas of haemorrhage. Metastatic foci consisted of neoplastic cells with features similar to that observed in the primary neoplastic mass. Metastatic foci in the lungs displayed an increased cellularity with more pronounced chondroid differentiation compared to the primary mass.

A diagnosis of myxoid extraskeletal chondrosarcoma was based on the observed histological pattern. The absence of skeletal involvement was confirmed on complete post mortem examination. Immunohistochemistry revealed diffuse vimentin positivity (Figure 5) and widespread S100 positivity (Figure 6), especially observed in the cartilaginous cells. Alcian blue staining was performed and the myxoid stroma stained blue (Figure 7), this excluded a diagnosis of extraskeletal osteosarcoma due to the exclusion of osteoid production. There was no cytokeratin or desmin reactivity.

DISCUSSION

Chondrosarcoma is a malignant neoplasm of mesenchymal origin in which neoplastic cells produce chondroid and fibrillar matrix in varying amounts (1). It occurs within bone or the periosteum. Extraskeletal chondrosarcoma is a rare soft tissue neoplasm that arises in numerous exstraskeletal locations (1). In humans, mesenchymal and myxoid forms have been described as the two most distinct variants of extraskeletal chondrosarcoma (6). Mesenchymal chondrosarcomas are characterised by a transition between undifferentiated mesenchymal cells and a range of differentiated chondroid and/or chondroid elements (1). Myxoid chondrosarcomas are well-circumscribed, multinodular masses characterised by variably shaped (fusiform to polyhedral to oval) neoplastic cells with scant, pale eosinophilic to occasionally vacuolated cytoplasm (4, 5). The neoplastic cells are separated by variable amounts of myxoid matrix or ground substance in addition to scattered areas of chondroid differentiation (5, 7, 8). Neoplastic cell nuclei are mostly oval to round, eu- to hyperchromatic with indistinct nucleoli and a variable mitotic rate (3, 4). The presence of large multinucleated cells have been reported (5, 7).

Exstraskeletal mesenchymal chondosarcoma has been described in humans, dogs, a cat and a cow (5, 7-11). In dogs, extraskeletal mesenchymal chondrosarcoma has been reported, amongst others, in the omentum, pericardium, spleen and retroperitoneal space (7, 9-11). In the cat, it was located in the dorsal lumbosacral region and at the base of the head in the right cervical area in the cow (4, 5, 8).

In humans, skeletal chondrosarcomas are aggressive with frequent metastasis, while with extraskeletal chondrosarcoma metastasis is rare, even more so in the myxoid variant than in mesenchymal chondrosarcoma (6). Previously extraskeletal myxoid chondrosarcomas were thought to be slow growing with a low metastatic rate. Recent evidence in humans however indicate that they have a less favourable prognosis with a high rate of recurrence following

surgical excision and frequent distant metastasis, especially pulmonary metastasis (12). A report of a five month old dog with primary extraskeletal myxoid chondrosarcoma in the lungs and numerous metastasis elsewhere supports the aforementioned finding (3).

In our case, the diagnosis was confirmed, based primarily on the histopathology with the addition of immunohistochemistry and Alcian blue staining as reiteration of the final diagnosis. Alcian blue staining highlighted the presence of the abundant myxoid matrix, which could also be observed as abundant eosinophilic matrix on the cytological preparations. These findings conform to what has been described in extraskeletal myxoid chondrosarcomas in humans and animals (3). Our discovery of distant metastasis are supportive of the fact that this particular variant has a more malignant behaviour than once thought.

When evaluating soft tissue tumours that consist of spindle-shaped cells, reaching a definitive diagnosis can often be challenging, since most of these tumours have similar histologic features and biologic behaviour. Some of the shared features in this heterogenous group of tumours include similarities in; the principle neoplastic cell shape i.e. spindle-shaped, the overall pattern i.e. interwoven bundles, streams and/or whorls, and in the matrix production that is often collagenous or myxoid in nature (13, 14). The aforementioned highlights the need for the application of immunohistochemistry and/or special staining techniques in order to establish a more specific diagnosis. Currently there is no consistent immunohistochemical stain or group of stains that can accurately separate the different types of tumours contained within this group. The most commonly encountered types included in the soft tissue spindle-shaped tumour/spindle-shaped sarcoma group are peripheral nerve sheath tumour, perivascular wall tumour, fibrosarcoma, myxosarcoma and liposarcoma (13).

