Urology Case Reports 40 (2022) 101880

Contents lists available at ScienceDirect

Urology Case Reports

journal homepage: www.elsevier.com/locate/eucr

Metastatic atypical renal tumour with metanephric characteristics treated with Sunitinib

H. Mohammad [a,*], K. Madsen [b,c], O. Graumann [d,e], A.C. Loya [f,g], N.V. Jensen [a], R.H. Dahlrot [a,e]

[a] Department of Oncology, Odense University Hospital, Odense, Denmark
[b] Department of Pathology, Odense University Hospital, Odense, Denmark
[c] Department of Cardiovascular and Renal Research, University of Southern Denmark, Odense, Denmark
[d] Department of Radiology, Odense University Hospital, Odense, Denmark
[e] Department of Clinical Research, University of Southern Denmark, Odense, Denmark
[f] Department of Pathology, Rigshospitalet, Copenhagen, Denmark
[g] Institute for Clinical Medicine, University of Copenhagen, Copenhagen, Denmark

ARTICLE INFO

Keywords:
Metanephric adenoma
Tyrosine kinase inhibitor
Oncology
Renal tumour

ABSTRACT

Metanephric Adenoma (MA) is a rare and unclassifiable renal tumour with sparse reported clinical and morphological features. Generally MA's have a benign course without recurrence after nephrectomy, however a few cases received oncological treatment due to malignant progression.

We present a 42-year-old woman who years after an initial nephrectomy developed several processes and biopsy confirmed recurrence of MA. Sunitinib was given for only two weeks, as she developed side-effects and currently the patient undergoes control scans with only minimal growth of the processes.

This is the first case of MA treated with Tyrosin-Kinase-Inhibitor.

1. Introduction

Metanephric adenoma (MA) is a rare and unclassifiable renal tumour with metanephric characteristics, yet to be well recognized. The reported clinical and morphologic features are sparse, and it is radiologically difficult to distinguish from other renal tumours. We herein report a case of a 42-year-old female, with a metastatic atypical renal tumour with metanephric characteristics.

2. Case report

In 2010, the patient underwent a computed tomography (CT) due to abdominal pain. In the left kidney, a 5 × 4.5 cm tumour was identified and a nephrectomy was performed (Fig. 1). The tumour appeared partly cystic and well-circumscribed without an apparent pseudocapsule. The tissue was yellow and firm with focal hemorrhages. Microscopically, the tumour appeared highly cellular with tightly packed acini, papillary structures and rich with mitotic activity (Fig. 2A and B). Immunohistochemistry showed positive staining for CK8, WT1 and EMA and focal positive reaction for vimentin. The Ki-67 proliferation index varied but was up to 25% in hot spots (Fig. 2C). No invasion was detected in the renal capsule or sinus fat tissue, nor were any vascular embolism observed. Based on the morphology and immunohistochemistry, the tumour was primarily diagnosed as MA and thus no further treatment was given. Seven years later, the patient presented with blood-tinged diarrhea, vomiting and associated right abdominal pain which could be clinically provoked. An ultra-sound of the upper abdomen was performed, showing a cystic process in the left epigastrium. A subsequent CT-scan described a cyst (12x8x10cm) arising from the right ovary (Fig. 3A) and supplementing CA-125 was 31. Due to torsion and necrosis, the right adnexa was resected and macroscopically, the cyst appeared multilocular with a dark and hemorrhagic surface. The ovary's characteristics were inconclusive due to ischemia. Because of the unusual morphology, the current and original material from 2010 was revised with additional examination by next generation sequencing (NGS) analysis by the Department of Pathology, Copenhagen University Hospital and by Cleveland Clinic, Cleveland, USA. The high Ki-67 activity, lack of BRAF mutations and presence of trisomy 7/17, made the diagnosis of MA unlikely, and the tumour was reclassified as an atypical renal tumour with metanephric characteristics with an unknown malignancy potential. A year later upon CT-scan follow-up, several processes in the kidney bed, left flank, posterior wall of the cervix and liver

* Corresponding author.
E-mail address: hajer.mohammad@rsyd.dk (H. Mohammad).

https://doi.org/10.1016/j.eucr.2021.101880
Received 9 September 2021; Received in revised form 29 September 2021; Accepted 5 October 2021
Available online 8 October 2021

