Cardiovascular Pathology 39 (2019) 8–11

Contents lists available at ScienceDirect

Cardiovascular Pathology

Clinical Case Report

# Primary angiosarcoma of the femoral artery in patient with kidney and liver polycystosis and multiple arterial aneurysms: report of the case and review of the literature☆

Ondrej Fabian [a,*], Dana Mokra [b], Jan Masopust [b], Jiri Skorepa [c], Daniela Novakova Kodetova [a], Josef Zamecnik [a]

[a] Department of Pathology and Molecular Medicine, 2nd Faculty of Medicine, Charles University and Motol University Hospital, V Uvalu 84, Prague, 5, 150 06, Czech Republic
[b] Department of Internal Medicine, 2nd Faculty of Medicine, Charles University and Motol University Hospital, V Uvalu 84, Prague, 5, 150 06, Czech Republic
[c] 3rd Department of Surgery, 1st Faculty of Medicine, Charles University and Motol University Hospital, V Uvalu 84, Prague, 5, 150 06, Czech Republic

ARTICLE INFO

*Article history:*
Received 6 August 2018
Received in revised form 17 November 2018
Accepted 19 November 2018

*Keywords:*
Angiosarcoma
Femoral artery
Polycystic kidney
Aneurysm

ABSTRACT

The association between kidney and liver polycystosis and arterial aneurysms is well documented. However, it remains unclear whether these patients are at increased risk of malignant transformation. In this article, we describe a case of a primary angiosarcoma of the femoral artery with metastatic spread into the lungs and hilar lymph node arising in a 74-year-old man with kidney and liver polycystosis and multiple arterial aneurysms.


## 1. Introduction

Angiosarcomas are malignant tumors with vascular differentiation, occurring mostly in the skin and subcutaneous tissue [1]. In rare cases, they may develop in preexisting hemangioma or vascular malformation and also as a primary sarcoma of large vessels [2,3]. We describe a case of a primary angiosarcoma of the femoral artery with metastatic spread into the lungs and hilar lymph node arising in a 74-year-old man with kidney and liver polycystosis and multiple arterial aneurysms.

## 2. Case report

A 74-year-old man was admitted to the department of internal medicine with a chief complaint of tender swollen right leg. Medical history revealed longstanding hypertension but was otherwise unremarkable. Both ultrasound and computer tomography (CT) ruled out deep venous thrombosis but showed an extensive, completely thrombosed arterial aneurysm of the right popliteal artery and the distal segment of the right femoral artery. Neither thrombolysis nor bypass was indicated. Magnetic resonance imaging was performed, which revealed a cystic hemorrhagic lesion eroding the adjacent fibula in the middle of the right leg; the lesion was thought most likely to be a venous hemangioma or vascular malformation. As an accidental finding, multiple liver cysts and bilateral multicystic kidney were described. Over the next few days, the pain in the patient's leg aggravated, the cystic lesion enlarged, hemoglobin concentration had fallen, and the patient developed progressive renal and respiratory insufficiency. A CT scan showed extensive bilateral pulmonary hemorrhages. A decision was made to perform an urgent amputation of the right leg. After the operation, the patient's condition quickly deteriorated, with continuous massive bleeding into the pulmonary parenchyma and airways. The patient died of multiorgan failure soon after the operation.

The autopsy showed advanced atherosclerosis with numerous calcified fibroatheromatous plaques affecting mainly the aortic arch, abdominal aorta, bifurcation of common iliac arteries, and coronary arteries. A completely thrombosed fusiform aneurysm was found affecting the distal segment of the right distal femoral and proximal popliteal artery. The aneurysm was found to be 25 cm in length and had a maximum width of 8 cm. Another fusiform aneurysm was discovered affecting the left popliteal artery; it was partially thrombosed with a length of 10 cm. Additional aneurysms of the same type were found in both common iliac arteries as well. On the right coronary artery, a 10-mm saccular aneurysm was detected. In addition to these findings, tubular dilatation of the aortic arch a thoracic aorta was present. The dilated segment measured 15 cm in the length and had a maximum width of 8 cm. The dilatation was not confined to the atherosclerotic segment only but affected also a part of the thoracic aorta with only mild fibrous thickening of the

☆ Conflict of interest: none.