Preceding definitively diagnosing a spindle shaped tumour/soft tissue sarcoma it is often necessary to exclude the possibility of carcinoma due to the likelihood of spindle cell variants of

carcinoma. Cytokeratins are a group of polypeptide keratins that are expressed in epithelial cells whereas vimentin is the major member of the intermediate filament family; both are primarily indicated in order to discriminate between neoplasms of epithelial versus mesenchymal origin (1). Once established that sarcoma is more likely, additional histopathological features including the specific pattern, cellular histomorphology and intercellular matrix production need to be evaluated. Of the histopathological features mentioned, intercellular matrix production is often more informative in distinguishing one sarcoma type from another. The presence of intercellular myxoid matrix, confirmed by alcian blue reactivity, often recapitulates the need for additional immunohistochemical labelling in order to distinguish myxosarcomas from other myxoid containing neoplasms such as myxoid liposarcomas, myxofibrosarcomas and myxoid chondrosarcomas as in this case (15, 16).

In the absence of convincing chondroid differentiation, myxosarcoma would have been the primary differential diagnosis to consider in this case. Myxosarcomas are tumours of fibroblast origin in conjunction with the presence of abundant myxoid matrix and apart from its reactivity with alcian blue, a final diagnosis would be one of exclusion as is often the case with fibrosarcomas (14). S100 is a calcium flux regulator and has a wide distribution that includes glial cells, neurons, chondrocytes, schwann cells, melanocytes, histiocytic cells, myoepithelial cells, some glandular epithelium and muscle (1). Although the expression of S100 in chondrocytes (well differentiated or not) is not specific or limited to chondrocyte containing neoplasms i.e. chondrosarcomas, it does contribute in reaching a diagnosis in these cases by identifying the chondrocytes as such. In our case, the S100 positivity in conjunction with the histopathological features and myxoid matrix assisted in reaching a final diagnosis. Desmin is an intermediate filament of muscle cells, not expressed in myoepthelial cells and was included in our case to exclude some of the other possible mesenchymal tumours i.e. perivascular wall tumour (1). Contrary to our case, with an increased suspicion of perivascular wall tumour as a potential

differential diagnosis, smooth muscle actin would be the preferred marker compared to desmin due to its increased specificity. In our case, the application of desmin was sufficient, as the histopathology was more suggestive of chondrocarcoma than perivascular wall tumour or peripheral nerve sheath tumour and was only included for the sake of completeness.

To our knowledge, extraskeletal chondrosarcoma has not been reported in wild antelope to date. This is the first report of the myxoid variant in addition to distant metastasis. In our case, the chronic neoplastic disease, apart from dental attrition and lactation, most likely also contributed to the demise of the animal. Considering the time of year (late autumn/early winter in the southern hemisphere), the ambient temperatures would have been low necessitating the animal to generate heat from fat reserves. The cachexic state of this animal would however have hampered heat production resulting in terminal cold exposure and subsequent death due to hypothermia.

LEARNING POINTS/TAKE HOME MESSAGES

- Extraskeletal myxoid chondrosarcoma can occur in wild antelope.
- Extraskeletal myxoid chondrosarcoma appears to be less indolent than previously reported.
- Extraskeletal myxoid chondrosarcoma neoplastic cells display positive Vimentin and S100 immunoreactivity.
- The myxoid and chondroid matrix associated with extraskeletal myxoid chondrosarcoma stains with Alcian Blue special stain.

