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ЕЖЕМЕСЯЧНЫЙ НАУЧНЫЙ ЖУРНАЛ

Медицинские новости Грузии

საქართველოს სამედიცინო სიახლენი

GEORGIAN MEDICAL NEWS

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GMN: Georgian Medical News is peer-reviewed, published monthly journal committed to promoting the science and art of medicine and the betterment of public health, published by the GMN Editorial Board since 1994. GMN carries original scientific articles on medicine, biology and pharmacy, which are of experimental, theoretical and practical character; publishes original research, reviews, commentaries, editorials, essays, medical news, and correspondence in English and Russian.

GMN is indexed in MEDLINE, SCOPUS, PubMed and VINITI Russian Academy of Sciences. The full text content is available through EBSCO databases.

GMN: Медицинские новости Грузии - ежемесячный рецензируемый научный журнал, издаётся Редакционной коллегией с 1994 года на русском и английском языках в целях поддержки медицинской науки и улучшения здравоохранения. В журнале публикуются оригинальные научные статьи в области медицины, биологии и фармации, статьи обзорного характера, научные сообщения, новости медицины и здравоохранения. Журнал индексируется в MEDLINE, отражён в базе данных SCOPUS, PubMed и ВИНИТИ РАН. Полнотекстовые статьи журнала доступны через БД EBSCO.

GMN: Georgian Medical News – საქართველოს სამედიცინო სიახლენი – არის ყოველთვიური სამეცნიერო სამედიცინო რეცენზირებადი ჟურნალი, გამოიცემა 1994 წლიდან, წარმოადგენს სარედაქციო კოლეგიისა და აშშ-ის მეცნიერების, განათლების, ინდუსტრიის, ხელოვნებისა და ბუნებისმეტყველების საერთაშორისო აკადემიის ერთობლივ გამოცემას. GMN-ში რუსულ და ინგლისურ ენებზე ქვეყნდება ექსპერიმენტული, თეორიული და პრაქტიკული ხასიათის ორიგინალური სამეცნიერო სტატიები მედიცინის, ბიოლოგიისა და ფარმაციის სფეროში, მიმოხილვითი ხასიათის სტატიები.

ჟურნალი ინდექსირებულია MEDLINE-ის საერთაშორისო სისტემაში, ასახულია SCOPUS-ის, PubMed-ის და ВИНИТИ РАН-ის მონაცემთა ბაზებში. სტატიების სრული ტექსტი ხელმისაწვდომია EBSCO-ს მონაცემთა ბაზებიდან.

WEBSITE

www.geomednews.com

К СВЕДЕНИЮ АВТОРОВ!

При направлении статьи в редакцию необходимо соблюдать следующие правила:

1. Статья должна быть представлена в двух экземплярах, на русском или английском языках, напечатанная через **полтора интервала на одной стороне стандартного листа с шириной левого поля в три сантиметра**. Используемый компьютерный шрифт для текста на русском и английском языках - **Times New Roman** (**Кириллица**), для текста на грузинском языке следует использовать **AcadNusx.** Размер шрифта - **12**. К рукописи, напечатанной на компьютере, должен быть приложен CD со статьей.

2. Размер статьи должен быть не менее десяти и не более двадцати страниц машинописи, включая указатель литературы и резюме на английском, русском и грузинском языках.

3. В статье должны быть освещены актуальность данного материала, методы и результаты исследования и их обсуждение.

При представлении в печать научных экспериментальных работ авторы должны указывать вид и количество экспериментальных животных, применявшиеся методы обезболивания и усыпления (в ходе острых опытов).

4. К статье должны быть приложены краткое (на полстраницы) резюме на английском, русском и грузинском языках (включающее следующие разделы: цель исследования, материал и методы, результаты и заключение) и список ключевых слов (key words).

5. Таблицы необходимо представлять в печатной форме. Фотокопии не принимаются. **Все цифровые, итоговые и процентные данные в таблицах должны соответствовать таковым в тексте статьи**. Таблицы и графики должны быть озаглавлены.

