

CASE REPORT

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Mucinous tubular and spindle cell carcinoma with high-grade transformation: case report

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Abstract

Background: Mucinous tubular and spindle cell carcinoma (MTSCC) is a type of renal cell carcinoma (RCC) described as an entity with low-grade and low malignant potential. This report presents a high-grade transformation of MTSCC which is an uncommon finding in this subtype of RCC. Although most reported cases showed low malignant potential and good prognosis after surgical resection, a small subset of patients has been reported with aggressive phenotype and fatal outcome.

Case presentation: A case of a 23-year-old male is discussed with an incidental renal mass in the left kidney after a workup of bilateral flank pain. Morphologically, the tumor was composed of tubular structures lined by cuboidal cells mixed with spindle cells and sarcomatoid change was present in the tumor. Previously sarcomatoid change has been mostly reported along with conventional morphology in other common type of RCC with a worse prognosis.

Conclusions: The aim of this report is to draw the attention of pathologists and clinicians to the importance of high grade MTSCC owing to the unfavorable prognosis.

Keywords: Spindle-cell, Carcinoma, High-grade, Mucinous tubular, Sarcomatoid change

Background

There are various types of renal cell carcinomas with distinct underlying molecular features, unique immunophenotypes, varying degrees of clinical outcomes, and therapeutic implications. Originally, mucinous tubular and spindle cell carcinoma (MTSCC) was described as an unclassifiable tumor in 1998 (Lima et al. 2013). In 2004, it was described as a distinct entity (Yang et al. 2010). It is more commonly reported in females and the mean age at presentation is 53 years (Ferlicot et al. 2005). Although MTSCC itself has low malignant potential, rare cases with sarcomatoid change have been reported with aggressive behavior. The MTSCC is composed of spindle cells admixed with tubules lined by bland cuboidal

cells set in a background of a variable amount of myxoid stroma (Ellis and Flower 2004).

We present a case of a 23-year-old male who reported bilateral flank pain. A left renal mass was detected on computerized tomography (CT) scan followed by a histopathological diagnosis of MTSCC with 70% tumor showing the sarcomatoid change.

Case presentation

A 23-year-old male reported to the urology department with chief complaints of bilateral flank pain and fever from the last fifteen days associated with a history of weight loss. There was no history of hematuria. He was a non-smoker and had no history of tuberculosis, diabetes mellitus, hypertension, asthma, or ischemic heart disease. There is no family history of any kind of malignancy. On physical examination, the patient was

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vitality stable with unremarkable general and systemic examination.

All the hematological investigations including renal function tests were within normal limits. CT scan chest showed tiny pulmonary nodules suspicious to be metastatic. CT scan (Fig. 1) abdomen showed well-defined heterogeneously relatively hypo-enhancing, ball-shaped, left renal mass with loss of fat interface with adjacent large bowel, compressing and displacing pelvicalyceal system with no definite vascular extension. A large hypodense lesion in segment VI of the liver and additional smaller hypodense lesions in the right lobe were also noted. Multiple enlarged upper abdominal and left renal hilar lymph nodes were seen.

In wake of complete clinical, laboratory, and radiological assessment left radical nephrectomy and adrenalectomy with lymph node dissection was performed.

On gross examination, a $10.5 \times 9.0 \times 6.0$ cm well-circumscribed tumor mass was found at the lower pole with necrosis on the cut surface. The tumor was limited to the renal parenchyma, away from sinus fat. Histological analysis revealed a tumor comprised of tubular structures set in a mucinous background. The tubules were lined by cuboidal cells having highly pleomorphic nuclei. At places, the cuboidal cells merged with spindle cell areas. Almost 70% of the tumor showed sarcomatoid differentiation and tumor necrosis was also present. The sarcomatoid cells were pleomorphic with hyperchromatic nuclei and prominent nucleoli as in Fig. 2. Abundant

mitotic figures were also present. The tumor was found to be focally invading into the perinephric fat, beyond the renal capsule. Carcinoma was found positive in 09 out of 13 periaortic lymph nodes.

