Ischemic stroke due to dissection of the posterior cerebral artery in a patient with polycystic kidney disease

Maksimova M.Yu., Airapetova A.S.
Research Center of Neurology, Moscow
80, Volokolamskoe Sh., Moscow 125367, Russia

Polycystic kidney disease (PKD) is a genetic condition clinically manifested by the formation of multiple cysts in the kidneys, liver and pancreas, as well as cardiovascular pathology. One of the rare complications of PKD is the development of dissections of the aorta, coronary and cerebral arteries.
This article presents a clinical case of ischemic stroke due to dissection of the posterior cerebral artery in a young patient with PKD who had a history of recurrent bleeding in the deep parts of both cerebral hemispheres.

Keywords: *ischemic stroke; posterior cerebral artery dissection; polycystic kidney disease.*
Contact: *Marina Yuryevna Maksimova;* ***ncnmaximova@mail.ru***
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Polycystic kidney disease (PKD) is a genetic disease clinically manifested in the formation of multiple cysts in the kidneys, liver, pancreas, as well as the pathology of other organs and systems, including the cardiovascular system [1].

Cardiovascular pathology in patients with PKD typically manifests itself in hypertension, heart valves abnormalities, dilatation and aneurysms of the aortic root [2], aneurysms of the coronary and cerebral arteries [3, 4]. A rarer cardiovascular complication of PKD is dissection of the aorta, coronary and cerebral arteries.

Clinical observation

Patient B., 30 years old, was admitted to the Research Center of Neurology with complaints of blurred vision and unsteady gait. From the medical history it was known that since the age of 12 the patient had episodes of increased blood pressure (BP). The examination revealed PKD. Genetic testing was not performed. Despite the constant use of antihypertensive therapy, episodes of increased BP persisted, up to a maximum of 200/100 mm Hg. In 2017, the patient had a hemorrhage in the left cerebral hemisphere. In March 2020, hemorrhage occurred in the deep parts of the right cerebral hemisphere and was complicated by intraventricular hemorrhage. CT-angiography of intracranial arteries did not reveal any pathology. In June 2023, after overwork, his BP suddenly rose up to 180/100 mm Hg and his vision became blurred, mainly due to decreased vision in the left eye. The next day, numbness in the left limbs, unsteadiness of gait and disorientation in space developed, so he sought medical care in the Research Center of Neurology.

On admission: BP – 125/90 mm Hg; electrocardiography – sinus rhythm; heart rate – 72 beats per minute; blood glucose level – 7.2 mmol/L.

Neurological status: left-sided hemianopsia, facial asymmetry due to the left nasolabial fold, moderate dysarthria, bilateral Babinski reflex, dysmetria in the left heel-to-knee test, instability in the Romberg test, gait ataxia. The severity of the neurological deficit evaluated by the National Institutes of Health Stroke Scale (NIHSS) was 4 points; disability according to the Modified Rankin Scale (mRS) – 2 points; the Rivermead Mobility Index – 13 points.

Brain MRI: "acute" infarctions in the right cerebral hemisphere in the thalamus, splenium of the corpus callosum with partial spread to the medial parts of the temporal lobe; post-hemorrhagic changes in the subcortical structures of both hemispheres of the brain are visualized (Fig. 1).

MR-angiography of the intracranial arteries: lack of a signal from blood flow along the right posterior cerebral artery from the P2 segment and distal.

MRI T1 fat-saturated (fat-sat) sequence: an intramural hematoma (hyperintense signal in all sequences) is visualized in the wall of the right posterior cerebral artery. The external diameter of the artery is about 4 mm, the internal one is about 1 mm. The MRI corresponds to a dissection of the right posterior cerebral artery (Fig. 2).

Duplex ultrasound scanning of the brachiocephalic arteries: without significant pathology and blood flow disturbance.

Echocardiography: moderate eccentric hypertrophy of the basal interventricular septum without stenosis of the left ventricular outflow tract. The chambers of the heart are not dilated. The systolic and diastolic function of the left ventricle is not impaired. Hemodynamically insignificant prolapse of the anterior mitral valve leaflet with mitral regurgitation grade 1. Tricuspid regurgitation grade 1.

