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# Partial nephrectomy can be a successful treatment option for renal epithelioid angiomyolipoma: a case report and literature review

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**Background.** Renal epithelioid angiomyolipoma is a rare tumour which involves kidneys in most cases. It is known for its aggressive behaviour as a significant number of cases have been associated with metastatic epithelioid angiomyolipoma. Usually, radical treatment with systemic therapy is recommended. Only a small number of cases of epithelioid angiomyolipomas have been reported with the standard treatment being radical or partial nephrectomy. We present a case report showing that partial nephrectomy can be a successful treatment option for renal epithelioid angiomyolipoma. This is the first case of this nature in Lithuania.

**Case presentation.** In this case, a 40-year-old male with epithelioid angiomyolipoma of the left kidney is presented. In 2012, a cystic left renal mass 40 × 41 mm in size was diagnosed incidentally while performing ultrasound and later confirmed by MRI. Due to the size of the tumour and the possibility of renal cell carcinoma, surgery was scheduled. Left partial nephrectomy was performed successfully. Final pathology report came back with the diagnosis of renal epithelioid angiomyolipoma. The patient had yearly follow-up for six years by CT scan, and neither recurrence nor progression were observed.

**Conclusion.** Early detection and diagnosis are crucial for treatment as the tumour tends to have malignancy potential. With early diagnosis, partial nephrectomy can be performed with yearly follow-up and no systemic treatment required.

**Keywords:** epithelioid angiomyolipoma, magnetic resonance imaging, partial nephrectomy, systemic treatment

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## INTRODUCTION

Renal angiomyolipoma is a common benign tumour characterized by abnormal blood vessels, smooth muscles, and mature adipose tissue (1). Most of renal angiomyolipomas are small in size and asymptomatic. Angiomyolipoma of the kidneys appears in 0.3–3% of the general population (2). One of the variants of renal angiomyolipoma is epithelioid angiomyolipoma (EAML). It is a very rare tumour, which has been recognized as a mesenchymal tumour in the 2016 World Health Organization classification of renal tumours (3). EAML involves the kidney in most of the cases but can be found in different organs, such as the liver, lungs, the pancreas, and the bladder (4, 5). Middle-aged females have the highest incidence of renal EAML (6). EAML can occur sporadically or as a part of a tuberous sclerosis complex. Classic angiomyolipomas are usually found incidentally on imaging studies and are relatively easy to identify because of the fat component in the tumour, but epithelioid variants of angiomyolipomas are tricky as they mimic various neoplasms (7). Epithelioid angiomyolipomas usually have a high percentage of epithelioid cells (at least 80%) and have a malignancy potential as a significant number of cases have been associated with malignant EAML behaviour (8, 9). Although EAML is not always malignant, the first fatal case of this tumour was reported in 1994 by Martignoni et al. (10).

Clinically, EAML has similar symptoms to those of renal cell carcinoma and remains asymptomatic until the late stages of the disease. Presenting symptoms include: body weight loss, haematuria, abdominal pain, and cough in the advanced disease (11). In addition, patients with EAML frequently express lumbar pains (12). EAML should be taken into consideration by clinicians if the patient is of young age and the renal tumour is large in size (1).

## CASE

We report a 40-year-old male patient, whose ultrasound showed a 41 × 40 mm cystic mass in the upper pole of the left kidney. Non-contrast enhanced MRI was carried out and confirmed a 43 × 40 × 40 mm heterogeneous tumour in the upper pole of the left kidney without metastasis (Fig. 1a, b, c). The patient was asymptomatic and the physical examination

