

## RENAL ARTERY THROMBOEMBOLISM FOLLOWED BY RENAL INFARCTION: A RARE CAUSE OF ACUTE FLANK PAIN, MIMICKING APPENDICITIS

Irena Šidiškienė<sup>1</sup>, Žilvinas Barauskas<sup>2</sup>, Lina Minkevičiūtė<sup>2</sup>

<sup>1</sup>*Diagnostical Unit of Internal disease, Kaunas Clinical Hospital, Lithuania,*

<sup>2</sup>*Faculty of Medicine, Medical Academy, Lithuanian University of Health Sciences*

**Key words:** renal artery thromboembolism, atrial fibrillation, flank pain, appendicitis

### Summary

Renal artery thromboembolism (RATE) is a rare and serious condition, that is often hard to diagnose. It is very important for any physician to have in mind this pathology with unexplained flank pain, specially in patients with risk factors for this condition. Renal artery thromboembolism can cause partial or total renal infarction (RI), so early diagnostic and adequate treatment is necessary. **Materials and Methods:** We present a case report in elderly woman with risk factors for peripheral thromboembolism. A review of articles was done with intention to discuss this case, including common presenting symptoms, risk factors, diagnostic particularities, treatment options and complications, prevention. **Conclusions:** In a presence of symptoms - localised flank pain, nausea, vomiting and elevated C- reactive protein, white blood cells, creatinine, d- dimers - contrast enhanced CT scan should be performed as soon as possible. Anticoagulation therapy is thought to be the safest treatment strategy. Unfractionated heparine, if possible, can be replaced by low mass weight heparin in order to prevent anticoagulation therapy complications. To prevent embolic complications of AF – warfarine therapy can be replaced by rivaroxaban therapy.

### Introduction

Renal artery thromboembolism is a rare condition, that is hard to diagnose, due to the nonspecific clinical manifestation. It accounts for 2% of peripheral thromboembolism events. Many cases of acute renal artery occlusion occur in a present of thromboembolic events, blunt abdominal trauma, hypercoagulable conditions or are unknown etiology. Howe-

ver, the most common cause of RI is atrial fibrillation (AF) - 64% of published cases [1]. There were 0.004%–0.007% incidence of RI in emergency department according to some studies [2,3]. Clinical symptoms of RI varies, but the most common are localised pain, fever, nausea, vomiting and hematuria [4,5]. Also, it is known, that cancer can have influence on thromboembolic events because of hypercoagulable state and the prothrombotic effects of it's treatment, but usually it occurs in vein system [4,6].

**We present a case report** of 83 years old women with chronic AF and breast cancer. The patient was hospitalised with unexplained pain in pelvic area with suspected appendicitis.

### Case presentation

In November 2017, a 83 year old female was admitted to the emergency room (ER) because of nausea, vomiting and constant right flank pain, which at first was covering the entire abdominal area, then after 12 hours localised at the right flank (8 points of VAS).

Her medical history included breast cancer, three ischaemic strokes few years ago and chronic atrial fibrillation, essential hypertension. She was taking: Tamoxifen 20mg/day, Digoxin 0.25mg/day, Metoprolol 100mg/day, Isosorbidedinitrate 20mg/day and vit. K antagonist 2,5-5mg/day, which dose depended on International normalized ratio (INR). Nonsmoker.

Patient physical examination showed subfebrile body temperature - 37.4°C, blood pressure of 148/80 mmHg and heart rate of 82 beats/minute. The auscultation revealed non-regular heart beats. There was no tenderness in abdominal area, but painful palpation in the right flank. Jordan symptom negative. Other systems were unremarkable.

Laboratory tests revealed a white blood cell count  $22.6 \times 10^9/l$  which has decreased after four days till  $11.5 \times 10^9/l$ , erythrocytes  $4.3 \times 10^9/l$ , haemoglobin 130g/l, platelets 172

$\times 10^9/l$ . C-reactive protein rised from 7.5mg/l on the first day to 60.2 mg/l two days later. Potassium all of the hospitaliation time was in the normal range from 3.7 till 4.7 mmol/l, but urea was elevated to 10.8mmol/l. Creatinine has reached the peak at fourth day of hospitalisation – 135.8  $\mu\text{mol/l}$ , in the end of treatment it has decreased 117.3  $\mu\text{mol/l}$ . Troponin I was increased to 0.126 $\mu\text{g/l}$  on hospitalisation date, in the second day had reached 1.18  $\mu\text{g/l}$  and eventually dropped down to 0.016 $\mu\text{g/l}$  few days later. D-dimers was slightly elevated till 1,18 $\mu\text{g/ml}$ . During hospitalisation, INR was in normal range 2.3-2.2-1.5, Prothrombin time (PT) – 24 %. Before RATE, the patient had not reached therapeutic INR interval several times.

Liver function was insignificantly increased - ALT 62 U/L, AST 82 U/L. P-amylase was 24 U/l, diagnosis of acute pancreatitis was rejected. Urinalysis was positive for red blood cells (50 cells/ $\mu\text{L}$ ) and leukocytes (500 cells/ $\mu\text{L}$ ), protein – negative, bacteria – positive, nitrite – negative – urinal infection and pyelonephritis was excluded. The ECG showed an abnormal heart rhythm: atrial fibrillation – 139 beats per minute with T inversion in  $V_2, V_3, V_4, V_5$  chest leads.

