INTRODUCTION
Renal cell carcinoma (RCC) is the most common malignant neoplasm of the kidney with metastatic disease seen at presentation in 20 - 25% of patients. Even more unusual is the presentation of superior vena caval syndrome (SVCS) caused by infradiaphragmatic cancer. Lung cancer is by far the most common cause for SVCS. Although renal cell carcinoma is well known to invade into the renal vein and inferior vena cava, its association with SVCS is extremely rare with very few case reports in the literature. These cases were all reported in the pre-targeted therapy era. The mechanisms involved are direct venous spread of disease or direct invasion from surrounding lymph nodes or thyroid which harboured metastatic disease from renal cell carcinoma. The prognosis at this advanced stage of disease is dismal with limited treatment options. The rapid development of targeted therapy, primarily against the angiogenesis pathway, offers new hope in this scenario as shown by the pivotal trial by Motzer et al. There are many new targeted agents in the treatment of metastatic renal cell cancers (mRCC) which include tyrosine kinase inhibitors, monoclonal antibodies and mammalian target of rapamycin inhibitors. Tyrosine kinase inhibitors have been shown to increase progression free survival and overall survival in treatment of mRCC.

CASE REPORT
A 53-year-old male patient presented with a rapidly-growing right neck swelling over a period of 3 weeks. There was associated lethargy, loss of weight and appetite, but no respiratory or urinary symptoms. On examination, there was a large 10 x 10 cm right cervical mass extending to the right supraclavicular region. There was dilatation of veins of the right upper thorax and neck, with plethora and facial oedema. There were no significant positive findings on abdominal, intraoral and ENT assessment. Baseline chest X-ray and routine blood investigations did not reveal any significant abnormalities.

Urgent computed tomography (CT) scan of the neck and thorax revealed multiple enlarged right cervical and supraclavicular lymph nodes (Figure 1). An incisional biopsy of the enlarged right cervical lymph node was performed. Histopathology revealed tumour composed of nests of large polygonal tumour cells separated by a network of small thin-walled blood vessels. The tumour cells express abundant clear cytoplasm and oval nuclei with occasional prominent nucleoli and focal nuclear pleomorphism (Figure 2a). The tumour cytoplasm was rich with PAS-positive, diastase-sensitive material, indicating glycogen and not mucin. Immunohistochemistry revealed strong cytoplasmic membrane positivity for CK7 and EMA (Figure 2b) and focal positivity for vimentin and CD10. The cells were negative for CK20, S100 protein and synaptophysin. The conclusion was a metastatic clear cell renal cell carcinoma of Fuhrman nuclear grade 2.

With this result, an urgent CT scan of the thorax and abdomen was performed and revealed a left
hypervascular upper pole renal tumour measuring 2.8 x 1.8 cm with para-aortic and para caval lymphadenopathy. There was also evidence of pulmonary embolism in both lower lobes secondary to thrombus in the compressed right subclavian vein due to right neck metastases (Figure 3).

The patient was admitted for blood transfusion for anaemia and commenced on low molecular weight heparin for treatment of pulmonary embolism. Due to the superior vena caval syndrome with onset of right upper limb lymphoedema, a total of 10 fractions of radiotherapy were given to the right neck mass. He was started on Sunitinib, a tyrosine kinase inhibitor, after blood and clinical parameters were stabilized.

There was good and prompt clinical response after radiotherapy and one week of Sunitinib. The neck mass rapidly decreased in size. Upon discharge, he was progressing well with the tyrosine kinase inhibitor therapy with small residual neck mass and markedly reduced right upper limb lymphoedema.

The patient went on to complete two cycles of Sunitinib 50 mg once daily with minimal side effects initially. However, he represented later with lethargy, confusion and neck cellulitis and was admitted for antibiotics and blood transfusion. Sunitinib treatment was withheld as his condition was deteriorating. A repeat CT scan of the neck and brain showed right neck abscess with posterior fossa cerebral metastases. The patient finally succumbed to the disease 9 weeks from time of presentation.

DISCUSSION

In the few reported cases of SVCS secondary to renal cell carcinoma, SVCS developed at a later stage after the presentation and treatment of the primary tumour in the kidney. To the authors’ knowledge, the case illustrated here represents the first case report in which the initial clinical presentation was SVCS.

Sakura et al. reported a case of pT3aN1M1 papillary renal cell carcinoma initially managed by radical nephrectomy and adjuvant interferon α therapy but developed SVCS 7 years later.4 In the case reported by Strugnell et al., SVCS occurred 9 months after radical nephrectomy for a pT3a sarcomatoid renal cell carcinoma.2 In an earlier reported case by Davidson et al., SVCS developed more than a year after radical nephrectomy for a pT3a clear cell carcinoma.3 All the patients invariably succumbed to the disease. This reaffirmed the aggressive nature of the disease once SVCS develops. It is also obvious that development of SVCS is not confined to any pathological subtype of renal cell carcinoma.

It is postulated that the metastatic disease might have acquired further mutations with enhanced metastatic potential. For instance, studies have shown that metastatic renal cell carcinoma expressed VEGF, interleukin-8, matrix metallo-proteinase type 9 (MMP-9) and MMP-2 at higher level than the primary tumour.7 In this case, histopathological examination of the lymph node biopsy using an appropriate panel of immunohistochemical markers was invaluable in making the diagnosis. Concurrent EMA and vimentin positivity is
typical of renal cell carcinoma, as is the presence of abundant cytoplasmic glycogen and absence of mucin. Immunonegativity for synaptophysin excluded the diagnosis of paraganglioma.

The present case had a relatively small primary renal tumour, thus the decision was made to proceed with radiotherapy and targeted therapy to relieve the debilitating symptoms of SVCS as the initial treatment strategy. As conventional adjuvant therapy of interferon and interleukin-2 offer low response rates, newer targeted therapy appeared attractive for advanced disease as in the case of SVCS. In this case, we opted to treat the patient with radiotherapy followed by Sunitinib. The patient responded rapidly to Sunitinib in the initial phase with reduction in the size of the supraclavicular lymph nodes and marked improvement of the lymphoedema of the upper limb. The patient tolerated the medication well and the symptomatic relief was remarkable.

Tyrosine kinase inhibitor did not appear to prolonged the overall survival in this case but the patient was able to enjoy a higher quality of life. As SVCS is an extremely rare condition, a proper trial comparing different kinds of targeted therapies will be difficult, if not impossible, to conduct. Therefore, experience gathered with case reports such as the current case will help in the accumulation of clinical information for the future treatment of renal cell carcinoma with SVCS.

**REFERENCES**