On immunohistochemistry, cytokeratin 7 (CK7) and alpha-methyl co-A racemase (AMACR) were positive, paired-box gene 8 (PAX-8) and carbonic anhydrase IX (CA-IX) were focal positive, CD10 was focal weak positive while TFE3 was negative in the tumor as illustrated in Fig. 3. According to these morphological and immunohistochemical findings, a diagnosis of high-grade MTSCC was made.

The postoperative course of the patient was uneventful and was discharged on day 3 in a stable condition. On sixth month follow-up, the patient was in good health.

Discussion

MTSCC is a rare neoplasm, mostly following an indolent course, but some cases of MTSCC have been reported showing sarcomatoid change (Dhillon et al. 2009; Pillay et al. 2008; Simon et al. 2008; Isono et al. 2020; Arafah and Zaidi 2013; Sugimoto et al. 2019; Kenney et al. 2015; Gong et al. 2020). The characteristic features of seven cases are compared with our case in Table 1. Sarcomatoid change has been previously more commonly reported in other common types of renal cell carcinoma. Patients with renal cell carcinoma showing sarcomatoid change presented at an advanced stage and followed a bad prognosis (Venturina et al. 2001).

The tumor is prevalent in females with a ratio of 4:1 against males and an age group of 13 to 82 years (Yang et al. 2010; Zhao et al. 2015). MTSCC was previously considered to be originating from the loop of Henle or collecting duct but later immunohistochemical analysis showed it to be CK7 and AMACR positive. This suggested its origin from the proximal segment of the nephron showing its close relation to papillary renal cell carcinoma. Occasionally, the differentiation between both types of carcinomas becomes difficult based on routine histology and immunohistochemistry, necessitating the use of genetic studies for making a proper diagnosis (Shen et al. 2007).

Imaging studies show that the tumor mostly appears well-circumscribed and homogenous with heterogeneous and slow progressive enhancement in the corticomedullary and nephrogenic phase of CT and MRI. It has a high T2 and a low ADC value on MRI. (Cornelis et al. 2017).

On gross examination, the tumor has distinct borders with most of the tumor bulk to be found in the medullary area. Morphological analysis shows