Kidneys' ultrasound: the kidneys are enlarged, the renal tissue is represented by a conglomerate of anechoic lesions with clear, smooth contours, the largest size up to 8_6 cm. Ultrasound signs of PKD (Fig. 3).

Renal arteries' ultrasound: without pathology.

24-hour BP monitoring on losartan 100 mg/day and amlodipine 5 mg/day therapy: average day-time BP – 132/97 mm Hg, average night-time BP – 130/90 mm Hg. The highest BP is 149/108 mm Hg, the lowest one is 112/70 mm Hg. The rate of night-time decrease in systolic BP is 1.6% (Non-dipper), in diastolic BP – 6.6% (Non-dipper).

Laboratory tests: elevated serum creatinine level up to 127 U-mol/L, proteinuria up to 0.081 g/L. Fasting blood glucose concentration from 6.0 to 4.8 mmol/L. Glycated hemoglobin – 6.5%. The patient was examined by an endocrinologist, the condition was regarded as stress hyperglycemia. The lupus anticoagulant was 0.99 (negative). Anticardiolipin antibodies: IgG – 5.6 U/ml (normal range: 0–10 U/ml), IgM – 4.2 U/ml (normal range: 0–7 U/ml). Beta-2 glycoprotein 1 antibodies: IgG – 6.1 U/ml (normal range: 0–10 U/ml), IgM – 4.8 U/ml (normal range: 0–7 U/ml). Homocysteine level – 16.4 U-mol/l (normal range: 0–15 U-mol/L). Cystatin C – 0.89 mg/L (normal range: 0.50–1.20 mg/L).

Diagnosis: acute ischemic stroke in the right posterior cerebral artery circulation system from June 2023. Dissection of the right posterior cerebral artery. The post-stroke period of hemorrhages in the deep parts of the left cerebral hemisphere from 2017 and in the deep parts of the right cerebral hemisphere with intraventricular hemorrhage from March 2020. Hypertension stage 3. Very high cardiovascular risk. Polycystic kidney disease. Chronic kidney disease stage 2.

From the family history (Fig. 4) it was found that the PKD was diagnosed in the patient's maternal grandmother (died at 48 years old, the cause is unknown), maternal aunt (died at 28 years old from "stroke"), mother (55 years old), sister (28 years old) and her son (8 years old). The patient's sister had hemorrhagic stroke due to an aneurysm rupture at the age of 28; she has three children: the 8-year-old son was diagnosed with PKD, a 5-year-old daughter and a 2-year-old son were not examined. A genetic examination of family members was not performed.

Antiplatelet, antihypertensive, neuroprotective therapy, rehabilitation exercises, balance and speech therapy were carried out during the treatment. As a result, the regression of hemianopsia, a decrease in the severity of dysarthria and gait discoordination, stabilization of hemodynamics was achieved. At the discharge the severity of the neurological deficit by NIHSS was 3 points; disability by mRS – 1 point; the Rivermead Mobility Index was 15 points.

Discussion

There is a large data about aneurysms of various localizations in patients with PKD, however, dissections of the coronary arteries [5–8] and aorta [9–12] are described less often. Clinical cases of spontaneous cerebral arteries dissections in patients with PKD are found only in a small number of studies [13–16].

M. Windpessl et al. [13] reported a case of the spontaneous internal carotid artery dissection in a 35-year-old female with PKD. T. Kuroki et al. [14] described two cases of the vertebral and internal carotid arteries dissection in a 32-year-old man with PKD, and dissection of both vertebral arteries in a 52-year-old patient. The article by S. Roth et al. [15] presented a clinical case of dissection of both internal carotid arteries in a 39-year-old

