Pathology - Research and Practice 215 (2019) 152359

Contents lists available at ScienceDirect

Pathology - Research and Practice

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

Case report

Intravascular (post-hysterectomy) leiomyoma (IVL) as late tumor thrombus within the inferior vena cava (IVC)—A rare case primarily imposing as IVC thrombus originating from left renal vein after former left nephrectomy status

M. Ghanem[a], F. Meyer[a], D. Jechorek[b], V. Schoeder[b], A. Ignatov[c], M. Fadel[d], Z. Halloul[a,*]

[a] Division of Vascular Surgery, Dept. of General, Abdominal, Vascular and Transplant Surgery, University Hospital, Otto-von-Guericke University at Magdeburg, Germany
[b] Institute of Pathology, University Hospital, Otto-von-Guericke University at Magdeburg, Germany
[c] Dept. of Gynecology and Obstetrics, University Hospital, Otto-von-Guericke University at Magdeburg, Germany
[d] Dept. of Cardiothoracic Surgery, University Hospital, Otto-von-Guericke University at Magdeburg, Germany

ARTICLE INFO

Keywords:
Tumor thrombus
Intravascular
Endocaval
Leiomyoma
Post hysterectomy
Interdisciplinary approach
Laparotomy
Sternotomy
Heart-Lung machine

ABSTRACT

Introduction: Intravascular leiomyoma is a rare type of myoma. It was firstly described by Birch-Hirschfeld in 1896, however, its intracardiac subtype was firstly reported by Durck in 1907. Most patients are asymptomatic. The tumor invades mostly the tributaries of the inferior vena cava (IVC) with upward extension that may approach the intracardiac space.

Aim: By means of a scientific case report, a patient with the very rare diagnosis of an endocaval leiomyoma thrombus post-hysterectomy is described based on the clinical experiences obtained in the specific case management and selective references from the literature.

Case presentation: A 48-years old female was diagnosed with intravascular tumor growth within the IVC with intracardiac extension using chest and abdominal CT scan, ECG and echocardiography which was approached by an interdisciplinary (vascular and cardiothoracic) surgical intervention (278 min) including heart-lung machine (99 min) with favorable postoperative result (R0 resection status with mid-term outcome, no recurrent tumor growth). Histopathological investigation diagnosed leiomyoma origin already from ovarian vein most likely in context to the former hysterectomy (3 years ago).

Discussion and conclusion: Intravascular leiomyoma is a benign tumor with invasive tendency, which can be considered a diagnostic and therapeutic challenge. It should be thoroughly investigated to be planned for a radical surgical removal. By possible adherence to the intraabdominal or -thoracic organs, an interdisciplinary and eventually step-wise surgical approach (combining vascular, abdominal, thoracic and heart surgery as well as gynecology and urology), which can be demanding, is recommended to be seriously considered to i) reliably achieve R0 resection status and, thus, ii) provide best outcome, quality of life and prognosis.

1. Introduction

Endocaval leiomyoma is one of the rare intravascular tumor manifestations [1–8], which arises primarily from the uterus, embolises into parauterine tributaries of the inferior vena cava (IVC) and can further grow endoluminally up to the right atrium with subsequent blockade of the tricuspid heart valve. Jing Du et al. [1] have reported in their study from October 2010 that most patients are asymptomatic with histopathologically detectable expression of the tumor lesion in the small vessels inside the uterine wall and further intravascular extensions. Three of the cases included in their study showed that the relatively small beginning of tumor growth consists of 0.5- to 1-cm worm-like strands of neoplastic smooth muscle cells, which are found to be extending into the nearby veins at the margin of the uterine mass. Fuat et al. [2] stated in their study from 2014 that the first documented case of the intravascular leiomyoma (IVL) was published by Birch-Hirschfeld in 1896, and the first presented case of intracardiac extension of IVL was described by Durck in 1907. Topcuoglu et al. [3] asserted in a

* Corresponding author at: Division of Vascular Surgery, Dept. of General, Abdominal, Vascular and Transplant Surgery, Otto-von-Guericke University with University Hospital, Leipziger Str. 44, 39120 Magdeburg, Germany.
E-mail address: zuhir.halloul@med.ovgu.de (Z. Halloul).

https://doi.org/10.1016/j.prp.2019.02.009
Received 26 September 2018; Received in revised form 28 January 2019; Accepted 26 February 2019

dissertation from 2004 that overall, at least 34 cases have been reported involving the right ventricle.