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FIGURES

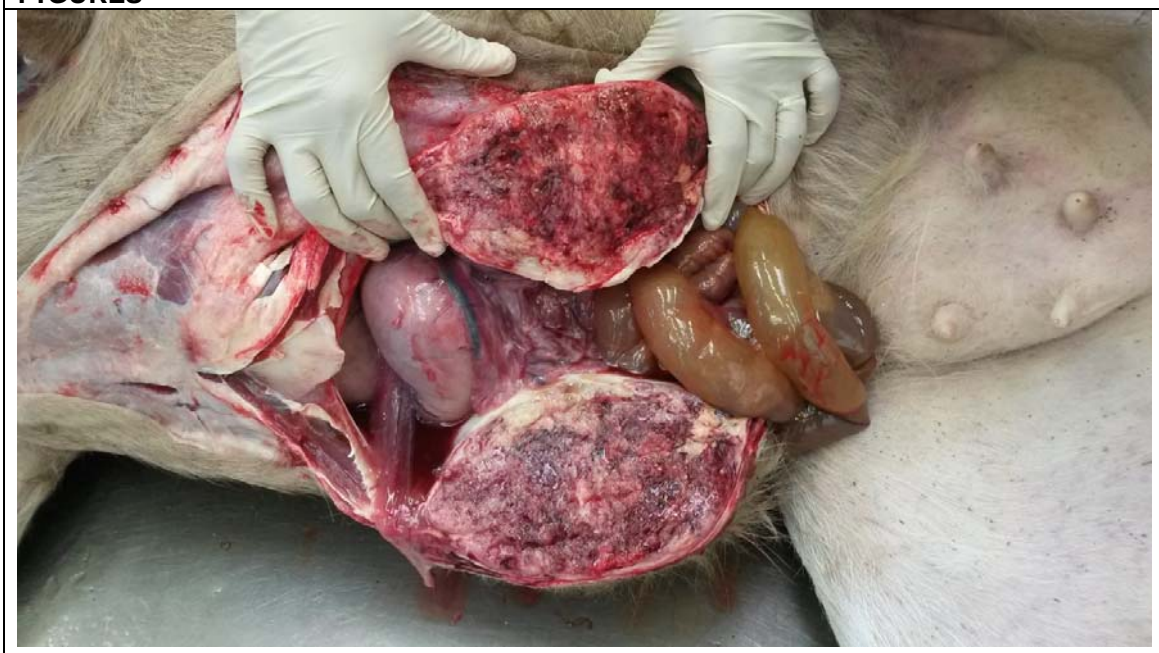

Figure 1: Large (20cm x 10cm), firm, well-circumscribed, retroperitoneal neoplastic mass on the ventral midline.

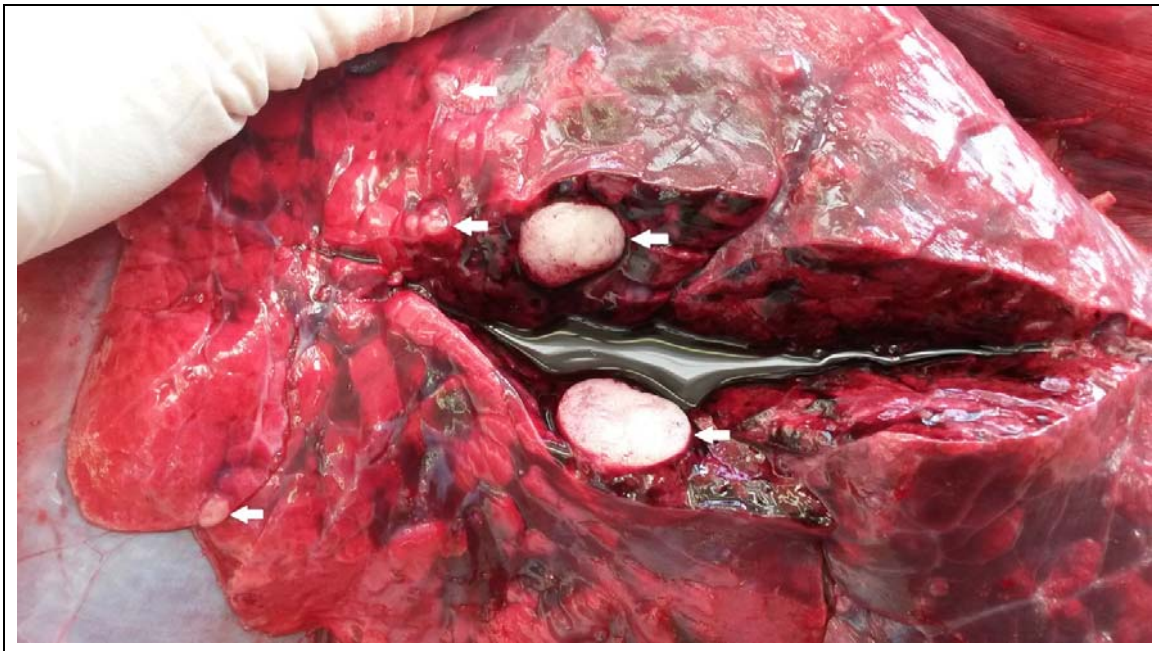

Figure 2: Multiple pulmonary metastatic foci of various sizes (*arrows*).