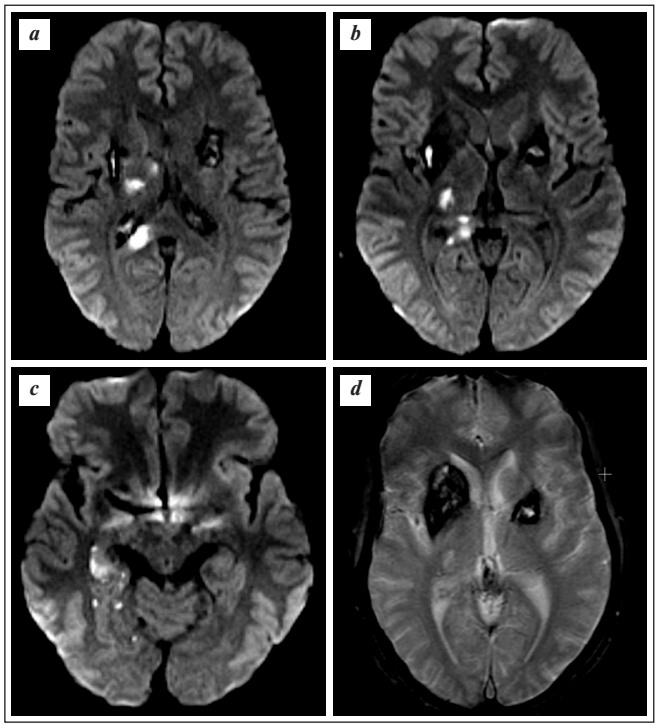

Fig. 1. *MRI of the brain of patient B. Acute ischemic foci in the right hemisphere of the brain (a–c); post-hemorrhagic changes in the subcortical structures of both hemispheres of the brain (d)*

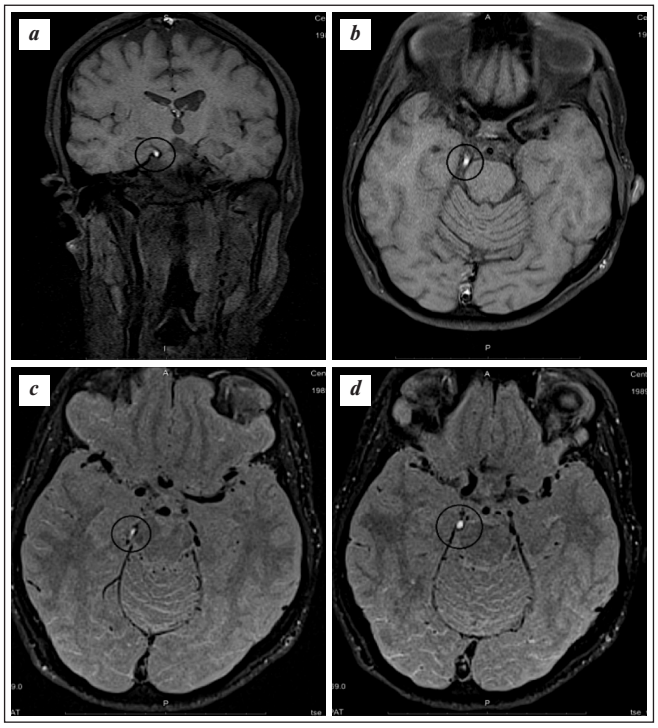

Fig. 2. *MRI of the brain of patient B. in T1 fat-sat mode. An intramural hematoma is visible in the wall of the right posterior cerebral artery. The MR-image corresponds to a dissection of the right posterior cerebral artery*