The aim was to describe - by means of a scientific case report - a patient with the very rare diagnosis of an endocaval leiomyoma thrombus post hysterectomy based on

(i) The clinical experiences obtained in the specific case management, and
(ii) Selective references from the literature.

2. Case presentation

2.1. Medical history and clinical examination

A 48-years old female patient introduced herself in the interdisciplinary emergency room (ER) with accidentally discovered intravascular tumor(-like) growth within the IVC by abdominal Angio CT scan (characterized by 3-mm sagittal and 1-mm coronary scans) which was primarily interpreted as suspicious for a tumor thrombus expanding from the left renal vein up to the right atrium. The medical history was significant for a left nephrectomy because of a renal cell carcinoma in 2006 as well as hysterectomy (not including ovarians) because of uterine leiomyoma in 2014. In addition, the patient had a renal dysfunction characterized by a GFR of 72 ml/min and creatinine of 83 µmol/l. The patient was under periodic routine oncological follow-up controls using CT scan. Symptomatology has been characterized by recurrent sporadic symptoms such as dizziness, impaired vision, increased heart rate, leg swelling and headache since October 2015. At the time of admission, patient did not report any complaints. Physical examination revealed no abdominal pain, no tenderness, no resistance and no muscular guarding.

2.2. Further aspects – diagnostic findings, therapeutic management and clinical course

2.2.1. CT scan (Abdominal Angio CT scan with contrast media, with stratification of 3-mm coronary and 1-mm sagittal-scans)

Suspected tumor thrombus was confirmed by the institutional radiologists. However, it was primarily questionable whether the thrombus originated from the left renal vein as a consequence of post-nephrectomy status (left panel). Interestingly, as additional findings there was a retro-aortic course of the left renal vein, and an intravascular tumor growth crosses the tricuspid valve and ends in the right ventricle without complete blockade of the valve (Figs. 1 and 2).

2.2.2. Echocardiography

An intracardiac tumor growth was also seen echocardiografically, with 2 parts: an apical part measuring 2.1 × 2.4 cm with expansion into the right ventricle through tricuspid valve without relevant reflux, and a basal part, with contact to IVC measuring 2.5 × 3.2 cm.

Further investigations were 24-h electrocardiogram and heart catheterization (not shown).

2.3. Peri- and intraoperative details

Decision-making resulted in the indication for surgical intervention using an interdisciplinary approach by vascular and cardiothoracic surgery. First, cardiac surgeon performed sternotomy with sequential cannulation of the distal part of IVC, superior vena cava (SVC) and aortic arch, then connecting the heart/lung machine. After laparotomy had been done, renal and hepatic veins as well as the inferior vena cava were dissected. The endocaval tumor was tried to be excised from the primarily suspected origin within the left renal vein including excision of its mouth into the IVC. The tumor was partially attached to the endothelium of the inferior vena cava, therefore, the endoluminal tumor lesion was cut out at the tumor adherences to the vascular wall – then, the tumor could be pulled out of the lumen of the IVC. It turned out that growth of tumor thrombus included also the left ovarian vein; therefore, this vein was also excised finally achieving R0 status, the excision included preventively the left ovary. IVC was sutured at the opening site near the mouth of former left renal vein using Prolene 4/0 prolene suture. The closure of the retroperitoneum, abdominal cavity as well as the sternotomy was achieved in the typical manner (Figs. 3 and 4).

A specimen of extirpated tumor-thrombus as well as parts of the inferior vena cava, renal vein as well as left ovarian vein with attached ovary were sent to the Histo-Lab.