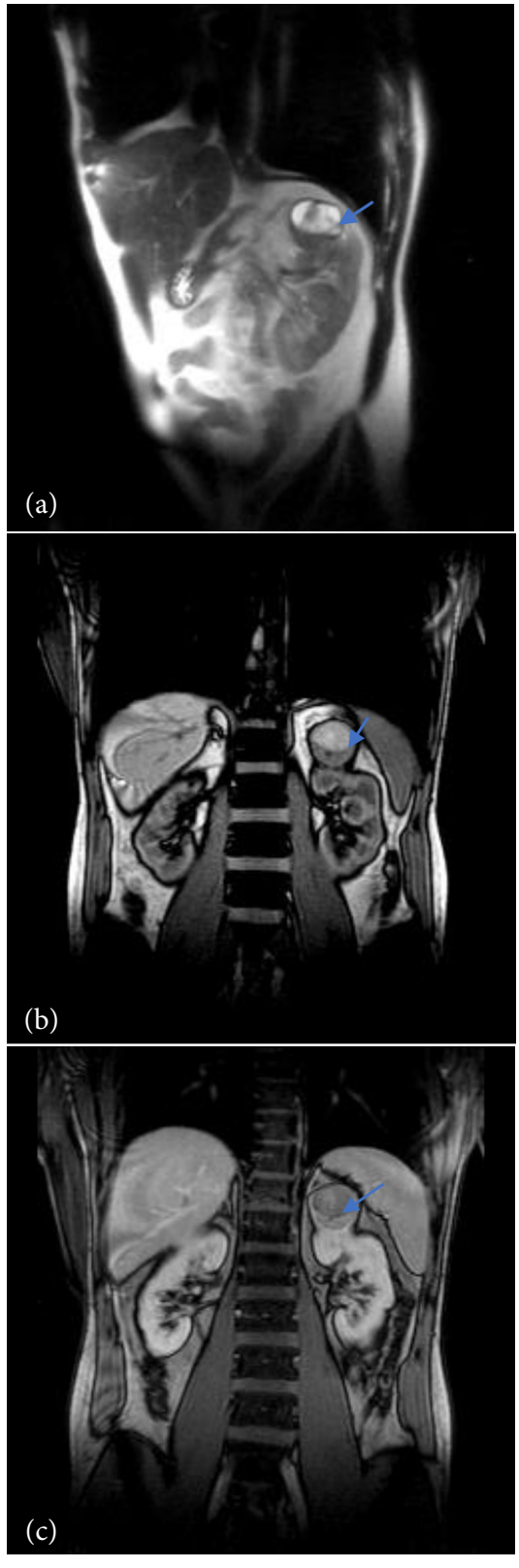


**Fig. 1.** Non-contrast MRI T2 and T1 weighted images. (a) T2 image shows left kidney heterogenous mass (arrow). (b) in-phase image shows hyperintensity (arrow). (c) out-of-phase image shows decreased siganla intensity, indicating microscopic fat (arrow)

was within normal limits. Due to the size of the tumour and its potential for malignancy, left partial nephrectomy was performed. The histological analysis showed a tumour that contained large polygonal cells with eosinophillic cytoplasm and polymorphic nuclei; it also showed invasion of the capsule of the kidney and of the surrounding fatty tissue (Fig. 2, 3). The centre of the tumour had an area of necrosis and an area of haemorrhage in it (Fig. 4). The margins were free of tumour. Immunohistochemical analysis showed HMB45+ 90%, SMA+ 5%, S100-, PanCk-, Synapt-, and the final diagnosis came back as epithelioid angiomyolipoma (Fig. 5a, b). The patient had a yearly follow-up CT scans for six years with the last CT in 2019. Through the years, no recurrence and progression was observed.