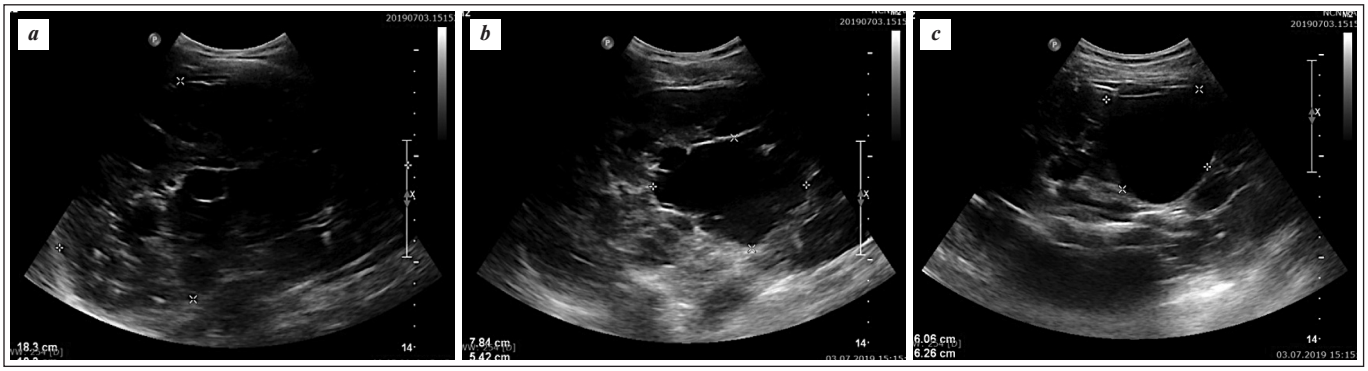

Fig. 3. *Kidneys' ultrasound in patient B. The kidneys are enlarged, the renal tissue is represented by a conglomerate of anechoic lesions with clear, smooth contours. Ultrasound signs of PKD*

female with PKD, with additionally identified multiple aneurysms in one of these arteries. G. Bobrie et al. [16] described two cases of spontaneous internal carotid artery dissection in 48- and 49-year-old patients with autosomal dominant PKD (ADPKD), a clinical case of dissection of the extracranial segments of the vertebral artery in a 68-year-old patient, dissection of the basilar artery in a 34-year-old patient with ADPKD, and a case of myocardial infarction due to coronary artery dissection in a 36-year-old patient with PKD.

The pathogenesis of arterial dissections in PKD is not well understood. According to some authors, the main predisposing factor is hypertensive angiopathy [2, 17, 18]. Y. Osawa et al. [19] previously proposed three possible risk factors for aortic dissection in patients with ADPKD: cystic degeneration of connective tissue, hypertension, and hemodialysis.

Pathological changes in the arterial wall in patients with ADPKD may be caused by the *PKD1* and *PKD2* gene mutations and low expression of polycystin-1 and polycystin-2 in the muscular layer of blood vessels, including the aorta and cerebral arteries [20–22]. Mutations in the *PKD1* and *PKD2* genes lead to dysfunction of calcium-permeable ion channels in endothelial cells, and an increase in the concentration of cyclic adenosine monophosphate in cells, inducing endothelial dysfunction and angiogenesis impairment [23,24]. Pathological changes associated with low polycystins expression lead to dysfunction of extracellular matrix proteins, including type IV collagen, proteoglycans, fibronectin, undulin, and tenascin, resulting in "weakness" of the vessel wall [25, 26]. Microscopically, ruptures of the elastic membrane and muscular layer of the arterial wall are revealed. Histological examination reveals disruption of collagen fiber organization and decreased density of smooth muscle cells at the site of dissection, as well as thinning and ruptures in the elastic layer of the arterial wall [27].

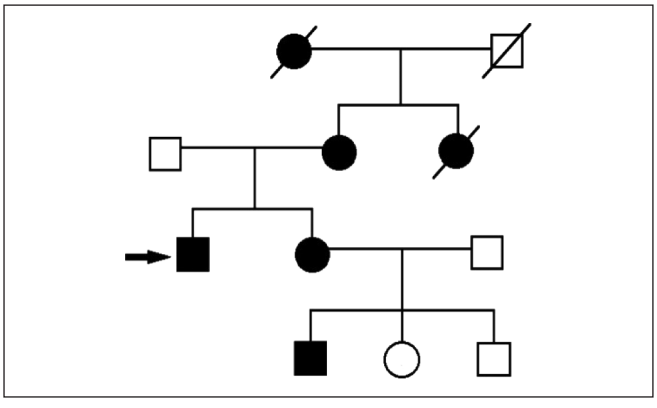

Fig. 4. *Clinical genealogical tree of the family of patient B. (indicated by the arrow)*

The distinctive feature of our observation is verification of intracranial artery dissection as the cause of acute ischemic stroke in a young man with PKD and a detailed analysis of his genealogy.