* Corresponding author at: Department of Pathology and Molecular Medicine, Motol University Hospital, V Uvalu 84, Prague 5, 15006, Czech Republic. Tel.: +420 224435645.
*E-mail address:* ondrejfabian5@gmail.com (O. Fabian).

https://doi.org/10.1016/j.carpath.2018.11.001
1054-8807/

intima. Among other gross pathological changes, the enlarged multicystic kidneys stood out. The total weight of the both kidneys was 1400 g, and biggest diameters were 27 and 30 cm, respectively. The size of the cysts ranged from 5 to 15 cm in diameter and contained clear serous fluid. The amount of renal parenchyma was massively reduced by the presence of cysts. The liver contained numerous membranous cysts as well, ranging between 1 and 7 cm in diameter. Both lungs were massively hemorrhagic and edematous. Multiple subpleural nodules were found in both lungs; some of them were white and firm, while some were brown and soft with hemorrhagic rims. The brain showed mild edema, and the arteries of the circle of Willis displayed sporadic atheromatous plaques. No intracranial aneurysms were found.

The amputated distal right leg was part of the autopsy as well. In the mid of the leg, close to the fibula, a large blood-filled cavity was found, with 15 cm in its largest diameter. Adjacent part of the fibular shaft was eroded. Second hemorrhagic cavity was present in the talocrural joint with similar erosion of the trochlea of talus. No macroscopically visible signs of neoplasia were present in either cavity.

Microscopic examination of the right femoropopliteal aneurysm displayed a thick exulcerated fibroatheromatous plaque with adjacent thrombus. Tunica media showed severe degenerative changes with almost complete loss of elastic fibers and fibrosis. However, a neoplasm was found in several places. It consisted of middle-sized oval or spindle-shaped cells with high-grade nuclear atypia and mitotic activity, forming numerous vascular spaces. In some parts, the tumor displayed a solid pattern of growth. Minor areas of the neoplasia contained clear cells. Neoplastic cells were diffusely immunohistochemically positive for CD31 and CD34 antigens. Accordingly, the diagnosis of angiosarcoma was made (Fig. 1A–C). The tumor was primarily intimal but penetrated the arterial wall infiltrating the surrounding soft tissues. Histopathologic examination of the hemorrhagic cavities in the leg did not reveal any neoplastic cells, but the eroded parts of the adjacent bones showed angiosarcoma infiltration. The aforementioned subpleural white nodules were revealed to be metastases of the angiosarcoma, and the brown nodules turned out to be morphologically consistent with *Candida* species mycotic infection. Metastasis was also found in one of the pulmonary hilar lymph nodes. Generalization of the primary angiosarcoma of the femoral artery and extensive pulmonary hemorrhage were therefore considered to be the cause of the death. Histopathology of the kidneys showed numerous thin-walled cysts lined with flat atrophic epithelium accompanied with atrophy of the residual renal parenchyma. The liver cysts were of biliary origin. Severe degenerative changes were found also aside from the femoral and popliteal aneurysms. These changes were especially pronounced in the dilated part of the thoracic aorta and showed marked disorganization of the arterial wall with almost complete loss of elastic fibers, fibrosis, substantial reduction of smooth muscle layer, and diffuse translamellar collections of mucoid substances (Fig. 2). In the lungs, numerous atypical arteries were found (Fig. 3). The arteries were branching, thick-walled, and with intimal fibroplasia, reduced elastic membranes, and mild adventitial fibrosis. An accidental finding of a tiny venous malformation in one from the hilar lymph nodes was also noted.

## 3. Discussion

We presented a case of the patient with primary angiosarcoma of the femoral artery with metastatic spread into the lungs and pulmonary lymph node arising in the terrain of multiple arterial aneurysms and polycystic kidney and liver disease. This case is unique from several reasons. It represents an unusual type of the malignant tumor exhibiting very rare localization with untypical clinical presentation. Also, the combination of kidney and liver polycystosis together with multiple arterial aneurysms of various types is rather rare. To the best of our knowledge, a case of angiosarcoma in this specific clinical setting has not been described before.