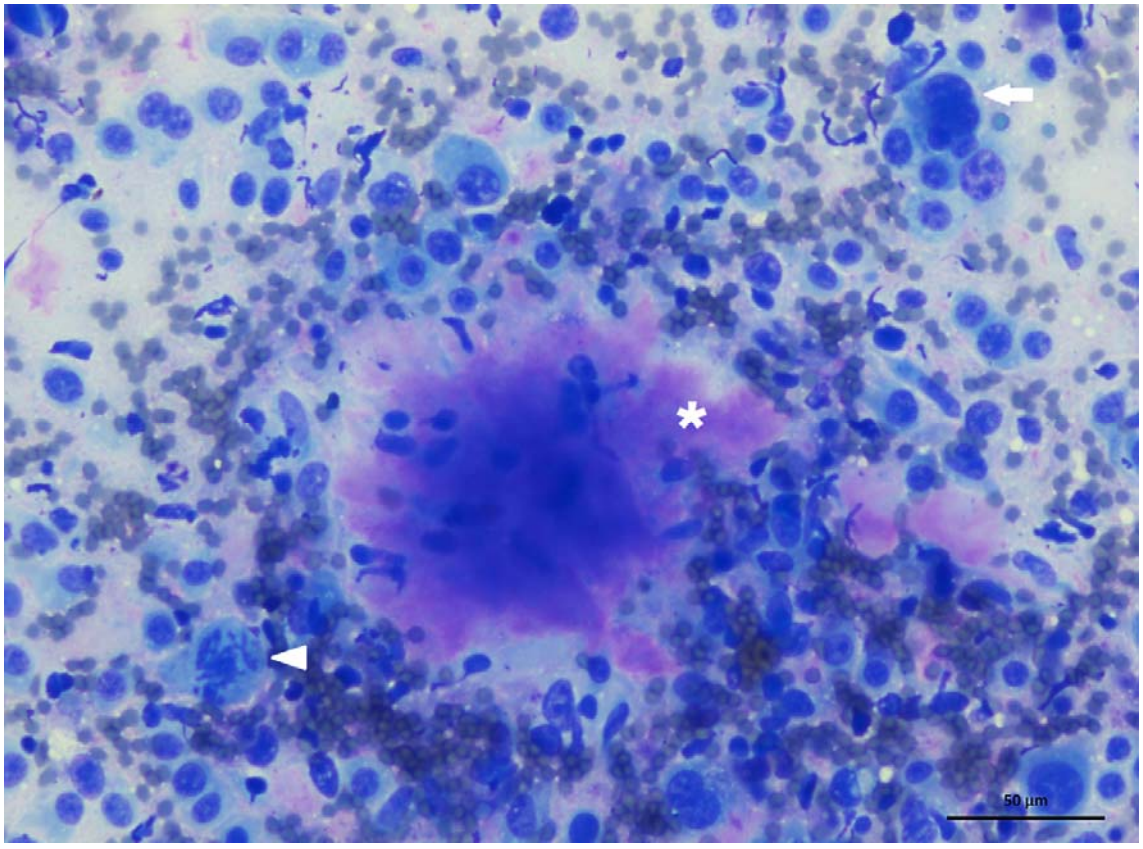

Figure 3: Scrape cytology smear revealing moderately pleomorphic spindle-shaped to polygonal neoplastic cells with the presence of multinucleated cells (*arrow*) and mitotic figures (*arrowhead*) interspersed by ample eosinophilic matrix (*asterisk*). (Diff-Quick stain, 200x magnification).