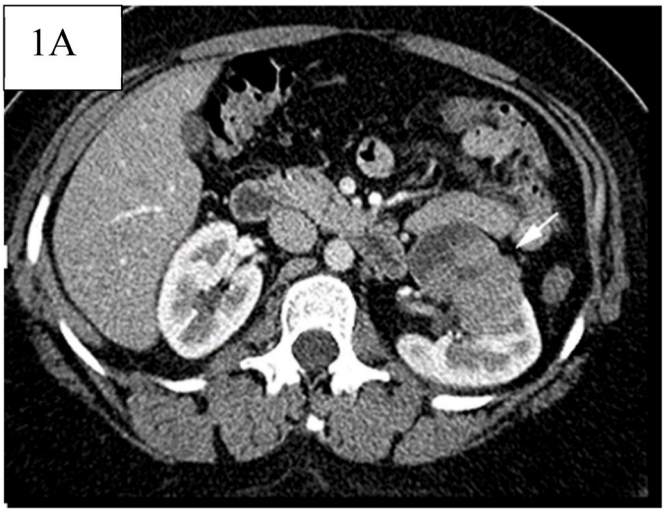

Fig. 1. CT from 2010 with intravenous contrast. Tumour is seen in the left kidney (white arrow).

were noted (Fig. 3B). An additional FDG-PET-scan showed activity in small changes, laterally and posteriorly of the abdomen and around the uterus. Biopsy from the left kidney's bed, confirmed recurrence of the atypical, metastatic renal tumour and the patient was treated with Sunitinib. After two weeks' treatment, the patient was admitted with fever and diarrhea, treated for infection of unknown focus and the symptoms were interpreted as side-effects to the medical treatment. At present, the patient undergoes CT-scans every 3–4 months, with only minimal growth and as she is asymptomatic, no treatment has been given.

3. Discussion

Macroscopically, MA often appear well-circumscribed with a pseudocapsule, tan to yellow in color, where both necrosis and hemorrhages may be present[1,2] Histologically, MA is a highly cellular tumour, composed of small, uniform epithelial cells arranged in tightly packed acini.[1] The present case appears with metanephric features, but with higher mitotic rate and higher Ki-67 proliferation index than usually reported, as in Papillary renal cell carcinoma (PRCC) and epithelial-predominant Wilms tumour (WT), the two main differential diagnosis.[1,2] Along with the findings of trisomy 7/17 and deficient BRAF V600E mutation, classic MA was excluded, although approximately 90% of MA lesions have BRAF V600E mutations.[3,4] Thus, based on the histopathology, immunochemistry and molecular findings combined with the clinical behavior, the tumour was classified as a metastatic atypical renal tumour with metanephric characteristics.

Generally, MA's have a benign course without recurrence after nephrectomy, however our patient had an unusual, aggressive course. As PRCC and WT were excluded, it complicated the choice of this case's treatment. There is no standard treatment for this type of tumour, and according to guidelines for nonclear cell Renal Cell Carcinoma (RCC),

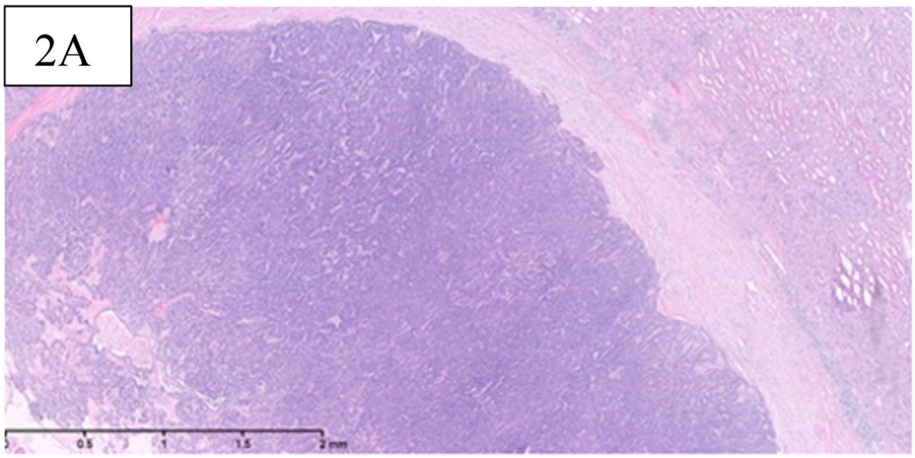

Fig. 2a. Overview of the tumour in relation to surrounding renal parenchyma (HE, x 2.5).