Fig. 1 CT Scan Abdomen showing left renal mass

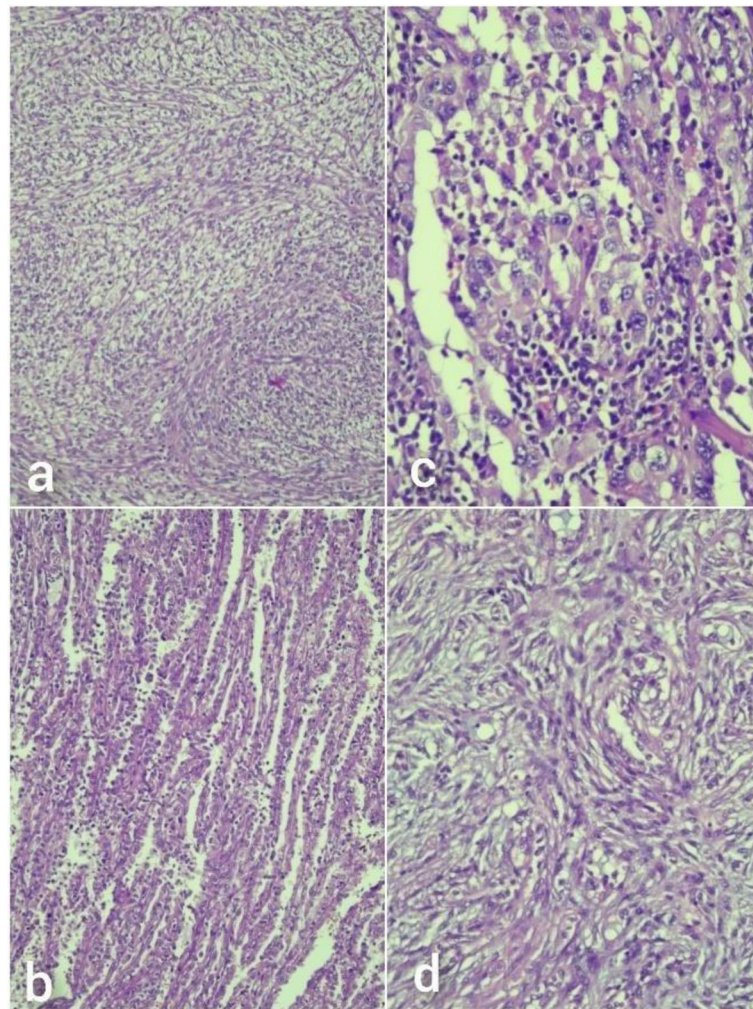


Fig. 2 **A** Spindle cell proliferation against myxoid stroma (**B**) with areas containing cords or tubules of cuboidal cells (H&E X10M), (**C**) foci showing higher nuclear grade and (**D**) sarcomatoid change (H&E X 20 M)

that the tumor is composed of elongated branching tubules and cords admixed with spindle cell areas. The tubular structures are lined by cuboidal cells containing scant eosinophilic cytoplasm and low-grade nuclei. Mucinous stroma is almost always present in all cases. Sometimes papillary structures, foamy macrophages, sarcomatoid change, and necrosis can be identified in tumors. The sarcomatoid cells have a high nuclear to cytoplasmic ratio, pleomorphic hyperchromatic nuclei, and prominent nucleoli (Ro et al. 1983).

In our case, the sarcomatoid change was present constituting 70% of the tumor. In addition, 40% of the tumor was showing necrotic areas. This upgraded the tumor to ISUP grade four which shows its deviation from commonly reported cases of a low-grade type of MTSCC.

Immunohistochemically, the tumor usually shows positivity for CK7, AMACR, renal cell carcinoma (RCC) antigen, and Lewis X (CD15) in both tubular and mucinous areas. CD 10 is negative most of the time however in some cases it may be positive (Sternberg et al. 2010).

Genetic studies have shown various chromosomal abnormalities including losses of chromosomes 1, 4, 6, 8, 9, 13, 14, 15, 22 and X (Rakozzy et al. 2002) and gains of chromosomes involving 2, 4, 5, 7, 9, 10, 12, 16, 17, 18, 19, 20, 22 and X (Dhillon et al. 2009; Brandal et al. 2006). Recently genetic study of MTSCC using array comparative genomic hybridization showed losses involving chromosomes 1, 4, 6, 8, 9, 13, 14, 15, 22 without any gains in chromosomes, in low and high-grade MTSCC of classical type, while