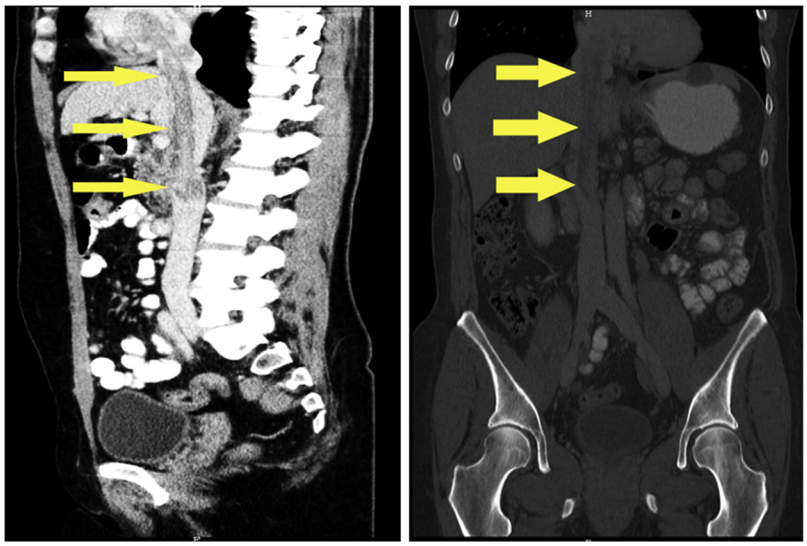
The surgical intervention lasted for 278 min, the use of heart/lung machine took long of 99 min.

The patient was monitored and further treated postoperatively on the surgical intensive care unit.

2.4. Pathological investigation

2.4.1. Gross pathology

Tumor specimen (thrombus, IVL) reached a total length of 250 mm consisting of a tumor-filled vessel wall part of 130 mm length and



Figs. 1 and 2. Abdominal Angio CT scan: Left panel: Sagittal 3-mm scan revealing IVC tumor thrombus extending from the juxtrarenal part with projecting intracardiac part within the right atrium and into the right ventricle through the tricuspid valve (yellow arrows); Right panel: 1-mm coronary scan.

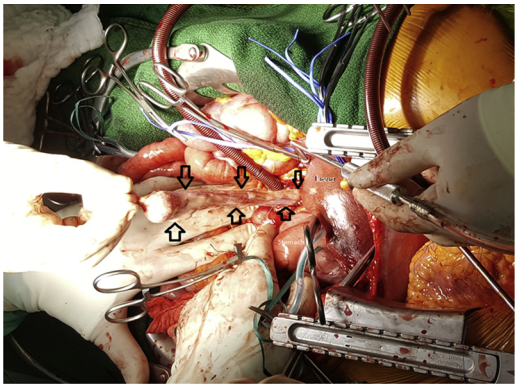


Fig. 3. Photo documentation of intraoperative situs: IVL (its course is marked with open black arrows) was longitudinally incised for extraction of tumor thrombus (intravascular leiomyoma) from IVC.

Fig. 4. Tumor specimen (thrombus, IVL) extending approximately 25 cm after extraction from ICV.

12 mm diameter and an uncovered nodular tumor part of 120 mm length and 25 mm thickness with smooth and shiny surface (Fig. 5A). Additionally, there was tumor containing fat and muscle tissue of 35 × 35 × 15 mm (Fig. 5B).

2.4.2. Histopathology

Tumor lesion consists of spindle cell proliferations, which were partially adhered to the wall of IVC. The proliferations are characterized by desmin-, vimentin- und partially sm-actin-positive myocytes bundles, forming intersecting fascicles and whirls. A strong expression of the estrogen receptor was detected. There was no expression of CD31, CD34, factor VIII or D2-40 Ki-67 proliferation index was stained positive (MIB1) in 2% of cells. Correspondingly, 3 mitoses per 10 HPF were found. Necrosis or hemorrhage was not seen. The histopathological picture matches a leiomyoma, which had deeply infiltrated the IVC (Fig. 5C–I).

The left ovarian specimen showed no malignancy, otherwise no specific finding.

2.5. Postoperative examination and follow up

Gynecological examination of the patient was performed postoperatively with primary exclusion of further necessary gynecological treatment such as operative intervention. Postoperative course was uneventful. The patient was transferred to a rehabilitation clinic (after discharge from the reporting clinic). There, the patient experienced a lack of normal body activity and irregular bowel movement as a possible adverse effect of analgetics (Palexia®; Tapentadol, Grünenthal GmbH, Aachen, Germany). Therefore, she presented herself after discharge with recurrent lower abdominal pain and a clinical as well as radiological finding suspicious for a subileus, which was treated with laxative therapy. The patient was discharged after relieve of her complaints with good bowel movement again to further postoperative rehabilitation therapy.