6. Фотографии должны быть контрастными, фотокопии с рентгенограмм - в позитивном изображении. Рисунки, чертежи и диаграммы следует озаглавить, пронумеровать и вставить в соответствующее место текста **в tiff формате**.

В подписях к микрофотографиям следует указывать степень увеличения через окуляр или объектив и метод окраски или импрегнации срезов.

7. Фамилии отечественных авторов приводятся в оригинальной транскрипции.

8. При оформлении и направлении статей в журнал МНГ просим авторов соблюдать правила, изложенные в «Единых требованиях к рукописям, представляемым в биомедицинские журналы», принятых Международным комитетом редакторов медицинских журналов - http://www.spinesurgery.ru/files/publish.pdf и http://www.nlm.nih.gov/bsd/uniform_requirements.html
В конце каждой оригинальной статьи приводится библиографический список. В список литературы включаются все материалы, на которые имеются ссылки в тексте. Список составляется в алфавитном порядке и нумеруется. Литературный источник приводится на языке оригинала. В списке литературы сначала приводятся работы, написанные знаками грузинского алфавита, затем кириллицей и латиницей. Ссылки на цитируемые работы в тексте статьи даются в квадратных скобках в виде номера, соответствующего номеру данной работы в списке литературы. Большинство цитированных источников должны быть за последние 5-7 лет.

9. Для получения права на публикацию статья должна иметь от руководителя работы или учреждения визу и сопроводительное отношение, написанные или напечатанные на бланке и заверенные подписью и печатью.

10. В конце статьи должны быть подписи всех авторов, полностью приведены их фамилии, имена и отчества, указаны служебный и домашний номера телефонов и адреса или иные координаты. Количество авторов (соавторов) не должно превышать пяти человек.

11. Редакция оставляет за собой право сокращать и исправлять статьи. Корректура авторам не высылается, вся работа и сверка проводится по авторскому оригиналу.

12. Недопустимо направление в редакцию работ, представленных к печати в иных издательствах или опубликованных в других изданиях.

При нарушении указанных правил статьи не рассматриваются.

REQUIREMENTS

Please note, materials submitted to the Editorial Office Staff are supposed to meet the following requirements:

1. Articles must be provided with a double copy, in English or Russian languages and typed or compu-ter-printed on a single side of standard typing paper, with the left margin of **3** centimeters width, and **1.5** spacing between the lines, typeface - **Times New Roman** (**Cyrillic**), print size - **12** (referring to Georgian and Russian materials). With computer-printed texts please enclose a CD carrying the same file titled with Latin symbols.

2. Size of the article, including index and resume in English, Russian and Georgian languages must be at least 10 pages and not exceed the limit of 20 pages of typed or computer-printed text.

3. Submitted material must include a coverage of a topical subject, research methods, results, and review.

Authors of the scientific-research works must indicate the number of experimental biological species drawn in, list the employed methods of anesthetization and soporific means used during acute tests.

4. Articles must have a short (half page) abstract in English, Russian and Georgian (including the following sections: aim of study, material and methods, results and conclusions) and a list of key words.

5. Tables must be presented in an original typed or computer-printed form, instead of a photocopied version. **Numbers, totals, percentile data on the tables must coincide with those in the texts of the articles.** Tables and graphs must be headed.

6. Photographs are required to be contrasted and must be submitted with doubles. Please number each photograph with a pencil on its back, indicate author's name, title of the article (short version), and mark out its top and bottom parts. Drawings must be accurate, drafts and diagrams drawn in Indian ink (or black ink). Photocopies of the X-ray photographs must be presented in a positive image in **tiff format**.

Accurately numbered subtitles for each illustration must be listed on a separate sheet of paper. In the subtitles for the microphotographs please indicate the ocular and objective lens magnification power, method of coloring or impregnation of the microscopic sections (preparations).

7. Please indicate last names, first and middle initials of the native authors, present names and initials of the foreign authors in the transcription of the original language, enclose in parenthesis corresponding number under which the author is listed in the reference materials.

