

Case report and review: A rare case of sarcomatoid renal cell carcinoma manifesting with supraclavicular lymph node metastasis

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Abstract

Sarcomatoid renal cell carcinoma (SRCC) is a highly aggressive form of dedifferentiated renal cell carcinoma. We report a 65-year-old man who presented to the emergency department with respiratory symptoms, obstructive jaundice with deranged liver function tests and raised inflammatory marker. General physical examination showed a swelling in left supraclavicular region. The initial differential diagnosis was pancreatic cancer, bronchogenic carcinoma, gastric cancer and lymphoma. Computer tomography (CT) scan showed a solid right renal lesion, multiple liver metastases, florid chest, lymphadenopathy in left supraclavicular region and a right adrenal mass. Patient had biopsy of left supraclavicular node which diagnosed it as a metastatic high grade sarcomatoid renal cell carcinoma. We present the findings and a brief review.

Case report

65-year-old male presented with a 3-4-week history of increasing dyspnoea, loss of appetite, weight loss and dark urine to the emergency department. His history included a back pain over a period of three months and worsening jaundice over a period of one week prior to the emergency admission. Patient had past diagnosis of benign prostatic hyperplasia and was on tamsulosin 400 micrograms capsules once daily. He underwent a CT (Computer tomography) scan of his abdomen and pelvis, which showed metastasis in liver, right kidney mass, enlarged lymph nodes in the left supraclavicular, anterior mediastinum, anterior trachea, sub carinal and hilar region. Patient's blood tests showed deranged liver function tests with levels of bilirubin-206 Units/Litre (U/L), ALT-278 U/L, ALP-824 U/L and Amylase-26 U/L. The CT findings also showed the intrahepatic ducts were significantly dilated down to the origin of the common hepatic duct. Below this, the common hepatic duct and common bile duct were not dilated. Obstruction was due to enlarged nodes at the porta hepatis obstructing the common hepatic duct. Patient was resuscitated and stabilised with antibiotics, intravenous fluids and booked for ERCP (Endoscopic retrograde cholangio-pancreaticography).

During ERCP, a stent was inserted into the common bile duct to relieve the obstruction. But developed pancreatitis post procedure with an amylase of 1200 U/L. This was treated conservatively, and patient made a good recovery with return of liver function tests to normal levels. While in the hospital, he had biopsy of the left supraclavicular lymph node which confirmed the diagnosis of metastatic high grade sarcomatoid renal cell carcinoma. Patient's case was discussed in the multi-disciplinary team meeting and was referred to a medical oncologist for palliative chemotherapy. Patient was also referred to the local cancer nurse specialist and palliative care team before being discharged home for follow-up in the community. The patient's clinical presentation had aberration in the normal presentation and serves a good learning point about sarcomatoid renal cell carcinoma (SRCC).

Investigations

CT thorax abdomen and pelvis

Figures 1-3.

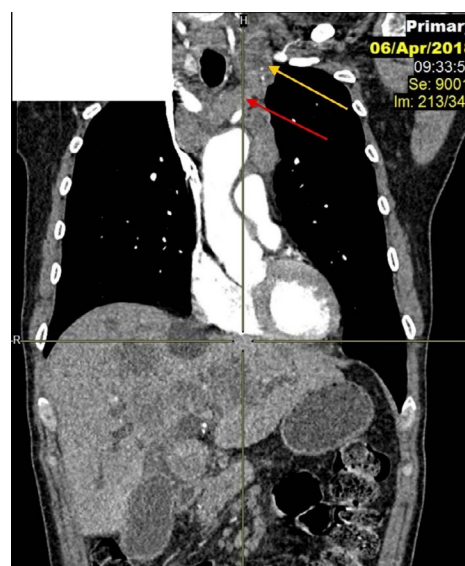


Figure 1. Post contrast coronal CT chest reformatting showing left supraclavicular LN (yellow arrow) and left pre-vascular mediastinal LN (red arrow)

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Histology

Histological features and immunoprofile of metastatic high grade sarcomatous renal carcinoma of left supraclavicular lymph node were depicted in Figures 4-11.