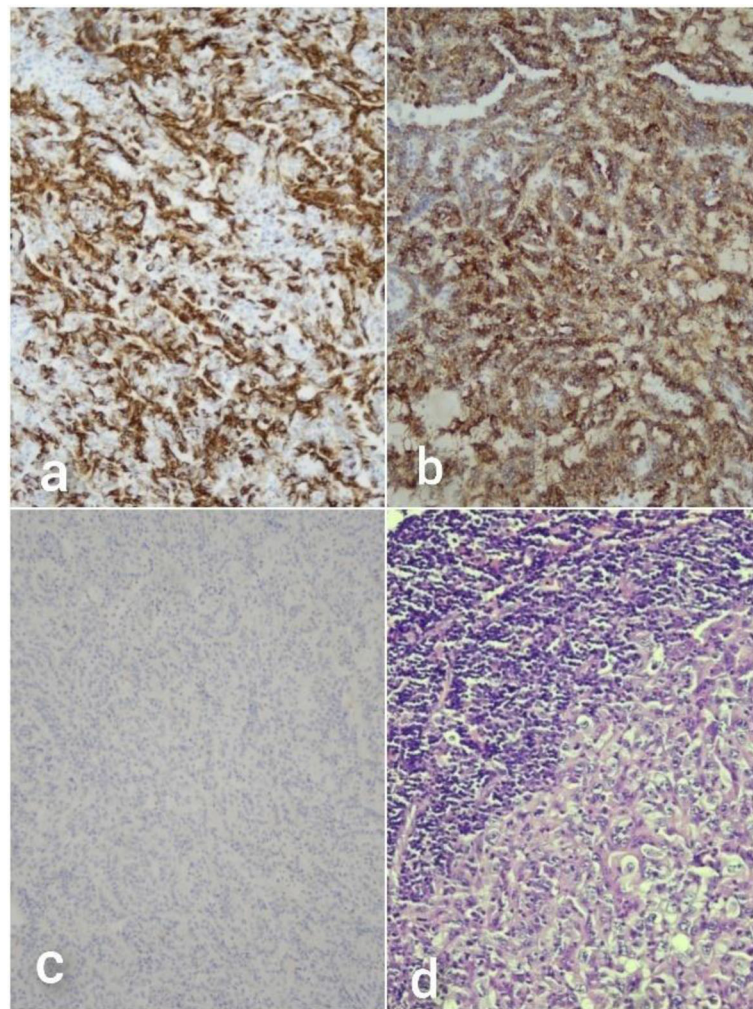


Fig. 3 A CK7 (X10M), (B) AMACR (X20M), (C) CD10 (X10M) and (D) lymph node showing metastatic carcinoma (H&E X20M)

the tumors having histopathological features overlapping with papillary RCC showed a variable pattern of losses and gains in chromosomes, including gains involving chromosomes 7 and 17 in 2 out of 4 analyzable tumors (Peckova et al. 2015). However, FISH based studies show that MTSCC does not show gains of chromosomes 7 and 17 (Cossu-Rocca et al. 2006). This emerging evidence has proved that although morphological and immunohistochemical features overlap with those of papillary RCC, genetically it is a separate entity.

There are no definite guidelines for the treatment of MTSCC, however surgical excision remains adequate for localized cases. For metastatic tumors, improvement in patient survival and reduced tumor burden have been achieved in some cases by benefiting from the use of sunitinib, a tyrosine

kinase inhibitor (Volpe et al. 2011). In a recent case report, combined immunotherapy with ipilimumab and nivolumab showed complete recession of the metastatic MTSCC (Fuchizawa et al. 2021). In a study (Lebacle et al. 2019), renal cell carcinomas with sarcomatoid change showed better expression of PD-1/PD-L1 as compared to conventional carcinomas. So, sarcomatoid RCC will respond better to targeted immunotherapy. However, further studies are required for setting proper management plan for metastatic MTSCC.

Conclusions

MTSCC is a rare tumor. This case report presents rare renal carcinoma subtype with sarcomatoid change. The sarcomatoid change is associated with aggressive behavior which is why the identification

Table 1 Characteristics of MTSCC cases with sarcomatoid change (Dhillon et al. 2009; Pillay et al. 2008; Simon et al. 2008; Isono et al. 2020; Arafah and Zaidi 2013; Sugimoto et al. 2019; Kenney et al. 2015; Gong et al. 2020)