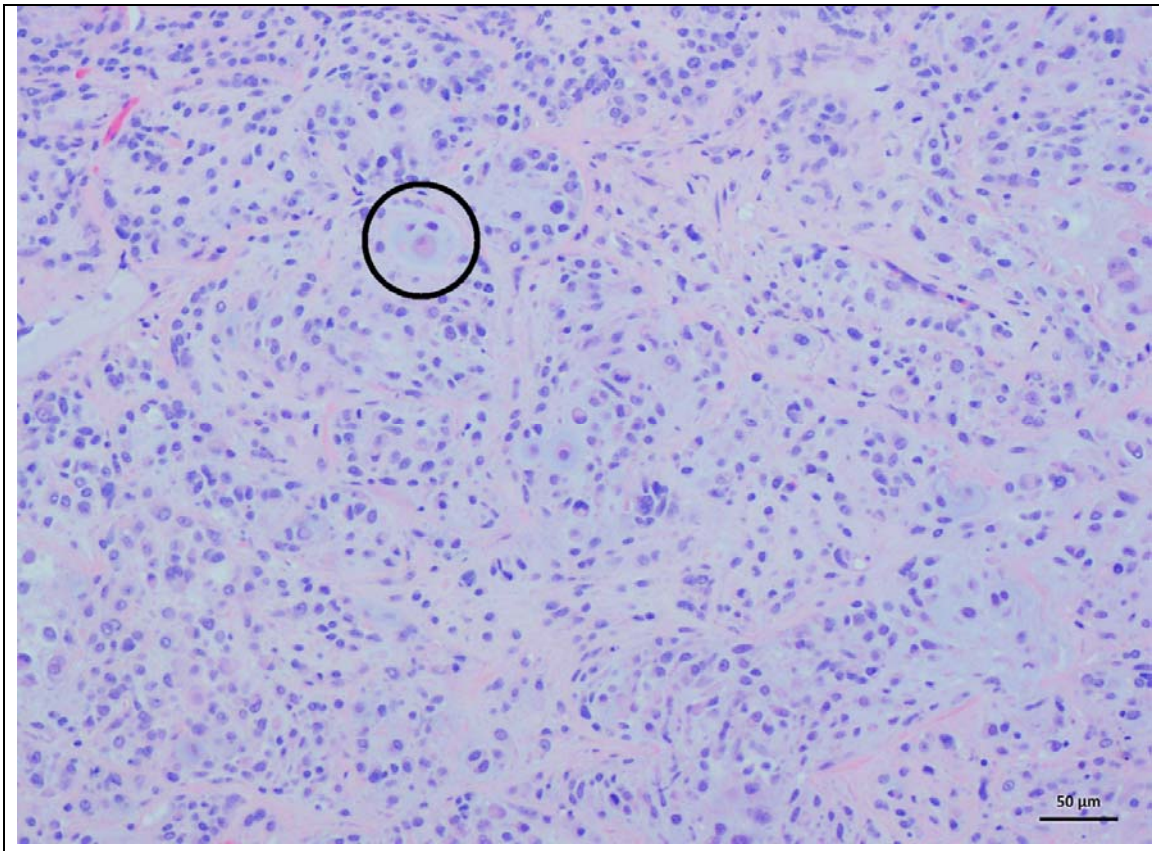

Figure 4: Histopathology of the neoplastic mass revealing neoplastic mesenchymal cells arranged in cords or strands immersed in a myxoid matrix with areas of chondroid differentiation (*circle*). (HE stain, 100x magnification)