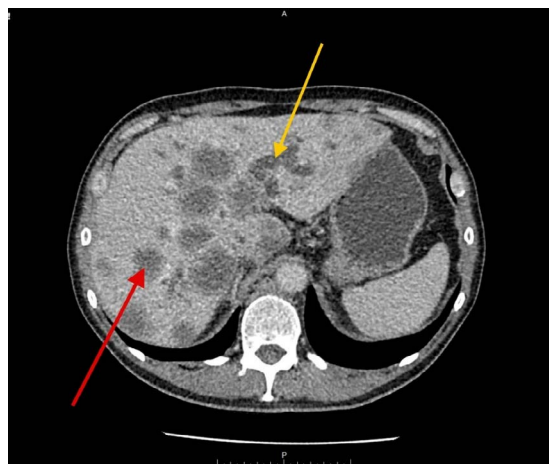


Figure 2. Post contrast axial CT abdomen axial showing dilated intra-hepatic biliary radicals (IHBR) (yellow arrow) and multiple hepatic focal lesions likely metastatic (red arrow)



Figure 3. Post contrast axial CT of the abdomen showing para-aortic LN (yellow arrow) and right renal mass lesion (red arrow)

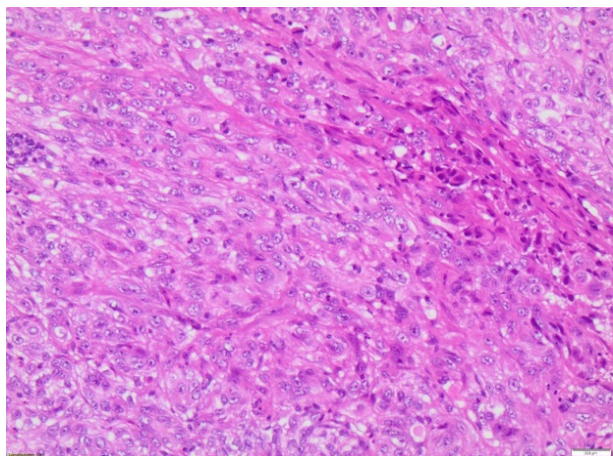


Figure 4. H&E X100 (Haematoxylin and Eosin stain X100) shows poorly differentiated malignant tumour with no obvious squamous or glandular differentiation

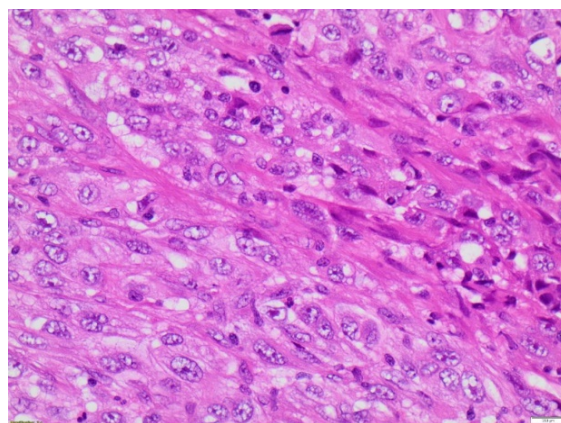


Figure 5. H&E X200 (Haematoxylin and Eosin stain X200). Tumour cells are spindle shaped with pleomorphic nuclei and eosinophilic cytoplasm

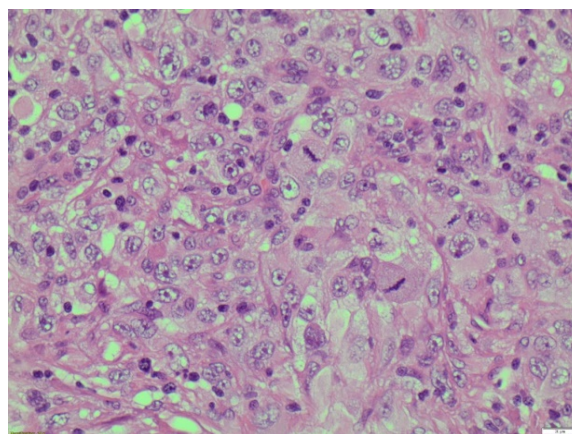


Figure 6. H&E X400 [Haematoxylin and Eosin stain X400]. Tumour cells show pleomorphic nuclei, prominent nucleoli and frequent mitoses