Case no.	Age/ Sex	Clinical Presentation	Radiological features	Gross features	Morphology	Immunohistochemistry	Treatment	Metastases	Prognosis
Our Case	23/ M	bilateral flank pain and fever	well-defined heterogeneously enhancing, ball-shaped, renal mass on CT scan.	Well circumscribed mass with necrosis on cut surface.	Tubular and spindle cell areas in a mucinous stroma and sarcomatoid change in 70% of tumor.	CK7: Positive AMACRPositive. PAX-8: Focal positive. CA-IX: Focal positive. CD10: Focal weak positive.	Radical nephrectomy.	Pulmonary and liver lesions on CT scan suspicious for metastases. Lymph node metastasis confirmed on histology.	Alive on six-month follow-up.
1	71/F	Back Pain	8 cm heterogeneous mass on CT scan	Poorly circumscribed tumor with heterogeneous tan yellow and white cut surface and necrotic areas.	Tubular and spindle cell morphology with sarcomatoid change in 60% of tumor	Tumor showed positivity for CK7/vimentin,Epithelial membrane antigen and CAM5.2	Radical nephrectomy.	Expansile lytic lesions in bilateral ribs, L4 vertebral body and multiple bilateral lung nodules on CT scan.	The patient died 9 months after the nephrectomy.
2	72/F	Flank Pain, hematuria	Not Available	well-circumscribed tumor in the upper pole measuring 7 × 7 × 5 cm with yellowish cut surface showing necrosis and hemorrhage.	cords and tubules lined by cuboidal cells with abrupt transition to spindle cell areas set in a mucinous stroma. Multiple foci of atypical spindle cells.	CK AE1/AE3 and CK7 positive while AMACR focal weak positive.	Radical nephrectomy.	Adrenal gland and lymph nodes metastasis were not present.	Alive and in a good state of health after 12 months of follow-up.
3	64/F	Back Pain with lower extremity weakness	MRI revealed a left kidney mass which was extending to retroperitoneum and was compressing the spinal cord.	Left kidney tumor with a tan yellow necrotic cut surface.	Bland tubular and spindle cell component in a mucinous stroma with sarcomatoid degeneration in 40% of viable tumor.	Tumor was positive for pancytokeratin, vimentin, CD10, CK7, CK18, CK19, epithelial membrane antigen, and AMACR	Radiotherapy followed by tumor embolization and radical nephrectomy with vertebral body resection.	Thoracic vertebral bodies, liver, malignant pleural effusion and adrenal gland metastasis	Patient expired 3 weeks after surgery.
4	80/ M	Discomfort and a palpable 3-cm mass in the right collarbone	CT revealed expansive lesions that involved the inferior pole of the left kidney.	A 3.0 × 3.0 × 2.5-cm, poorly-circumscribed tumor with greyish-white and focally tan colored cut-surface.	Tubules lined by bland cuboidal cells mixed with spindle cells with extracellular mucinous and sarcomatoid component.	CD10, AMACR, CK7, EMA, E-cadherin, ZE-B1, Slug, TWIST, and vimentin were positive.	Partial nephrectomy	peritonitis carcinomatosa and multiple metastases.	Patient died 7 months after surgery.
5	43/ M	Incidental finding	MRI showed a tumor with cystic degeneration measuring 50mm.	Tumor consisted of heterogeneous yellowish nodular cut-surface with hemorrhage.	Admixture of bland tubular and spindle cells mixed with atypical spindle cells in a mucinous stroma.	Positive for AMACR and PAX8. CK7, CD10 were negative.	radical nephrectomy with lymph nodes resection followed by tyrosine kinase inhibitor, sunitinib and axitinib.	lymph node metastases and peritoneal dissemination.	Patient died due to the disseminated disease 12 months after the surgery
6	64/ M	Pain abdomen, altered bowel habits, and swelling on the left side of the abdomen.	CT scan showed a 20 cm kidney mass with cystic and solid components.	A circumscribed mass with tan-yellow cut-surface and areas of hemorrhage and necrosis.	Bland tubular and spindle cell component in a mucinous stroma with sarcomatoid degeneration in 20% of viable tumor.	AMACR and CK7 were strong diffuse positive, while epithelial membrane antigen was focally positive	Radical nephrectomy	Liver, spleen and left pleural metastasis.	Patient died after 8 months of surgery due to multiple metastasis.
7	80/ M	Known case of chronic obstructive lung disease.	11 cm left kidney tumor.	Discrete pseudocapsule with focal infiltrative borders and extensive necrosis(70%)	Mucin poor MTSCC with high grade spindle cell sarcoma component comprising of 20% of tumor.	CK7, AMACR strong Positive in both tubular and spindle cell areas.	Radical nephrectomy.	No radiological evidence of metastasis.	Patient had disease free survival on 4 months of follow-up

of this high-grade feature is essential. Complete morphology, immunohistochemistry and cytogenetics are required for definite diagnosis of this tumor. Close follow-up of tumor is required for understanding of complete biological behavior of this tumor.

Abbreviations

MTSCC: Mucinous tubular and spindle cell carcinoma; RCC: Renal cell carcinoma; CK-7: cytokeratin 7; CT: Computerized tomography; MRI: Magnetic resonance imaging; CA-IX: Carbonic anhydrase IX; AMACR: alpha methyl co-A racemase

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Authors' contributions

NH: conception, acquisition, analysis, interpretation of data; has drafted the work and has approved the submitted version. AM: supervision, revised, analysis, interpretation of data; and has approved the submitted version. The author(s) read and approved the final manuscript.

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Availability of data and materials

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Declarations

Ethics approval and consent to participate

The research has been approved by the Institutional Review Board and Ethics Committee (IRB & EC), Shifa International Hospitals Limited.

Consent for publication

The manuscript does not contain data from any person, and hence the above statement is "Not applicable".

Competing interests

The authors declare that they have no competing interests.

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