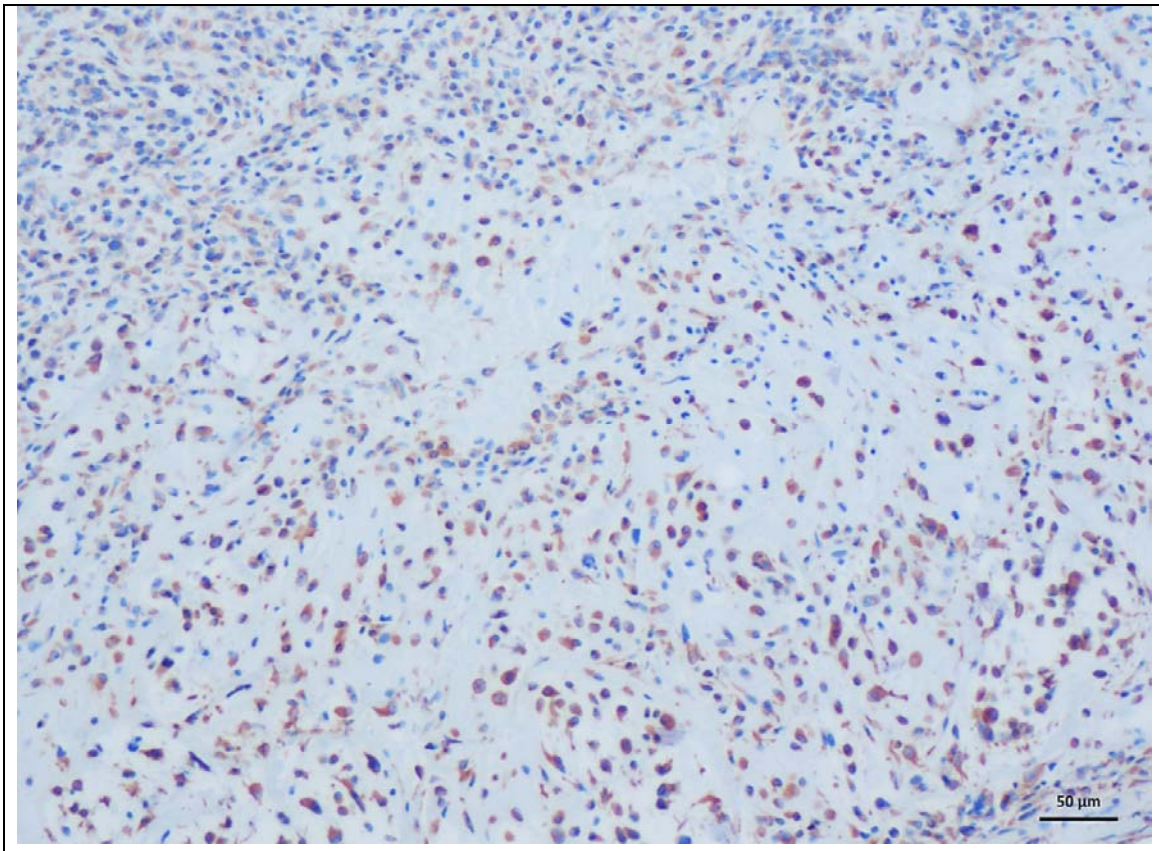

Figure 5: Diffuse cytoplasmic Vimentin positive immunohistochemical labelling of neoplastic cells. (Avidin-biotin peroxidase complex method, Mayer's haematoxylin counterstain, 100x magnification)