8. Please follow guidance offered to authors by The International Committee of Medical Journal Editors guidance in its Uniform Requirements for Manuscripts Submitted to Biomedical Journals publication available online at: http://www.nlm.nih.gov/bsd/uniform_requirements.html
http://www.icmje.org/urm_full.pdf
In GMN style for each work cited in the text, a bibliographic reference is given, and this is located at the end of the article under the title "References". All references cited in the text must be listed. The list of references should be arranged alphabetically and then numbered. References are numbered in the text [numbers in square brackets] and in the reference list and numbers are repeated throughout the text as needed. The bibliographic description is given in the language of publication (citations in Georgian script are followed by Cyrillic and Latin).

9. To obtain the rights of publication articles must be accompanied by a visa from the project instructor or the establishment, where the work has been performed, and a reference letter, both written or typed on a special signed form, certified by a stamp or a seal.

10. Articles must be signed by all of the authors at the end, and they must be provided with a list of full names, office and home phone numbers and addresses or other non-office locations where the authors could be reached. The number of the authors (co-authors) must not exceed the limit of 5 people.

11. Editorial Staff reserves the rights to cut down in size and correct the articles. Proof-sheets are not sent out to the authors. The entire editorial and collation work is performed according to the author's original text.

12. Sending in the works that have already been assigned to the press by other Editorial Staffs or have been printed by other publishers is not permissible.

Articles that Fail to Meet the Aforementioned Requirements are not Assigned to be Reviewed.

ავტორთა საყურადღებოდ!

რედაქციაში სტატიის წარმოდგენისას საჭიროა დავიცვათ შემდეგი წესები:

1. სტატია უნდა წარმოადგინოთ 2 ცალად, რუსულ ან ინგლისურ ენებზე,დაბეჭდილი სტანდარტული ფურცლის 1 გვერდზე, 3 სმ სიგანის მარცხენა ველისა და სტრიქონებს შორის 1,5 ინტერვალის დაცვით. გამოყენებული კომპიუტერული შრიფტი რუსულ და ინგლისურენოვან ტექსტებში - **Times New Roman (Кириллица)**, ხოლო ქართულენოვან ტექსტში საჭიროა გამოვიყენოთ **AcadNusx.** შრიფტის ზომა – 12. სტატიას თან უნდა ახლდეს CD სტატიით.

2. სტატიის მოცულობა არ უნდა შეადგენდეს 10 გვერდზე ნაკლებს და 20 გვერდზე მეტს ლიტერატურის სიის და რეზიუმეების (ინგლისურ, რუსულ და ქართულ ენებზე) ჩათვლით.

3. სტატიაში საჭიროა გაშუქდეს: საკითხის აქტუალობა; კვლევის მიზანი; საკვლევი მასალა და გამოყენებული მეთოდები; მიღებული შედეგები და მათი განსჯა. ექსპერიმენტული ხასიათის სტატიების წარმოდგენისას ავტორებმა უნდა მიუთითონ საექსპერიმენტო ცხოველების სახეობა და რაოდენობა; გაუტკივარებისა და დაძინების მეთოდები (მწვავე ცდების პირობებში).

4. სტატიას თან უნდა ახლდეს რეზიუმე ინგლისურ, რუსულ და ქართულ ენებზე არანაკლებ ნახევარი გვერდის მოცულობისა (სათაურის, ავტორების, დაწესებულების მითითებით და უნდა შეიცავდეს შემდეგ განყოფილებებს: მიზანი, მასალა და მეთოდები, შედეგები და დასკვნები; ტექსტუალური ნაწილი არ უნდა იყოს 15 სტრიქონზე ნაკლები) და საკვანძო სიტყვების ჩამონათვალი (key words).

5. ცხრილები საჭიროა წარმოადგინოთ ნაბეჭდი სახით. ყველა ციფრული, შემაჯამებელი და პროცენტული მონაცემები უნდა შეესაბამებოდეს ტექსტში მოყვანილს.