In the presented clinical case, a patient with PKD, a history of recurrent hemorrhages in the deep parts of brain against the background of uncontrolled hypertension was diagnosed with ischemic stroke due to dissection of the right posterior cerebral artery. From the family history it has been established that the disease is inherited in each generation, affecting both males and females. Of note is the fact that all family members had an early age of disease onset, and the patient has elevated fasting blood glucose and glycated hemoglobin levels, which may indicate endocrinopathy, that occurs in renal cysts and diabetes syndrome associated with a mutation in the *HNF1B* gene. However, given the lack of genetic examination of the patient and his family, it is impossible to definitively determine the type of PKD.

Conclusion

Practicing physicians of various specialties, especially cardiologists and neurologists, should be aware of the systemic pathological changes in PKD and the risk of dissection of the aorta, coronary and cerebral arteries in patients with PKD. Given the small number of studies devoted to this problem, further research aimed at clarifying the pathogenesis and risk factors of arterial dissections in PKD is needed to develop algorithms for prevention, timely diagnosis and treatment.

REFERENCES

1. Horie S, Mochizuki T, Muto S, et al. Evidence-based clinical practice guidelines for polycystic kidney disease 2014. *Clin Exp Nephrol.* 2016 Aug;20(4):493-509. doi: 10.1007/s10157-015-1219-7. Erratum in: *Clin Exp Nephrol.* 2016 Aug;20(4):510. doi: 10.1007/s10157-016-1285-5

2. Torres VE, Harris PC, Pirson Y. Autosomal dominant polycystic kidney disease. *Lancet*. 2007 Apr 14;369(9569):1287-301. doi: 10.1016/S0140-6736(07)60601-1

3. Gieteling EW, Rinkel GJ. Characteristics of intracranial aneurysms and subarachnoid haemorrhage in patients with polycystic kidney disease. *J Neurol.* 2003 Apr;250(4):418-23. doi: 10.1007/s00415-003-0997-0

4. Cornec-Le Gall E, Alam A, Perrone RD. Autosomal dominant polycystic kidney disease. *Lancet*. 2019 Mar 2;393(10174):919-35. doi: 10.1016/S0140-6736(18)32782-X. Epub 2019 Feb 25.

5. Basile C, Lucarelli K, Langialonga T. Spontaneous coronary artery dissection: One more extrarenal manifestation of autosomal dominant polycystic kidney disease? *J Nephrol.* 2009;22(3):414-6.

6. Itty CT, Farshid A, Talaulikar G. Spontaneous coronary artery dissection in a woman with polycystic kidney disease. *Am J Kidney Dis.* 2009 Mar;53(3):518-21. doi: 10.1053/j.ajkd.2008.08.027. Epub 2008 Nov 6.

7. Afari ME, Quddus A, Bhattarai M, et al. Spontaneous coronary dissection in polycystic kidney disease. *R I Med J* (2013). 2013 Dec 3;96(12):44-5.

8. Lee CC, Fang CY, Huang CC, et al. Computed tomography angiographic demonstration of an unexpected left main coronary artery dissection in a patient with polycystic kidney disease. *J Thorac Imaging.* 2011 Feb;26(1):W4-6. doi: 10.1097/RTI.0b013e3181dc2a53

9. Gignon M, Defouilloy C, Montpellier D, et al. Sudden death caused by aortic dissection in a patient with polycystic kidney disease. *Genet Couns.* 2011;22(4):333-9.

10. Paynter HE, Parnham A, Feest TG, Dudley CR. Thoracic aortic dissection complicating autosomal dominant polycystic kidney disease. *Nephrol Dial Transplant.* 1997;12(8):1711-3. doi: 10.1093/ndt/12.8.1711

11. Adeola T, Adeleye O, Potts JL, et al. Thoracic aortic dissection in a patient with autosomal dominant polycystic kidney disease. *J Natl Med Assoc.* 2001;93(7-8):282-7.