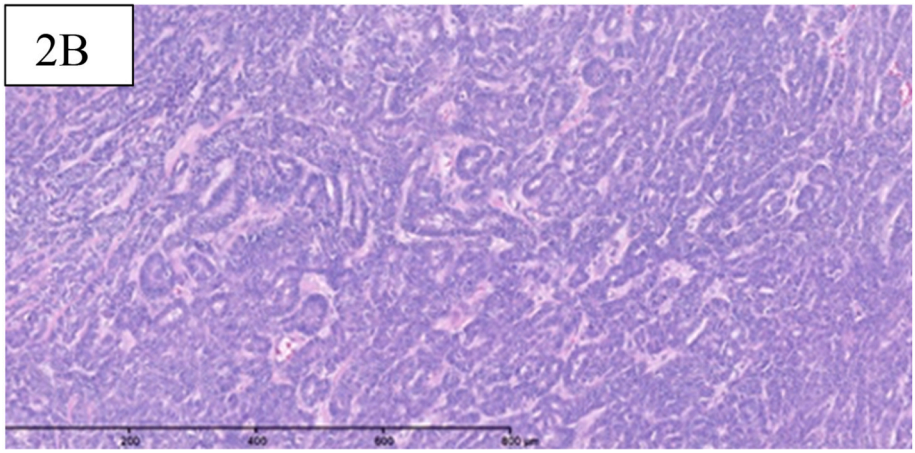

Fig. 2b. Close-up of the tumour with visible acinar and papillary structures (HE, x20).

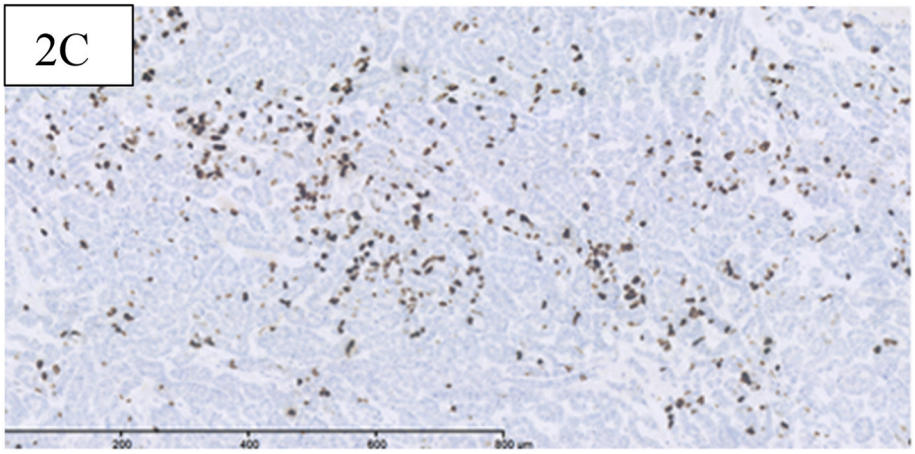

Fig. 2c. Proliferation marker.

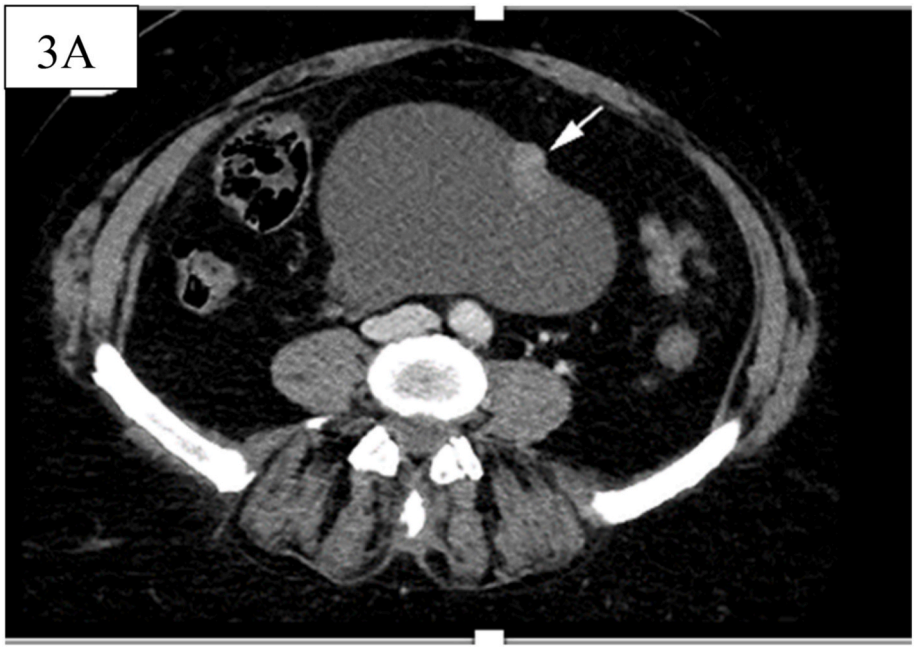

Fig. 3a. CT from 2017 with intravenous contrast. Large cystic mass is seen with solid component contrast enhancing (white arrow).