6. ფოტოსურათები უნდა იყოს კონტრასტული; სურათები, ნახაზები, დიაგრამები - დასათაურებული, დანომრილი და სათანადო ადგილას ჩასმული. რენტგენოგრამების ფოტოასლები წარმოადგინეთ პოზიტიური გამოსახულებით **tiff** ფორმატში. მიკროფოტოსურათების წარწერებში საჭიროა მიუთითოთ ოკულარის ან ობიექტივის საშუალებით გადიდების ხარისხი, ანათალების შეღებვის ან იმპრეგნაციის მეთოდი და აღნიშნოთ სურათის ზედა და ქვედა ნაწილები.

7. სამამულო ავტორების გვარები სტატიაში აღინიშნება ინიციალების თანდართვით, უცხოურისა – უცხოური ტრანსკრიპციით.

8. სტატიას თან უნდა ახლდეს ავტორის მიერ გამოყენებული სამამულო და უცხოური შრომების ბიბლიოგრაფიული სია (ბოლო 5-8 წლის სიღრმით). ანბანური წყობით წარმოდგენილ ბიბლიოგრაფიულ სიაში მიუთითეთ ჯერ სამამულო, შემდეგ უცხოელი ავტორები (გვარი, ინიციალები, სტატიის სათაური, ჟურნალის დასახელება, გამოცემის ადგილი, წელი, ჟურნალის №, პირველი და ბოლო გვერდები). მონოგრაფიის შემთხვევაში მიუთითეთ გამოცემის წელი, ადგილი და გვერდების საერთო რაოდენობა. ტექსტში კვადრატულ ფჩხილებში უნდა მიუთითოთ ავტორის შესაბამისი N ლიტერატურის სიის მიხედვით. მიზანშეწონილია, რომ ციტირებული წყაროების უმეტესი ნაწილი იყოს 5-6 წლის სიღრმის.

9. სტატიას თან უნდა ახლდეს: ა) დაწესებულების ან სამეცნიერო ხელმძღვანელის წარდგინება, დამოწმებული ხელმოწერითა და ბეჭდით; ბ) დარგის სპეციალისტის დამოწმებული რეცენზია, რომელშიც მითითებული იქნება საკითხის აქტუალობა, მასალის საკმაობა, მეთოდის სანდოობა, შედეგების სამეცნიერო-პრაქტიკული მნიშვნელობა.

10. სტატიის ბოლოს საჭიროა ყველა ავტორის ხელმოწერა, რომელთა რაოდენობა არ უნდა აღემატებოდეს 5-ს.

11. რედაქცია იტოვებს უფლებას შეასწოროს სტატია. ტექსტზე მუშაობა და შეჯერება ხდება საავტორო ორიგინალის მიხედვით.

12. დაუშვებელია რედაქციაში ისეთი სტატიის წარდგენა, რომელიც დასაბეჭდად წარდგენილი იყო სხვა რედაქციაში ან გამოქვეყნებული იყო სხვა გამოცემებში.

აღნიშნული წესების დარღვევის შემთხვევაში სტატიები არ განიხილება.

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RETROPERITONEAL PERIVASCULAR EPITHELIOID CELL NEOPLASM (PECOMA) RESPONSE TO MTOR KINASE INHIBITION. A CASE REPORT WITH LITERATURE REVIEW

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Abstract.

Perivascular epithelioid cell tumors (PEComas) are a very rare group of neoplasms and were first reported in 1996. These tumors represent a family of mesenchymal neoplasms, related through activation of the mammalian target of rapamycin (mTOR) inhibitor signaling pathway. The objective of this case report is to demonstrate significant regression of the tumor after neoadjuvant treatment with an oral mTOR inhibitor, following surgical removal of the mass to avoid a multiorgan resection. We present a case of a 27-year-old female with retroperitoneal PEComa and evaluated the tumor with MRI and integrated ^{18}F-FDG-PET/CT scans at presentation and serially during treatment with everolimus. After 6 months of treatment with everolimus the tumor showed a substantial size reduction. Therefore, a multiorgan resection could be omitted. The patient has not demonstrated any disease recurrence after nearly 2 years of follow-up. PEComas are tumors with unpredictable behavior. Our report indicates that treatment of PEComas with everolimus may achieve a significant clinical response. As indicated by our case and past reports, mTOR inhibitors may be one of the best treatment options for this disease.