12. Fukunaga N, Yuzaki M, Nasu M, Okada Y. Dissecting aneurysm in a patient with autosomal dominant polycystic kidney disease. *Ann Thorac Cardiovasc Surg.* 2012;18(4):375-8. doi: 10.5761/atcs.cr.11.01756

13. Windpessl M, Stadler K, Lampl R, Wallner M. Horner syndrome in renal clinic: a woman with polycystic kidney disease and spontaneous carotid artery dissection. *Nephrology (Carlton).* 2013;18(4):315. doi: 10.1111/nep.12042

14. Kuroki T, Yamashiro K, Tanaka R, et al. Vertebral artery dissection in patients with autosomal dominant polycystic kidney disease. *J Stroke Cerebrovasc Dis.* 2014;23(10):e441-e443. doi: 10.1016/j.jstrokecerebrovasdis.2014.05.028

15. Roth C, Kleffmann J, Bergmann C, et al. Ruptured cerebral aneurysm and acute bilateral carotid artery dissection in a patient with polycystic kidney disease and polycystic liver disease. *Cerebrovasc Dis*. 2013;35(6):590-1. doi: 10.1159/000350727

16. Bobrie G, Brunet-Bourgin F, Alamowitch S, et al. Spontaneous artery dissection: is it part of the spectrum of autosomal dominant polycystic kidney disease? *Nephrol Dial Transplant.* 1998 Aug;13(8):2138-41. doi: 10.1093/ndt/13.8.2138

17. Pirson Y. Extrarenal manifestations of autosomal dominant polycystic kidney disease. *Adv Chronic Kidney Dis.* 2010;17(2):173-80. doi: 10.1053/j.ackd.2010.01.003

18. 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. doi: 10.5414/cnp73478

19. Osawa Y, Omori S, Nagai M, et al. Thoracic aortic dissection in a patient with autosomal dominant polycystic kidney disease treated with maintenance hemodialysis. *J Nephrol.* 2000 May-Jun;13(3):193-5.

20. Torres VE, Cai Y, Chen XI, et al. Vascular expression of polycystin-2. *J Am Soc Nephrol.* 2001 Jan;12(1):1-9. doi: 10.1681/ASN.V1211

21. Pirson Y, Chauveau D, Torres V. Management of cerebral aneurysms in autosomal dominant polycystic kidney disease. *J Am Soc Nephrol.* 2002 Jan;13(1):269-76. doi: 10.1681/ASN.V131269

22. Liu D, Wang CJ, Judge DP, et al. A Pkd1-Fbn1 genetic interaction implicates TGF-β signaling in the pathogenesis of vascular complications in autosomal dominant polycystic kidney disease. *J Am Soc Nephrol.* 2014 Jan;25(1):81-91. doi: 10.1681/ASN.2012050486. Epub 2013 Sep 26.

23. Yanda MK, Liu Q, Cebotaru V, et al. Role of calcium in adult onset polycystic kidney disease. *Cell Signal.* 2019 Jan;53:140-50. doi: 10.1016/j.cellsig.2018.10.003. Epub 2018 Oct 5.

24. Fick-Brosnahan GM. Endothelial dysfunction and angiogenesis in autosomal dominant polycystic kidney disease. *Curr Hypertens Rev.* 2013 Feb;9(1):32-6. doi: 10.2174/1573402111309010006

25. Carone FA, Kanwar Y. Tubular cell and matrix changes in renal cystic disease. *Contrib Nephrol.* 1993;101:1-6. doi: 10.1159/000422098

26. Klingel R, Ramadori G, Schuppan D, et al. Coexpression of extracellular matrix glycoproteins undulin and tenascin in human autosomal dominant polycystic kidney disease. *Nephron*. 1993;65(1):111-8. doi: 10.1159/000187451

27. Haruta S, Gunji K, Kawamura T, Hiroshima K. Generalized Vascular Dissection on Pathological Examination in a Patient With Polycystic Kidney Disease and Acute Aortic Dissection. *J Natl Med Assoc.* 2019 Oct;111(5):563-8. doi: 10.1016/j.jnma.2019.04.008. Epub 2019 May 27.

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Conflict of Interest Statement

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Maksimova M.Yu. https://orcid.org/0000-0002-7682-6672
Airapetova A.S. https://orcid.org/0000-0002-9397-3746