the patient received treatment with Sunitinib, a VEGF-receptor Tyrosine-Kinase Inhibitor (TKI). An immune check-point inhibitor could have been another option, but has only later become a standard treatment. Chemotherapy and radiotherapy generally lack efficacy in RCC and were not considered. Due to diarrhea, a known side-effect to Sunitinib, the patient refused further treatment. As it was only given over two weeks, no definitive conclusions can be drawn as to whether Sunitinib is efficient in MA's. However, it can be speculated if the short-term treatment stabilized the course and if persistent treatment could have resulted in complete regression. Currently, only two cases with progression and metastasis have been reported.[2,5] Renshaw et al. reported a 7-year-old child with metastatic MA in several lymph nodes treated with nephrectomy, beam irradiation to the lymph nodes and adjuvant chemotherapy. Neither dose nor chemotherapeutic regimen are further described.[5] In the second case, a patient underwent a radical nephrectomy with postoperatively radiotherapy (50 Gy). After developing bone lesions, the patient received chemotherapy with Actinomycin D and Vincristine over several courses and palliative irradiation and resection of some lytic lesions. The patient survived 17 years after her initial nephrectomy.[2]

The initial symptoms of this case were in accordance with the ones reported for MA (subjective weakness, abdominal pain, hematuria, dysuria, pollakiuria, abdominal mass and fever), although many patients are asymptomatic and MA is detected incidentally by diagnostic imaging. MA patients are often younger, mean age 41 (range 5–83) years, with a female to male ratio of 2:1. On diagnostic imaging, MA's differ in size from 2.5 to 15 cm, located unilaterally, equally distributed between the right and left kidney, complicating the distinguishment from other renal tumours by imaging alone.[1,2]

Our case is the first reported of a metastatic RCC with MA characteristics, treated with a TKI, and one of the very few patients to receive anti-neoplastic treatment. As there is extreme sparse literature describing the clinical characteristics and treatment modalities of a renal tumour with these histological features, it remains a clinical challenge.

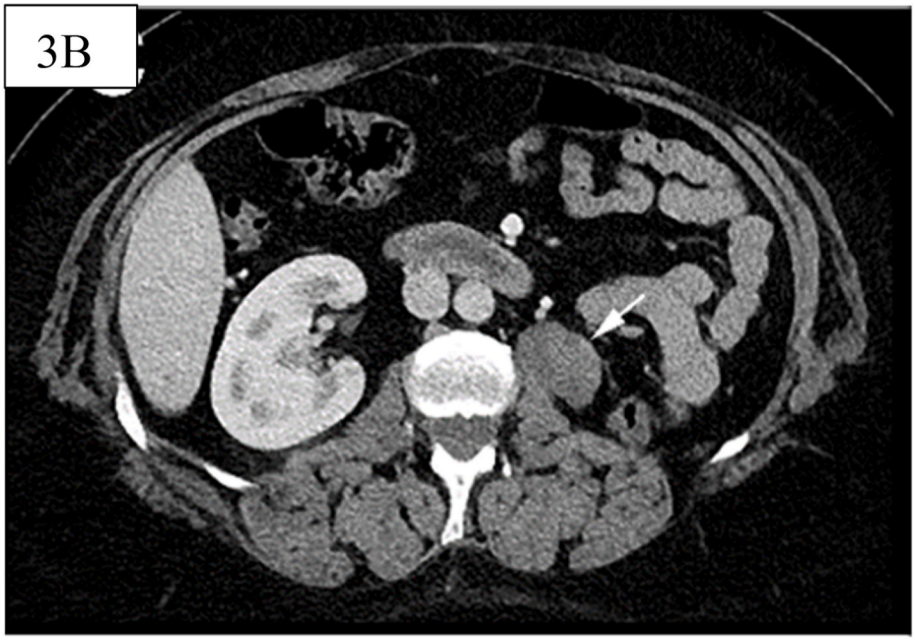

Fig. 3b. CT from 2018 with intravenous contrast. Soft tissue process in the left kidney's bed (white arrow).

References

1. Davis C, Barton J, Sesterhenn I. Clinicopathological study of fifty patients. *Am J Surg Pathol*. 1995;19(10):1101–1114.
2. Pins M, Jones E, Martul V, Kamat B, Unlas J, Renshaw A. Metanephric adenoma- like tumor of the kidney. Report of 3 malignancies with emphasis on discriminating features. *Arch Pathol Lab Med*. 1999;123(5):415–420.
3. Choueiri T, Cheville J, Palescandolo E, et al. BRAF mutations in metanephric adenoma of the kidney. *Eur Urol*. 2012;62(5):917–922.
4. Brown JA, Anderl KL, Borell TJ, Qian J, Bostwick DG, Jenkins RB. Simultaneous chromosome 7 and 17 gain and sex chromosome loss provide evidence that renal metanephric adenoma is related to papillary renal cell carcinoma. *J Urol*. 1997;158:370–374.
5. Renshaw AA, Freyer DR, Hammers YA. Metastatic metanephric adenoma in a child. *Am J Surg Pathol*. 2000;24(4):570–574.