Key words. PEComa, mTOR kinase inhibition, retroperitoneal tumor.

Introduction.

Perivascular epithelioid cell tumors (PEComa) are a rare type of neoplasms that take origin from mesenchymal tissue. They were first reported in 1996 [1]. Patients with retroperitoneal PEComas generally do not present any discomfort, but sometimes exhibit some non-specific symptoms, such as back pain, and abdominal pain and may sometimes be accidentally found [2-4]. PEComa is defined by the World Health Organization as mesenchymal tumors composed of histologically and immunohistochemically distinctive perivascular epithelioid cells. The PEComa family includes the renal and extrarenal types of angiomyolipoma (AML), the pulmonary and extrapulmonary types of clear-cell "sugar" tumors (CCST), the pulmonary and extrapulmonary types of lymphangioleiomyomatosis (LAM), a clear-cell myomelanocytic tumor of the ligamentum teres/falciform ligament (CCMMT) and the malignant form as the PEComa not otherwise specified (PEComa NOS) [5]. A lymphangioleiomyomatosis and angiomyolipoma are seen at high frequency in patients with tuberous sclerosis complex (TSC), a disorder caused by mutation of TSC1 and/or TSC2 genes [6]. These genes encode the proteins hamartin/tuberin that combines to form a TSC1-TSC2 protein complex. This complex then regulates the mammalian target of rapamycin (mTOR) protein, through the mTORC1 signaling pathway. This is the main regulator of cell proliferation and lymphangiogenesis. The absence of the TSC1-TSC2 protein complex leads to uncontrolled activation of mTOR [7]. Pharmacologic inhibitors of mTOR, such as everolimus and related compounds directly inhibit T-lymphocyte proliferation. Although there is a limited number of previous reports of patients with retroperitoneal or abdominal PEComas described clinical response under mTOR inhibitors, no effective neoadjuvant therapy for retroperitoneal PEComas in large series has been reported yet [8-11]. Here we report a case of retroperitoneal PEComa, who was also treated with everolimus to achieve a major clinical response following surgical removal of the tumor to avoid a multiorgan resection by the young patient. We also review the current literature on the treatment of retroperitoneal PEComa with this class of compounds.

Case presentation.

An otherwise healthy 27 old female was referred to our hospital in the context of unclear left flank pain in January of 2016. A CT and MRI scan showed a well-defined, round, hypodense mass measuring 9.8 x 4.5 x 3.2 cm, originating from the left-sided retroperitoneum, extending superiorly up to splenic hilum with contact to splenic vessels, pancreas body and tail, the left colon flexure and the left kidney with left adrenal gland respectively (Figure 1A). No lymphadenopathy or distant metastases were detected in the primary CT and integrated ^{18}F-FDG-PET/CT scans. A CT-guided biopsy of the tumor indicated PEComa. Due to the young age of the patient and possible side effects of everolimus, it was decided to start with the lowest dose of the medication with 2.5 mg daily PO. Everolimus treatment was well tolerated, with grade 1 stomatitis, which did not require any dose modifications during treatment. Although there was an initial modest decrease in SUV uptake on integrated ^{18}F-FDG-PET/CT scan (SUVmax 4.9 to 4.2) [12], there was no decrease in tumor volume four weeks after therapy started. The interval between integrated ^{18}F-FDG-PET/CT scans were three months. During continuing treatment, a significant reduction in the size of the retroperitoneal mass was seen on day 90 on follow-up scans (Figure 1B) and stable disease on day 180 of therapy. The patient underwent surgery with resection of the mass with partial left nephrectomy, left adrenalectomy, and resection of mesocolon transversum. Histology of the tumor demonstrated the presence of poorly pleomorphic, spindle-shaped medium-sized tumor cells in fascicular orientation. Immunohistochemically, these cells showed staining for smooth muscle actin, desmin, caldesmon, bcl-2, and estrogen and progesterone receptors. S100, MART1, CD34, CD117 CD99, and Pan-cytokeratin staining were negative and only a few cells demonstrated reaction for human melanoma black HMB-45. The Ki-67 associated proliferation index was 1%. Thus, the final diagnosis was retroperitoneal PEComa/Angiomyolipoma without any signs of malignancy. At 20 months of follow-up, the patient had