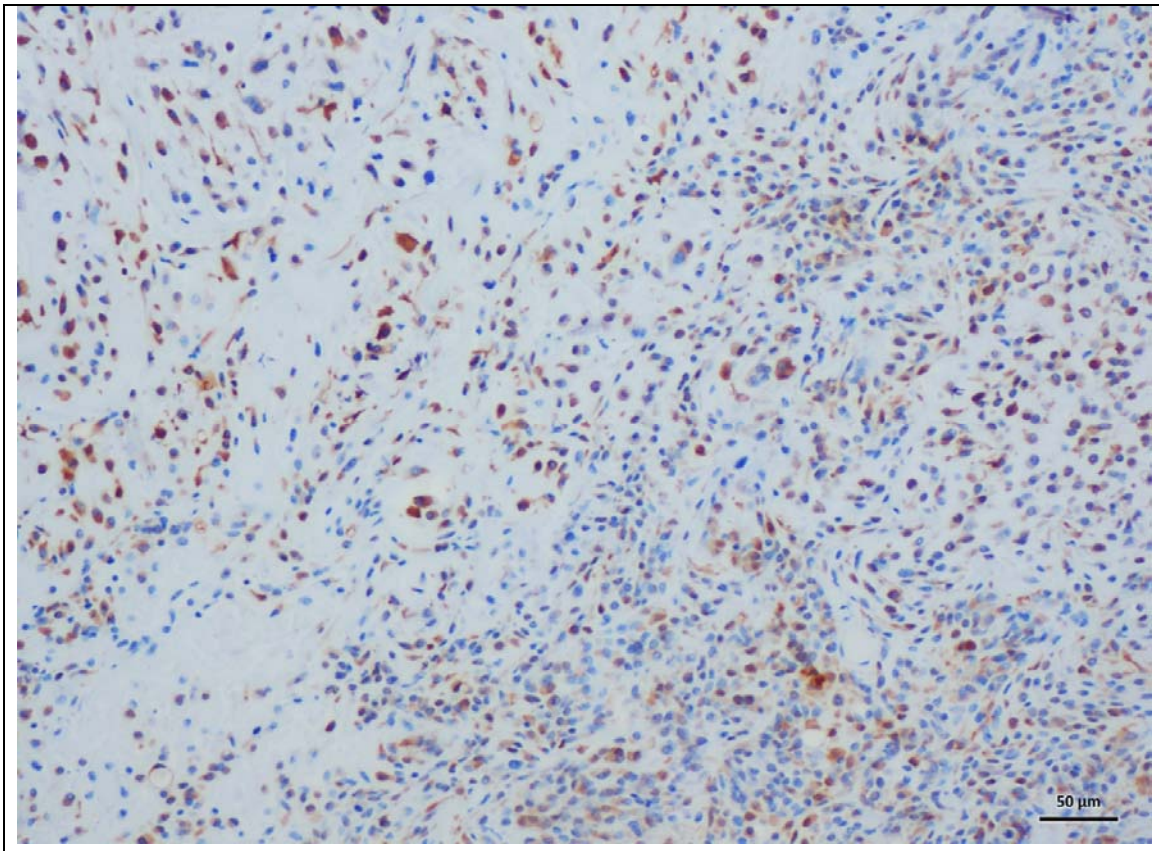

Figure 6: Widespread cytoplasmic S100 positive immunohistochemical labelling of neoplastic cells. (Avidin-biotin peroxidase complex method, Mayer's haematoxylin counterstain, 100x magnification)

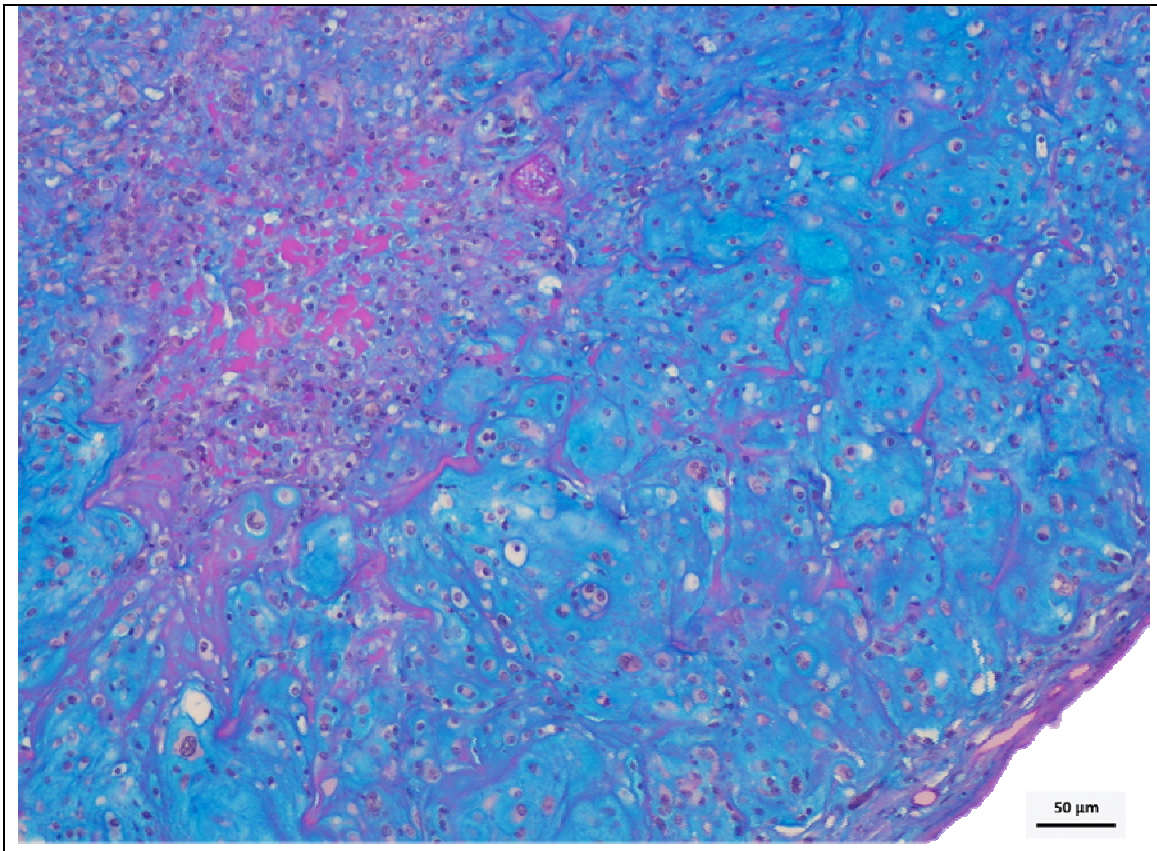

Figure 7: Intense blue staining of abundant myxoid and chondroid matrix between neoplastic cells. (Alcian blue stain, 100x magnification)