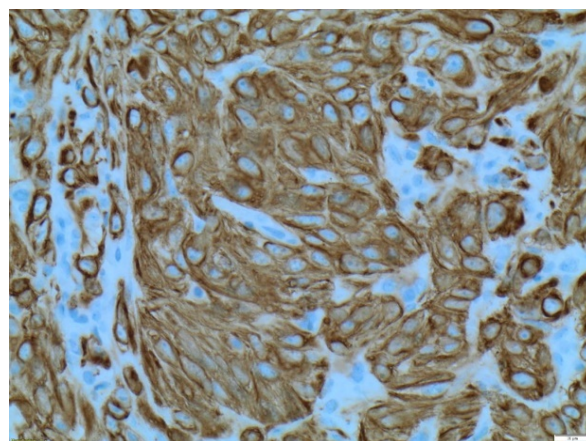


Figure 7. CK8/18 X200 immunohistochemistry-Tumour cells are positive for cytokeratin [CK] 8/18 X200

Discussion

Kidney cancer is the 12th most common cancer in the world along with pancreatic cancer, with around 338,000 new cases diagnosed in 2012 [1]. Czech republic and Lithuania constitutes the highest reported cases in the world with 59% of the cases occurring predominantly in developed countries. The incidence rates were reported highest in North America, Europe and lowest in Africa and Asia.

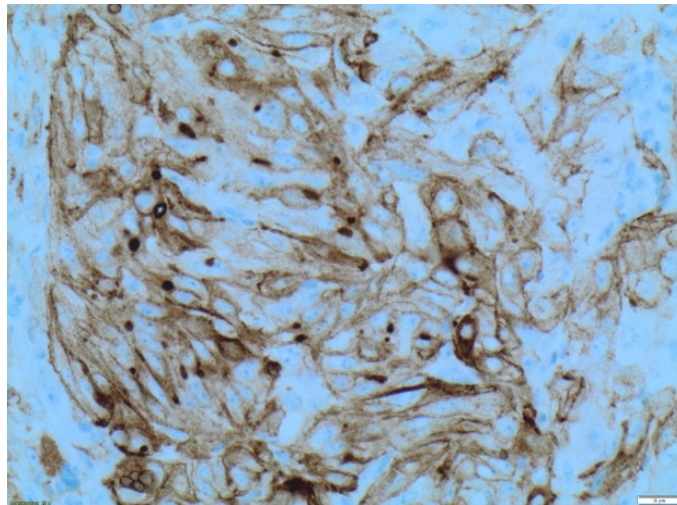


Figure 8. EMA X200 immunohistochemistry-Tumour cells are positive for epithelial membrane antigen [EMA] X200

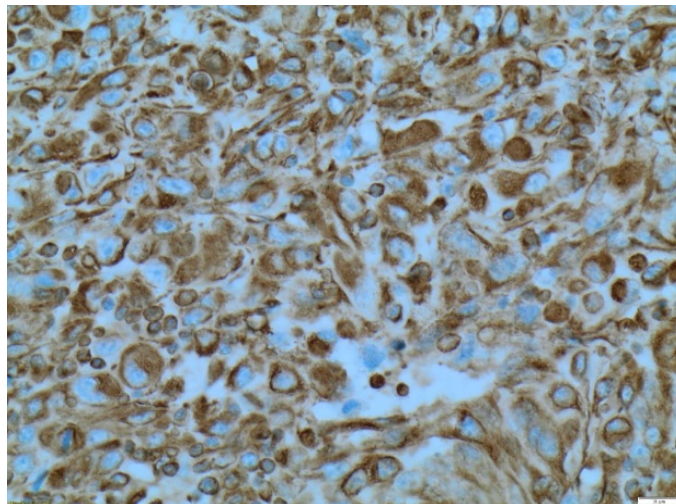


Figure 9. Vimentin X200 immunohistochemistry-Tumour cells are positive for vimentin X200