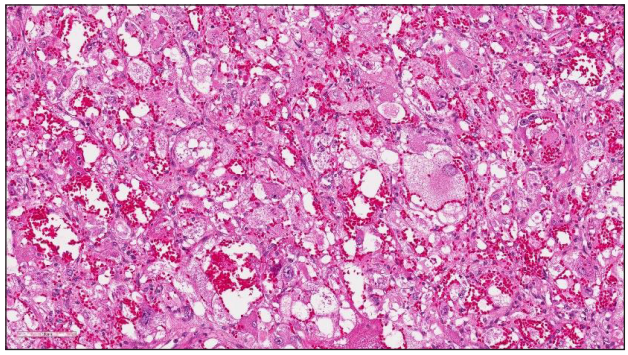

**Fig 2.** Tumour composed by large polygonal epithelioid cells with abundant eosinophilic granular cytoplasm. HE ×216

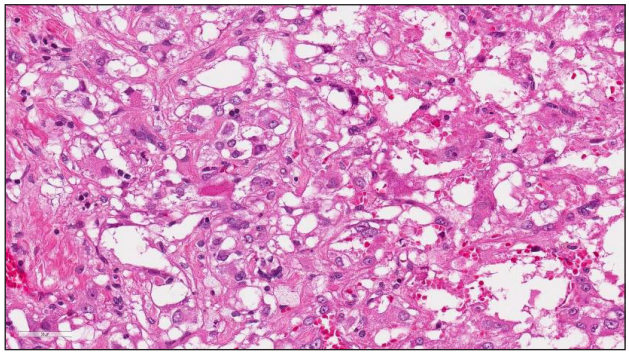

**Fig3.** Tumour cells exhibit large irregular nuclei and prominent nucleoli. HE ×400

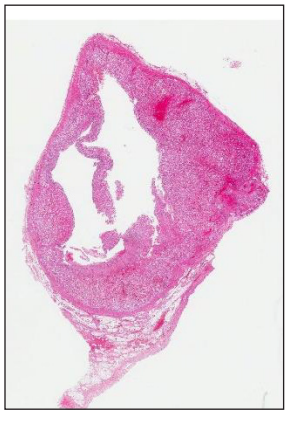

**Fig 4.** General view: encapsulated solid tumour with necrotic centre. HE ×70

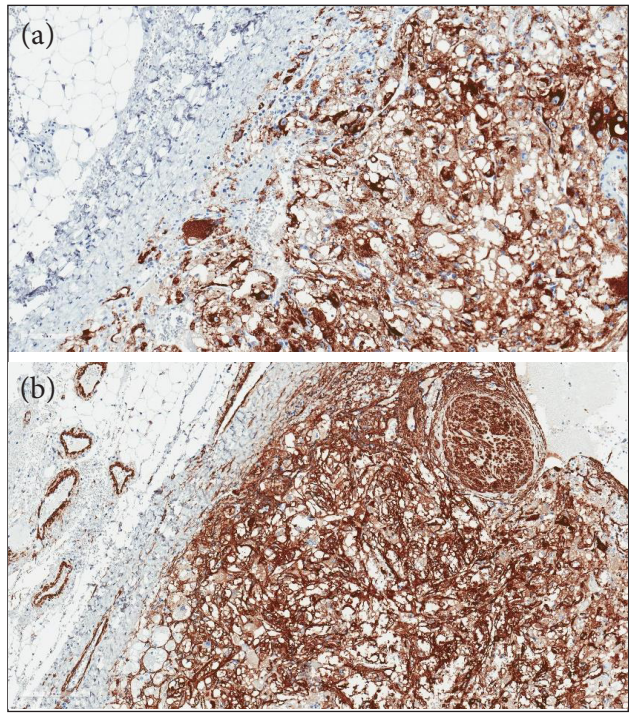


**Fig. 5.** Immunohistochemical stainings show positive reactions against smooth muscle actin (a) and HMB45 (b)

## DISCUSSION

Diagnosis of renal angiomyolipoma is considered to be relatively easy because of the presence of fatty cells is found (13). On the other hand, the epithelioid type of angiomyolipoma is challenging in most cases as it can mimic a majority of neoplasms, especially renal cell carcinoma (12). In our case, the tumour was first considered to be renal cell carcinoma and the diagnosis of epithelioid angiomyolipoma was only later confirmed by the histological analysis. There are several diagnostic tools that aid in diagnosing EAML of the kidney, including ultrasound, computer tomography, and magnetic resonance imaging. Contrast-enhanced ultrasound imaging may be beneficial (6). Even with all the advanced techniques in the medical field, renal EAMLs can still be challenging to diagnose, so the combination of various diagnostic tools and histological examination is very important.

Histologically, the proliferation of epithelioid cells and granular cytoplasm of eosinophils is observed (14). Because of its malignant behaviour, factors which determine the risk of malignancy in patients presenting with EAML were searched for (15). There are no definite histological criteria for malignancy except distant metastases, which confirm malignant EAML (12). However, few factors (a high percentage of epithelioid cells, marked atypia and large diameter of the mass) have been associated with EAML malignancy by Jun Lei et al. (16). In his study, four characteristics were found significant in predicting malignant EAML behaviour: tumour size >9 cm, tumour thrombus formation in the vein, epithelioid cells >70% or atypia cells >60%, and necrosis. (16) In a case by Amine Bani et al. necrosis, high mitosis index, marked atypia, vascular involvement, and predominant component of epithelioid cells were associated with malignancy and tumour progression (12). Recent studies by Jun Lei et al. demonstrated the role of HMB45 biomarker in predicting EAML malignancy. All 43 cases in the study presented HMB45-positive. Other markers, such as Ki-67, which were thought to serve as an antigen to indicate EAML malignancy, were proved to be less sensitive compared to HMB45 as only 10 out of 43 cases were Ki-67 positive (16). In our case, the tumour was positive for HMB45 biomarker, as well as SMA. Defects in genes also play a role in the development of epithelioid angiomyolipoma. Malignancy potential might be related to a mutation in p53 gene, as it was described in a few articles (13, 17). A mutation in TSC1 and TSC2 genes have been linked to malignant behaviour of epithelioid angiomyolipomas (16). Missense, non-sense, frame-shift, and splice-site mutations among the 41 coding exons are included in the mutation of TSC2 gene (18). Gene deficiencies in chromosome band 16p13 and clonal chromosomal aberrations were reported by Kattar et al. (19). Defining and systematizing specific EAML malignancy criteria and biomarkers is important to determine patient long term prognosis and to appoint right treatment, so further studies are needed.