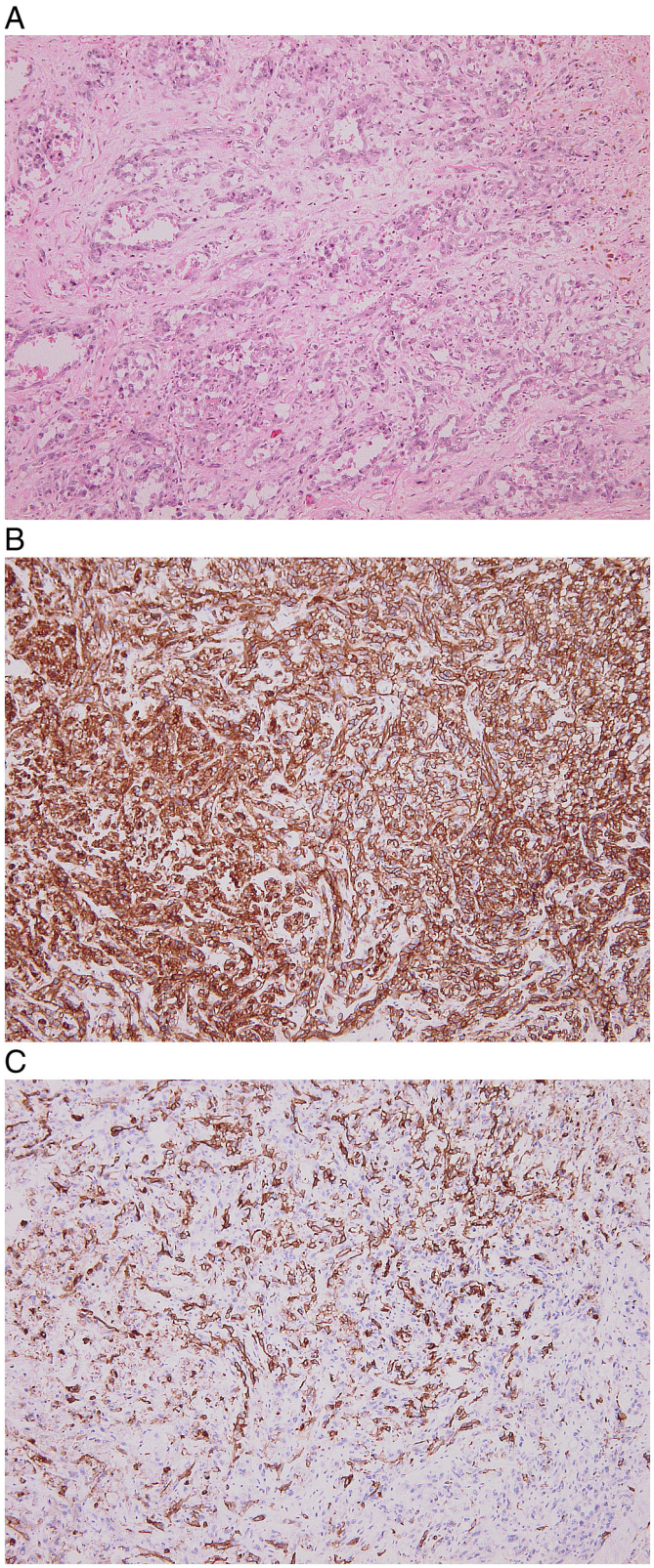


**Fig. 1.** (A) Angiosarcoma of the femoral artery, hematoxylin and eosin (H&E) stain, magnification 200×. (B) Strong and diffuse positivity of CD31 in the angiosarcoma, 200×. (C) Strong and diffuse positivity of CD34 in the angiosarcoma, 200×.