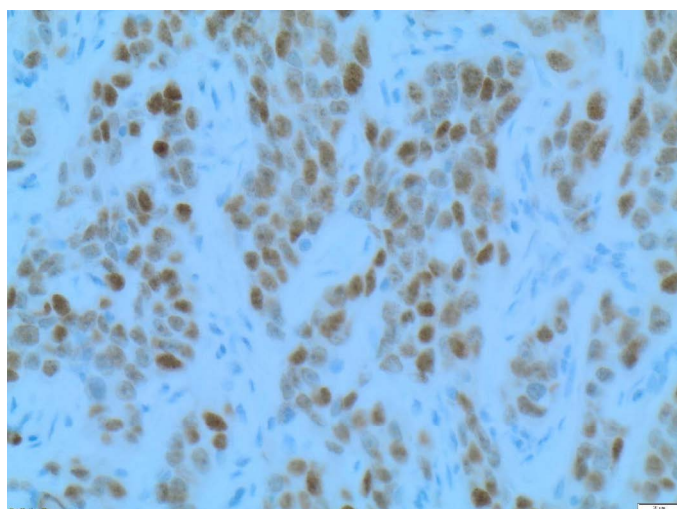


Figure 10. PAX8 X200 immunohistochemistry-Tumour cells are positive for PAX8 [Paired-box gene 8] X200

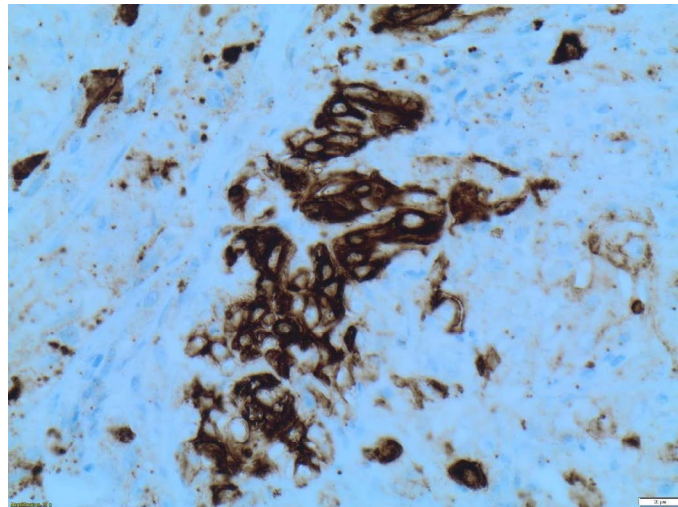


Figure 11. CD10 X200 immunohistochemistry-Tumour cells are positive for CD10 or CALLA (common acute lymphoblastic leukaemia antigen)