3. Discussion

The reported patient represents the very rare case of a late postoperative renal vein occlusion suspicious for tumor thrombus

A first assumed to occur in the long-term run of more than 10 years after nephrectomy because of renal cell carcinoma;
B second – more appropriately interpreted and finally confirmed by histopathological investigation – originating from uterine site after former hysterectomy because of a leiomyoma 3 years ago,

which grew progressively within IVC reaching the right atrium and combined with the non-frequent presence of retro-aortic course of left renal vein.

The aforementioned complaints of the patient with accelerated heart frequency, leg swelling and dizziness could be considered alarming signs of an intra-cardiac lesion that urges an intervention. After admission and suitable investigations, such as chest and abdominal CT scan for imaging, electrocardiography, and echocardiography, the urgent indication for surgical intervention was seen favoring an interdisciplinary approach of vascular and cardiothoracic surgery. Venography, in particular, was not considered to be necessary with the today's quality of 3-phase CT scan.

We speculated on grounds of the intraoperative finding, histopathological investigation details, and gross pathology aspects that the intravascular tumor growth started either as embolization originating from the uterine myoma before/or while hysterectomy, which in turn has grown slowly and unnoticed till developing symptoms and reaching the right atrium, or (as the second postulate) originally from the vessel wall.

Leiomyoma is the most common gynecological tumor in the reproductive age, is of benign nature, and originates from the smooth muscle cells of uterine wall, the etiology of which is still not yet clear but leading risk factors are now well known, such as nulliparity, obesity, and early menarche, with a greater exposure to sex steroids, especially estrogen [9].

The intravenous type is one of the aggressive forms of leiomyoma that shows malignant fashion of intravascular invasion [10]. Grossly, intravenous leiomyomatosis is a coiled or nodular growth with worm-like extensions into the uterine veins in the broad ligament or into other pelvic veins, with expansion through the IVC and in some extent to intracardiac site [6]. Histopathologically, it shows typical features of uterine leiomyoma, or it may show the histological features of its variants, such as cellular, atypical (leiomyoma with bizarre nuclei), epithelioid, myxoid, and lipoleiomyoma [6].

The intracardiac extension occurs in about 10% of cases described and is often clinically undetectable; such presentation is largely confused with a primary cardiac neoplasia or migrant venous thrombus [5]. And it may be primarily misdiagnosed as a primary cardiac tumor or a venous thrombus-in-transit [6].

Imaging studies can be helpful in the consideration of differential diagnosis or determination of the extent of the tumor lesion. Echocardiography, venography, and thoracic and abdominal CT scan, along with newer imaging modalities such as magnetic resonance venography or CT angiography should be performed preoperatively [4].

Complete surgical removal with R-0 status is the therapy of choice for intravenous leiomyomatosis. Mandelbaum et al. described the first successful resection of leiomyoma in the right heart in 1974, which had originated within the IVC just below the right atrium [11]. If the tumor is too extensive, or adherent to the cardiac and vascular structures requiring resection of the abdominopelvic and intrathoracic components,