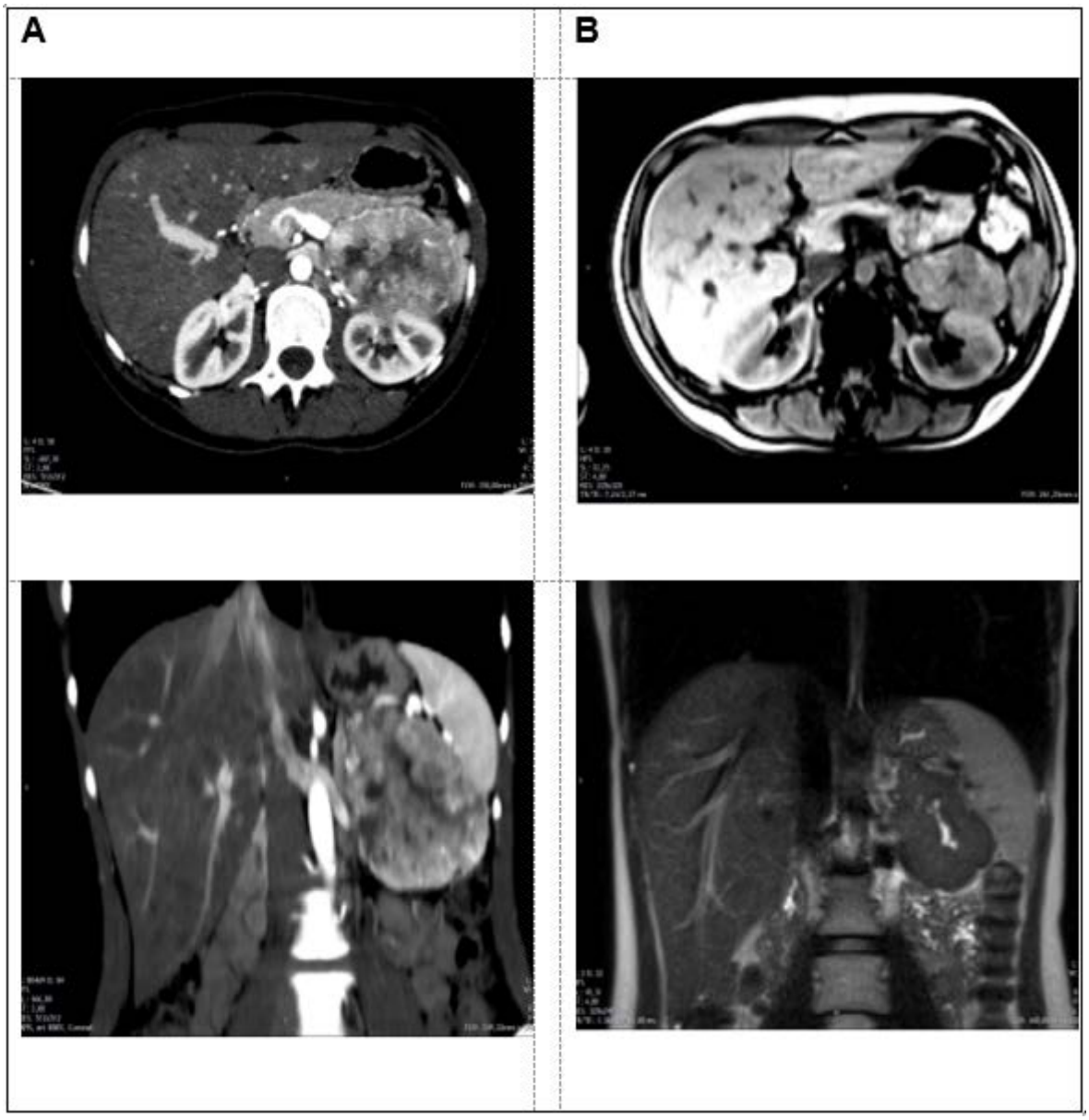

Figure 1. *Contrast-enhanced abdominal CT and MRI images of the patient before (A) and after (B) 3 months of everolimus 2.5 mg/day treatment.*

no evidence of disease. Everolimus was discontinued before surgery and has not been restarted since then. Our patient is scheduled for clinical and radiological follow-up evaluation with contrast-enhanced MRI every 12 months in the first three years and subsequent two years MRI examinations thereafter.

Discussion.

PEComas are a family of neoplasms that show considerable diversity in an organ of appearance, histological characteristics, and clinical presentation as well. A group of PEComas demonstrates malignant behavior with recurrences after surgery and the development of metastases. The management of these tumors remains to be not standardized yet. But if possible surgical resection seems to be a treatment of choice for this type of tumor. Furthermore, as activation of the mTOR signaling pathway is usual in these tumors, mTOR inhibitors – everolimus and similar compounds have been successfully applied as medical treatment. We have detected only nine reports of treatment of the retroperitoneal PEComas with mTOR inhibitors with a total amount of 12 cases in the PubMed database. In the case series mTOR kinase inhibitor was reported to be effective, especially in the therapy of unresectable tumors and cases with distant metastases [8]. Because the number of reported cases is limited (Table 1), there are no solid criteria for diagnosis and therapy of benign or malignant PEComas. According to Folp et al. criteria, the tumor in our patient with a size of >5cm along with further risk factors such as suspicious infiltrative growth shape was considered before surgery as „PEComa with uncertain malignant potential“ [5]. Based on the fact that PEComas share the activation of mTOR signaling pathway, we treated our patient with everolimus – an mTOR kinase inhibitor, in the hope to reduce tumor size to avoid a multiorgan resection in the young patient. We have observed a significant volume reduction of the tumor during of first three months and stable disease for further three months after therapy begin. After resection, our case is considered to be benign.