Sarcomatoid type is a rare type of cancer of kidney and is reported to occur in 5-8 percent of the (Renal Cell Carcinoma) RCC's. Most of the kidney cancer commonly starts in clear cells but can become sarcomatoid at any time due to a process called de-differentiation. Sarcomatoid cells contain elements of muscle, nerves, fat, blood vessels and fibrous tissue. The term "sarcomatoid renal cell carcinoma" (SRCC) was first coined in 1968 to describe tumours that had progressed or transformed to a high grade, pleomorphic often spindle cell malignancy with a resemblance in most cases to pleomorphic undifferentiated sarcoma [2,3]. Sarcomatoid renal cell carcinoma (SRCC) since 2016 WHO classification has been recognised as a form of dedifferentiated carcinoma rather than renal sarcoma known earlier. The tumour undergoes transformation into a high grade undifferentiated component with presence of spindle cells and show epithelial and mesenchymal differentiation by ultrastructural and immune histochemical analysis [4-6]. The Sarcomatoid transformation happens in all histologic subtypes of RCCs, the commonest being the chromophobe subtype. However, regardless of RCC subtype, sarcomatoid differentiation, if present is associated with aggressive behaviour and high mortality [5]. The clinical presentation of SRCC shows wide disparity in terms of presentation depending on the stage of the tumour. Most of the literature lacks high level evidence and there is no clear understanding of the disease, because of its rarity. De Peralta-Venturina *et al.* study on 101 case series showed the patients mean age at presentation was 60 years (33-80 years), more common in males than females (1.6:1). The average tumour size was 9.2 cms and more often involved the left kidney than the right [5]. Shuch *et al.* study on 104 patients showed median size of tumour of 9.5 cms (2.5-30). 65% were of clear cell histology, 13.6% papillary, chromophobe (10.7%), collecting duct 1% and rest unclassified. They also showed to have been more common in right than left kidney and have metastatic disease of 69.2% at presentation. Mortality was around 81.7% with a median survival of 5.9 months [7]. Several small studies have showed median overall survival of all patients with SRCC was 5.8 months. Patients without distant metastasis had a median overall survival of 35 months compared with 3 months of those with distant metastasis. The percentage of the Sarcomatoid components did not have an obvious influence on the prognosis [8].

Sarcomatoid RCC dedifferentiation originates from a process called epithelial to mesenchymal transition (EMT). EMT is a biological process where a polarised epithelial cell interacting with the basement membrane via basal surface undergo biochemical changes into

mesenchymal cell phenotype with ability to increased migratory capacity, invasiveness, and resistance to apoptosis and production of ECM components [9]. EMT is responsible for the cancer spread locally and metastasis and represents SRCC morphologically and immunochemically [10]. Investigations like fine needle aspiration (FNA), core biopsy, CT and MRI are used for diagnosis, although none is effective. There are studies which spoke of FNA [11,12] as a good diagnostic choice. Other studies have argued core biopsy [13] is better than FNA when evaluated along with immunocytochemistry.

Sarcomatoid renal cell carcinoma typically demonstrates aggressive features, such as necrosis, renal vein invasion and renal sinus invasion along with heterogeneous appearance due to non-enhancing necrotic areas with contrast in CT. MRI showed necrosis as hypo intense signal on T1 with corresponding T2 hyper intensity [14].

Patients with SRCC have the worst prognosis in comparison to all other RCC'S. Even when comparing high grade, SRCC in comparison to other high grade RCC's fares worst in prognosis. The presence of sarcomatoid changes is an independent predictor of poor survival and outcome [6,7].

The treatment options include nephrectomy and adjuvant chemotherapy if it is localised. Even though American college of urologist recommend partial nephrectomy as the choice, Eminaga *et al.* did a SEER based study which showed the localised SRCC to be at 13% and most of the SRCC are not amenable for a partial nephrectomy and total nephrectomy provides a oncological advantage [15,16]. As with SRCC with metastasis, there are no established standard guidelines and treatment options include targeted therapy, chemotherapy and immunotherapy.

VEGF (Vascular endothelial growth factor) targeted therapy has been administered as first line therapy in studies [17,18] by Kyriakopoulos and Golshayan and have reported survival of less than an year. Many trials are ongoing and few have evaluated the option of chemotherapy like gemcitabine-doxorubicin ECOG8802 phase II study [19] and doxorubicin-ifosfamide phase 2 trial [19,20]. But none give a survival more than 4 to 8 months. Immunotherapy like high-dose interleukin-2 (HD IL-2) has been administered [21,22] with reduced relative risk of death comparing to patients not receiving it at all. Even though, there are many trials going on in the world at present, there is no wide consensus among the medical fraternity about the SRCC in terms of diagnosis, management and treatment due to its aggressive nature

and associated poor prognostic outcome. The advent of molecular medicine and biomarkers should shed light about better understanding of the disease and its management in the future.

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