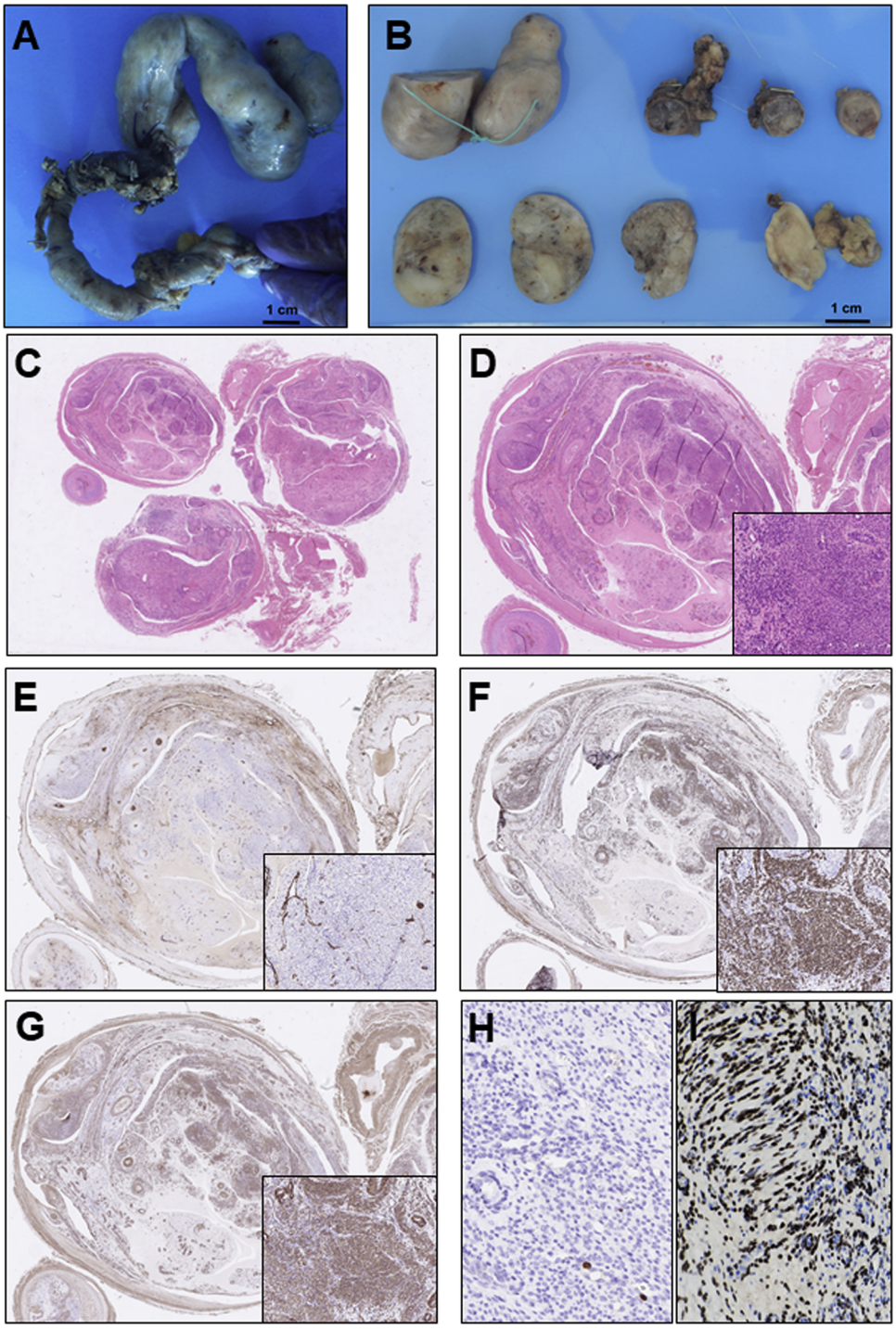


Fig. 5. Macroscopy, histology and immunohistochemistry of the tumor specimen after excision (50×-, 100×-, 400×-magnification).
A) Tumor specimen partially covered by vessel wall.
B) Tumor specimen of the atrium.
C) Cross sections of the vessel wall with intravascular tumor growth.
D) Spindle type tumor cells show a fascicular growth.
E) Negativity for factor VIII excludes a tumor originating from the vessel wall.
F) Desmin- and **G)** sm-actin-expression confirm leiomyoma.
H) Low Ki67-Index; **I)** Strong expression of estrogen receptor.

then, a separate operation may be mandatory. Otherwise, one-stage resection under total circulatory arrest and hypothermia can be used with success [3].

In summary, the presented instructive case reflects impressively the variable manifestations of intravascular / endocaval tumor thrombi as formerly shown in other tumor entities, such as renal cell carcinoma [12–14] and/or carcinoma of pararenal gland [13], besides the further differential diagnosis with leiomyoma of the presented case and the necessity and great prospect of an interdisciplinary diagnostic and therapeutic approach as also described before [13].

4. Conclusion

Intravascular leiomyoma represents a diagnostic and therapeutic challenge. It showed silent progressive growth which acquires application of ordinary and advanced diagnostic imaging to reach the right diagnosis and to exclude possible other differential diagnoses. Anticipating risky patients are female, post hysterectomy with known uterine leiomyoma. Its silent growth, which may reach right atrium manifests itself with some cardiac symptoms, which themselves are not uncommon and can include shortness of breath, and cardiac arrhythmia.