For patients with EAML, one of the treatment options is chemotherapy, as EAML is considered to be chemosensitive. Reports of response to the treatment with doxorubicin, dacarbazine, ifosfamide and cisplastin have been published (14). Treatment with mTOR inhibitors, such as everolimus was found to be effective, especially in more complicated cases with malignant EAML behavior, recurrent or unresectable cases (16, 20). Although there is a possibility and positive feedback from systemic treatment, because of its malignant nature, surgical treatment remains as a gold standard for EAML. A study by Kun-Han Lee et al. suggests surgery as main treatment for suspicious renal EAML (1).

Partial nephrectomy is also recommended as first choice treatment for small tumours that are located in the peripheral area of the kidney (17). Nephron-sparing surgery is one of the best treatment choice for classing renal angiomyolipomas when surveillance or conservative treatment is contraindicated (21). According to the literature, most cases of renal AML require adjuvant treatment for relapse and progression (22, 23).

Recurrences of EAML after partial nephrectomy are also possible and have to be taken into consideration, as radical nephrectomy or systemic treatment might be required (24). In the case above, a recurrence of EAML of the kidney was found three years after partial nephrectomy. In our case, partial nephrectomy was successfully performed for a tumour slightly over 4 cm in size and after the diagnosis of renal EAML the patient was observed instead of using systemic treatment and had yearly follow- up CTs were carried out for up to 6 years as there still was malignancy potential . No progression of the tumour or metastases were observed and no systemic treatment was required. This shows the importance of early diagnosis and treatment of patients with renal EAML, as there is a lack of case reports of this variant of tumour and no guidelines are provided.

## CONCLUSIONS

The usual treatment for renal EAML is radical nephrectomy and the use of systemic treatment in case of advanced disease. Early diagnosis with partial nephrectomy can be performed with yearly follow- up and no systemic treatment is required.

## CONFLICT OF INTEREST

The authors declare that there is no conflict of interest regarding the publication of this article.

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## INKSTO REZEKCIJA GALI BŪTI SĖKMINGAS INKSTO EPITELIOIDINĖS ANGIOMIOLIPOMOS GYDYMO BŪDAS: ATVEJO PRISTATYMAS IR LITERATŪROS APŽVALGA

*Santrauka*

**Apžvalga.** Inkstų epitelioidinė angiomiolipoma yra retas navikas, dažniausiai nustatomas inkstuose. Tai itin agresyvus darinys. Remiantis literatūros apžvalgomis, daugeliu atvejų buvo rekomenduojamas radikalus gydymas ir sisteminė terapija. Pristatome klinikinį atvejį, kai inksto rezekcija buvo sėkminga gydymo taktika inkstų epitelioidinės angiomiolipomos atveju.

**Klinikinis atvejis.** Keturiasdešimties metų vyrui 2012 m., atliekant ultragarsinį tyrimą, atsitiktinai nustatytas 40 × 41 mm dydžio cistinis kairiojo inksto darinys, vėliau patvirtintas MRT. Įtarus inksto vėžį buvo numatyta operacija. Kairiojo inksto rezekcija buvo atlikta sėkmingai. Galutinė patologijos išvada patvirtino inkstų epitelioidinę angiomiolipomą. Pacientas kasmet stebėtas atliekant kompiuterinę tomografiją, po 6 metų naviko progresavimo nepastebėta.

**Išvados.** Nors inkstų epitelioidinė angiomiolipoma yra labai reta ir itin piktybinė, ankstyva diagnostika yra labai svarbi gydymo sėkmei. Epitelioidinės angimiolipomos atveju gali būti atliekama inksto rezekcija.

**Raktažodžiai:** epitelioidinė amgiomiolipoma, magnetinio rezonanso tomografija, inksto rezekcija, sisteminis gydymas