Table 1. *Review of published retroperitoneal PEComa treated with mTOR inhibitors.*

Case Nr.	Sex	Age	Tumor type	Size in cm	mTOR inhibitor	Dose	Duration	Response according RECIST v-1.1	Other drugs combined with mTOR inhibitor	TSC1/2 mutation	Side effects of therapy	Autor, publish year
1.	m	65	PEComa	20	sirolimus	8 mg daily	16 months	CR	none	TSC2	mild fatigue	Wagner et al. [8]
2.	f	58	Metastatic PEComa	17	temsirolimus	10 mg IV weekly	2 cycles (8 weeks	progression	topotecan, bortezomib	n/a	n/a	Wagner et al. [8]
3.	n/a	n/a	metastatic PEComa	n/a	everolimus	10 mg daily	2 cycles (8 weeks)	progression	figitumumab	n/a	n/a	Quek et al. [14]
4.	f	63	recurrent and metastatic PEComa/ AML	n/a	everolimus	10 mg daily	10 months	CR of Mts and PR of recurrent tumor	none	n/a	stomatitis grad I and acneiform rash grad I	Gennatas et al. [9]
5.	f	40	PEComa	6	sirolimus	3 mg daily	> 16 months	CR	none	TSC2	diarrhea, chylous ascites	Dickson et al. [10]
6.	f	24	PEComa	25	sirolimus	4 mg daily	>22 months	CR	none	TSC2	chylous ascites	Dickson et al. [10]
7.	f	51	metastatic PEComa	20	temsirolimus	15 mg weekly	5 months	progression	none	n/a	n/a	Nakanishi et al. [15]
8.	n/a	n/a	metastatic PEComa	n/a	sirolimus	3 mg daily	0.25 months	n/a	none	n/a	n/a	Benson et al. [16]
9.	n/a	n/a	metastatic PEComa	n/a	sirolimus	3 mg daily	2 months	progression	none	n/a	n/a	Benson et al. [16]
10.	f*	26	PEComa/ LAM	8	sirolimus	2 mg daily	12 months	PR	none	n/a	acneiform rash grad I and hypercholesterolemia	Freitas et al. [17]
11.	f*	37	PEComa/ LAM	18	sirolimus	2 mg/ daily	6 months	PR	none	n/a	acneiform rash grad I and hypercholesterolemia	Freitas et al. [17]
12	f	42	recurrent and metastatic PEComa/ LAM	9	everolimus	10 mg/ daily	9 months	PR	none	n/a	acneiform rash grad I	Cihan et al. [18]
13.	f	27	PEComa/ AML	9.8	everolimus	2.5 mg/ daily	6 months	PR	none	n/a	stomatitis grad I	Case described in this report