The best modality of therapy is the complete surgical removal as interdisciplinary approach either

- in one set in case of intravascular or intracardiac tumor lesion, which is free of massive adherence to intraabdominal or -thoracic structures, or
- in 2 sets when it is required.

Crucial aim is the R-0 resection status without further intravascular postoperative remnants to provide best prospect for a long-term tumor-free outcome accompanied by periodic follow-up imaging.

Conflict of interest

The authors declare no conflict of interest; the research was achieved independent of any financial support.

References

[1] J. Du, X. Zhao, D. Guo, H. Li, B. Sun, Intravenous leiomyomatosis of the uterus. A clinicopathologic study of 18 cases, with emphasis on early diagnosis and appropriate treatment strategies, Hum. Pathol. 42 (2011) 1240–1246.
[2] F. Demirkiran, V. Sal, U. Kaya, C. Alhan, N. Tokgozoglu, Intravenous leiomyoma with extension to the heart: a case report and review of the literature, Case Rep. Obstet. Gynecol. 2013 (2013) 602407.
[3] M.S. Topcuoglu, H. Yaliniz, H. Poyrazoglu, A. Tokcan, S.C. Demir, A. Bozkurt, et al., Intravenous leiomyomatosis extending into the right ventricle after subtotal hysterectomy, Ann. Thorac. Surg. 78 (2004) 330–332.
[4] M.S. Nam, M.J. Jeon, Y.T. Kim, J.W. Kim, K.H. Park, Y.S. Hong, Pelvic leiomyomatosis with intracaval and intracardiac extension: a case report and review of the literature, Gynecol. Oncol. 89 (2003) 175–180.
[5] L. Oliveira, S. Ramos, Anesthetic approach for a clinical case of intravenous leiomyomatosis: case report, Rev. Bras. Anestesiol. 63 (6) (2013) 504–507.
[6] C. Vural, Ö.Ö zen, B. Demirhan, Intravenous lipoleiomyomatosis of uterus with cardiac extension: a case report, Pathol. Res. Pract. 207 (2011) 131–134.
[7] V. Valdés Devesa, C.R. Conley, W.M. Stone, J.M. Collins, J.F. Magrina, Update on intravenous leiomyomatosis: report of five patients and literature review, Eur. J. Obstetr. Gynecol. Reprod. Biol. 171 (2013) 209–213.
[8] T.D. Clay, J. Dimitriou, O.M. McNally, P.A. Russell, A.E. Newcomb, A.M. Wilson, Intravenous leiomyomatosis with intracardiac extension - a review of diagnosis and management with an illustrative case, Surg. Oncol. 22 (2013) e44ee52.
[9] R.M. Moroni, C.S. Vieira, R.A. Ferriani, R.M. dos Reis, A.A. Nogueira, L.G. Oliveira Brito, Presentation and treatment of uterine leiomyoma in adolescence: a systematic review, BMC Womens Health 15 (2015) 4.
[10] Z.F. Xu, F. Yong, Y.Y. Chen, A.Z. Pan, Uterine intravenous leiomyomatosis with cardiac extension: imaging characteristics and literature review, World J. Clin. Oncol. 4 (1) (2013) 25–28.
[11] I. Mandelbaum, F.J. Pauletto, W.K. Nasser, Resection of a leiomyoma of the inferior vena cava that produced tricuspid valvular obstruction, J. Thorac. Cardiovasc. Surg. 67 (4) (1974) 561–567.
[12] A. Janitzky, F. Meyer, Z. Halloul, M. Porsch, M. Daher, D. Kuester, et al., Successful interdisciplinary treatment of renal cell carcinoma with tumour thrombus into inferior vena cava using multimodal protocol and organ-extending R0 resection in rare horseshoe kidney and doubled right organ, BMJ Case Rep. 2010 (2010) pii: bcr0420091802.
[13] J. Dillner, F. Meyer, H. Lippert, C. Huth, S. Klose, A. Roessner, et al., Organ-invasive carcinoma of the pararenal gland involving the inferior vena cava: successful curative and interdisciplinary surgical management, Dtsch. Med. Wochenschr. 138 (6) (2013) 260–265.
[14] M. Weber, F. Meyer, U.B. Liehr, Z. Halloul, Surgery of inferior vena cava-associated urological tumor lesions, Urologe A 52 (10) (2013) 1438–1446.