Our systematic review of the literature confirms the extreme rarity of primary malignant tumors of the great vessels. They can be classified as mural, which arise from smooth muscle of tunica media and are predominantly leiomyosarcomas, or intimal (also referred to as luminal),

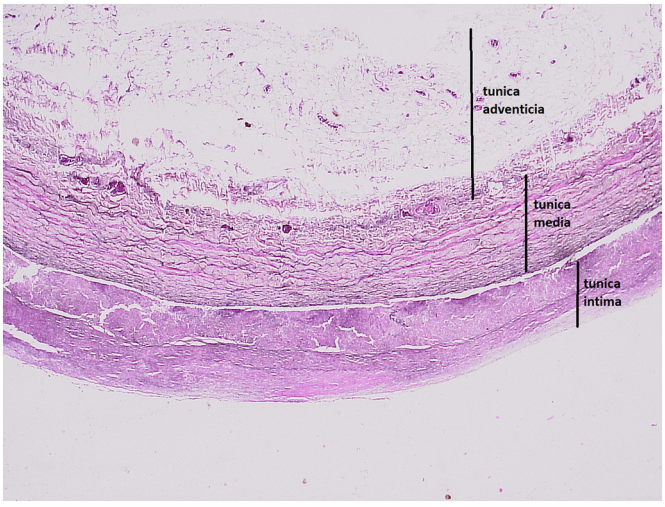


**Fig. 2.** Severe degenerative changes of the aortic wall, elastin stain, 100×.

which are predominantly high-grade sarcomas [4]. Most of the published cases reported primary malignant tumors originating from the superior vena cava or pulmonary arteries, while originating from other vessels seems to be very rare [4,5]. Primary angiosarcomas of great vessels are exceedingly rare, described only in few sporadic care reports, and consisted predominantly of intimal angiosarcomas of the aorta. A review by Seelig M.H. et al. from the year 1998 [3] describes 10 primary aortic angiosarcomas, majority of them (6 cases) arising in abdominal part. A more recent review by Thalheimer et al. from the year 2004 [6] denotes 21 cases of the aortic angiosarcoma, again with the predominance in the abdominal segment. Primary angiosarcomas of the femoral artery have been described only in four cases so far [7–10]. The most common clinical presentation was arterial occlusion [7,8,10], followed by aneurysm formation [9].

Approximately 60% of angiosarcomas affect a skin and subcutis, often with a background of long-term exposure to ultraviolet radiation or environmental toxins (especially vinyl chloride, thorotrast, or some insecticides). Secondary angiosarcomas arising in the terrain of chronic lymphedema or due to previous radiotherapy are also well known [1]. Occurrence in the internal organs is less frequent, most commonly in the liver, spleen, bones, and breast [11], sometimes arising from the preexisting benign or malignant lesion as Paget's bone disease, fibrous dysplasia, Wilms' tumor, retinoblastoma, or type 1 neurofibromatosis [1]. Primary angiosarcoma of the deep soft tissues is rare, with only a few case reports providing the limited information [11]. It seems to be a highly aggressive sarcoma with poor prognosis and is probably substantially underdiagnosed due to variable morphology and frequent aberrant expression of proteins, especially cytokeratines. A common complication of this subgroup of angiosarcoma is an extensive hemorrhage that can cause death by exsanguination or compression of surrounding organs. The extensive bleeding can lead to a diagnostic pitfall as well, as the voluminous blood clot can obscure the presence of the neoplastic cells [12].