AML = angiomyolipoma; f = female; LAM = lymphangioleiomyomatosis; m = male; mTOR= mammalian target of rapamycin; CR= complete response; PR = partial response; n/a = not available; Mts = metastasis.
**Freitas et al. personal communication.*

Table 1 provides a compilation of all published reports of retroperitoneal PEComa patients treated with mTOR inhibitors, including our patient. Most patients were female (69%). The median age was 43.3 years (range 24 - 65). Most patients (53.8%) had metastatic PEComa. The median tumor size was 14.7 cm (range 6 – 25 cm). The TSC2 mutation could be identified in three patients. Seven patients received sirolimus with the median dose of 3.5 mg daily, four received everolimus with the median dose of 8 mg daily, and two received temsirolimus with the median dose of 12.5 mg weekly. The median duration of treatment was 9.1 months. Treatment toxicities under mTOR inhibition were generally harmless and manageable. Of 13 patients, four (30.7%) presented acneiform rash grad I, two (15.3%) presented stomatitis grad I, two (15.3%) presented chylous ascites and one (7.6%) showed mild fatigue. In five patients no exact data about treatment safety and toxicity could be extracted from the reported cases. No treatment-related deaths were reported.

Given the response characteristics of this tumor group the RECIST v-1.1 criteria were used to assess the effects of sirolimus in our patient and is the most used system in oncology for response analysis. RECIST v-1.1 criteria describes standard approach to solid tumor measurement and definitions for objective assessment of change in tumor size [13]. Overall, three (23%) Patients had a complete response, four (30%) had a partial response, and four (30%) showed progressive disease by the RECIST v-1.1 criteria. One patient had a complete response of metastasis and a partial response of recurrent tumor but showed a new recurrent tumor located retroperitoneally 10 months after the therapy begin and was treated surgically. In one case described by Benson et al. no data regarding the therapy response of PEComa tumor under sirolimus could be retracted from the reported data.

Altogether these reports support the use of mTOR inhibitors in the treatment of retroperitoneal PEComa. The treatment is in most cases without any serious side effects and if necessary,

the dosage can be easily managed by orally administered drugs such as sirolimus and everolimus. Sirolimus, everolimus, and temsirolimus are similar compounds, however, two of two patients (100%) treated with temsirolimus, one of four patients (25%) treated with everolimus, and one of seven patients (14.2%) treated with sirolimus showed tumor progress. Which treatment options should be contemplated if PEComa shows size progression under mTOR inhibitions remains to be not clear. During the follow-up of 20 months our patient had no evidence of disease relapse on MRI scans. In the case of tumor relapse, we would perform repeat operation to achieve margin negative resection.

Despite the extreme rarity of these types of tumors further research is required to manage the optional dose and duration of therapy and to document long-term benefits.

Consent.

Written informed consent was obtained from the patient for publication of this case report and accompanying images. A copy of the written consent is available for review by the first author of this article.

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