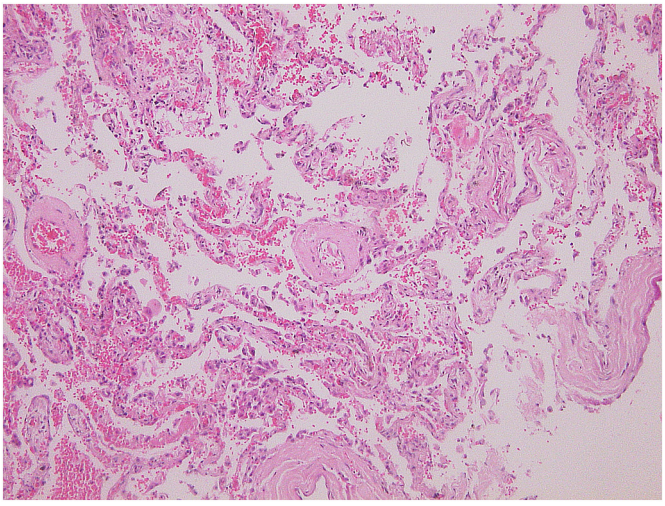

**Fig. 3.** Atypical thick-walled arterioles in the pulmonary parenchyma, H&E, 200×.

The relationship between polycystic kidney and liver disease, arterial aneurysms, and angiosarcoma is unclear. The association between adult polycystic kidney disease, liver polycystosis, and intracranial aneurysms is, however, well documented. Up to 50% of patients with polycystic kidney disease develop multiple cysts in the liver, which are mostly asymptomatic [13,14]. Approximately 10%–20% of those patients have solitary or multiple aneurysms affecting the circle of Willis [14–17]. Some authors therefore recommend routine screening for intracranial aneurysms in these patients [16]. These diseases probably share a common genetic background, which is a congenital laxity of connective tissue. Previous studies showed that genes for polycystin 1 and 2, which are mutated in the most of the cases of adult polycystic kidney disease, are strongly expressed in the smooth muscle of larger muscular and elastic arteries but poorly expressed in the wall of intracranial aneurysms and some cases of aortic dissections [17]. It remains unclear why the majority of the aneurysms manifest in the circle of Willis. Any other arterial complications associated with kidney and liver polycystosis seem to be extremely rare. Aneurysms of the abdominal aorta, valvar heart diseases, and aortic dissections have been reported. The microscopy in these cases showed severe degeneration of the arterial wall with massive translamellar mucoid deposits (formerly known as cystic medionecrosis) [18–20]. The risk of developing angiosarcoma is probably increased in those patients, but the evidence is not convincingly documented. There are some reports of angiosarcomas arising from preexisting hemangioma or vascular malformations, but the exact number is not clear because a large portion of the cases subsequently showed to be other histopathological diagnoses or secondary angiosarcomas arising in the terrain of previous radiotherapy [2]. There is only one case report of angiosarcoma arising from duplicate polycystic kidney [21].

Regarding coronary aneurysms, most of them are acquired, predominantly in the settings of advanced atherosclerosis, Kawasaki disease, or as a consequence of previous surgical intervention. They occur mainly in the right coronary artery and are often multiple. A small proportion of the cases arise as a consequence of congenital defects in the connective tissue (Marfan or Ehlers–Danlos syndrome) [22]. We are not aware of a single published case of coronary aneurysm being associated with polycystic kidney and liver disease.

## 4. Conclusions

The main purpose of this case report was to emphasize the aforementioned association of the polycystic kidney and liver disease, multiple arterial aneurysms, and primary angiosarcoma of the femoral artery, which, to the best of our knowledge, has not been described before. We also intend to highlight the often-neglected increased risk of angiosacroma development in these patients. It is still unclear whether the aneurysms were purely atherosclerotic or had a genetic background, especially when no intracranial aneurysm was found. However, due to the severe degenerative changes of the aortic wall in combination with kidney and liver polycystosis beside the atypical intraparenchymal pulmonary arteries in the absence of pulmonary hypertension, congenital background is presumed to play a role as well.

## Acknowledgments

We would like to thank Adam Whitley, M.D., and Azzat Al-Redouan, M.D., for reviewing the manuscript.

## References

[1] Mark RJ, Poen JC, Tran LM, Fu YS, Juillard GF. Angiosarcoma. A report of 67 patients and a review of the literature. Cancer 1996;77(11):2400–6.
[2] Rossi S, Fletcher CD. Angiosarcoma arising in hemangioma/vascular malformation: report of four cases and review of the literature. Am J Surg Pathol 2002;26(10):1319–29.
[3] Seelig MH, Klingler PJ, Oldenburg WA, Blackshear JL. Angiosarcoma of the aorta: report of a case and review of the literature. J Vasc Surg 1998;28(4):732–7.
[4] Burke AP, Virmani R. Sarcomas of the great vessels. A clinicopathologic study. Cancer 1993;71(5):1761–73.
[5] Goldblum JR, Rice TW. Epithelioid angiosarcoma of the pulmonary artery. Hum Pathol 1995;26(11):1275–7.
[6] Thalheimer A, Fein M, Geissinger E, Franke S. Intimal angiosarcoma of the aorta: report of a case and review of the literature. J Vasc Surg 2004;40(3):548–53.
[7] Otto RC, Pouliadis GP, Bollinger A. Angiosarcoma of the superficial femoral artery with distal embolization. Radiology 1977;123(2):310.
[8] Sattout AH, Deolekar MV, Tait WF, Williams GT. Femoral artery angiosarcoma presenting with distal embolization: report of a case. Surg Today 2008;38(6):541–4.
[9] Choi SY, Min SK, Kim KI, Kim HY. Intimal angiosarcoma presenting with common femoral artery aneurysm. J Vasc Surg 2012;56(3):819–21.
[10] Miyamoto T, Mihara M, Iwasaki K, Mishima E, Shimao S, Miyamoto H. Angiosarcoma of the thigh with thrombosis in the femoral artery. J Dermatol 1992;19(4):242–5.
[11] Meis-Kindblom JM, Kindblom LG. Angiosarcoma of soft tissue: a study of 80 cases. Am J Surg Pathol 1998;22(6):683–97.
[12] Rosai J. Ackerman's surgical pathology. . 8th ed.St. Louis: CV Mosby; 1996.
[13] Hoevenaren IA, Wester R, Schrier RW, McFann K, Doctor RB, Drenth JP, et al. Polycystic liver: clinical characteristics of patients with isolated polycystic liver disease compared with patients with polycystic liver and autosomal dominant polycystic kidney disease. Liver Int 2008;28(2):264–70.
[14] Geevarghese SK, Powers T, Marsh JW, Pinson CW. Screening for cerebral aneurysm in patients with polycystic liver disease. South Med J 1999;92(12):1167–70.
[15] Gieteling EW, Rinkel GJ. Characteristics of intracranial aneurysms and subarachnoid haemorrhage in patients with polycystic kidney disease. J Neurol 2003;250(4):418–23.
[16] Graf S, Schischma A, Eberhardt KE, Istel R, Stiasny B, Schulze BD. Intracranial aneurysms and dolichoectasia in autosomal dominant polycystic kidney disease. Nephrol Dial Transplant 2002;17(5):819–23.
[17] Nacasch N, Werner M, Golan E, Korzets Z. Arterial dissections in autosomal dominant polycystic kidney disease — chance association or part of the disease spectrum? Clin Nephrol 2010;73(6):478–81.
[18] Chien-Chang L, Wei-Tien C, Cheng-Chung F, I-lun T, Wen-Jone C. Sudden death caused by dissecting thoracic aortic aneurysm in a patient with autosomal dominant polycystic kidney disease. Resuscitation 2004;63:93–6.
[19] Torra R, Nicolau C, Badenas C, Brú C, Pérez L, Estivill X, et al. Abdominal aortic aneurysms and autosomal dominant polycystic kidney disease. J Am Soc Nephrol 1996;7(11):2483–6.
[20] Torres VE. Systemic manifestations of renal cystic disease. In: Gardner KD, Berstein J, editors. The cystic kidney. Dordrecht: Kluwer; 1990. p. 207–45.
[21] Nazirov RA. Angiosarcoma of a duplicate polycystic kidney in a girl. Urol Nefrol 1970;35(3):58–9.
[22] Abou Sherif S, Ozden Tok O, Taşköylü Ö, Goktekin O, Kilic ID. Coronary artery aneurysms: a review of the epidemiology, pathophysiology, diagnosis, and treatment. Front Cardiovasc Med 2017;4:24.