Firstly, infectious disease of unknown etiology was suspected and denied after laboratory tests results came. Then patient was transferred to surgical department for farther investigation and treatment of acute abdominal pain. The patient was consulted by surgeon and gynecologist. Later was performed abdominal ultrasound, which identified free-flowing stretch of liquid in the lower right abdominal area, about 1.1 cm thickness, the appendix was not visualised. Ultrasound did not show any renal abnormalities, so surgeons diagnosed acute appendicitis.

In surgery department patient was treated with drotaverin 80mg/4ml, ketoprophen 100mg/2ml and metoclopramid 10mg/2ml intramusculous injections and intravenous 0.9% 500ml sodium chloride.

Because of chronical AF, patient was transferred to intensive care unit (ICU) for preoperative preparation. As patient still remained symptomatic, a contrast-enhanced CT scan was performed in order to identify the etiology of pain localised on the right flank. D-dimers was increased to 1,18  $\mu\text{mol/l}$  at that moment. Artery thrombosis was suspected. The CT scan showed right renal artery contrasting defect (0.6x0.5x2.1cm floating thromb) followed by renal infarction signs - hypodential DI, not accumulating contrast in the inferior pole of the kidney (Figure 1). Additionally, the CT scan revealed some fluid in the pleural cavity: in the right cavity 1.1 cm, in the left – 0.7 cm thickness and 0.4 cm thickness stretch of liquid near liver.

The echocardiography revealed ejection fraction 48%, I° MV, AoV, TV regurgitations. Dilation of heart chambers or thrombi was not detected.

The diagnosis of renal artery thromboembolism with acute renal infarction was made. Thrombolysis or thromboaspiration was declined because of additional procedure risk. The patient was treated with heparin 1000VV/hour, following on APTT.

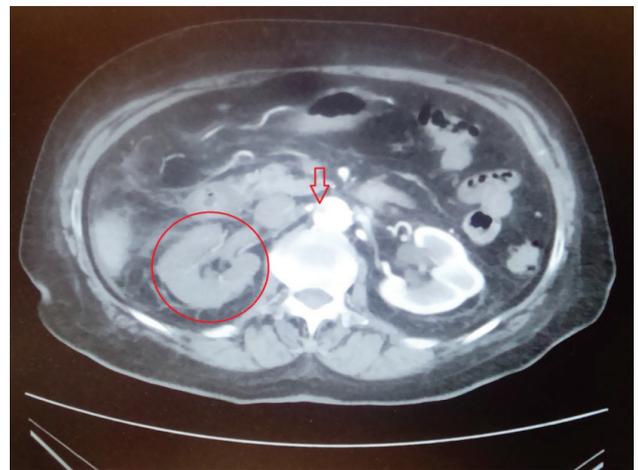
After 2 days in ICU an improvement of patient general status was noticed, so she was transferred to department of Internal medicine, where anticoagulation therapy was continued with heparin (50000VV overall). After 5 days of treatment with heparin, it was replaced byfraxiparin 0.6ml x 2/d (10,8ml overall) for 9 days, then fraxiparin was replaced by rivaroxaban 15mg x 1/d (45mg overall) for 3 days.

During anticoagulation therapy, patient bleed from gastrointestinal tract. Fibrosophago- gastroduodenoscopy was performed and shown few hemorrhagic erosions in stomach. Hemoglobin was decreased to 86g/l. After examination two units of erithrocyte mass transfusion was done, because of tissue hypoxia.

Eventually, abdominal pain have disappeared, signs of kidney supuration or other complications have not been observed. The renal function partially recovered and the serum creatinine was 117  $\mu\text{mol/l}$  in the end of the treatment. The patient after discharge was recommended to continue the treatment with rivaroxaban, metoprolol, tamoxifen and omeprisol and was suggested to perform a renal ultrasound after a month. From that time till now, patient had not experienced any anticoagulation therapy complications.

## Discussion

Renal artery thromboembolism is a rare condition, that is hard to diagnose, due to the nonspecific clinical manifestation. It accounts for 2% of peripheral thromboembo-



**Figure 1.** Enhanced CT scan - right renal artery contrasting defect with noncontrasting right kidney

lism events. Other localisation includes aorta (7%), pelvic arteries (9%), mesenteric arteries (29%), upper and lower extremities (61%) [7].

Clinical symptoms usually varies and can mimic nephrolithiasis, pyelonephritis, appendicitis or any other acute abdomen cause, but mostly it consists of localised pain (89.4%), nausea/vomiting (43.8%) and fever (26.8%). Laboratory tests mostly shows elevated lactate dehydrogenase (92.1%), C-reactive protein (75.4%), white blood cells (72.3%), creatinine (42.7%), proteinuria (58.1%) and hematuria (53.2%) [8]. Our patient was hospitalised with acute flank pain, nausea and vomiting. Laboratory results showed slightly elevated alanine transaminase and asparagine transaminase. C-reactive protein and white blood cell count also were elevated. Troponin I increasing was secondary, because of thromboembolic complication and stressful situation. D-dimers was slightly increased. There were microhematuria and leucocyturia without proteinuria.

Many cases of acute renal artery occlusion occur in a present of thromboembolic events, blunt abdominal trauma, hypercoagulable conditions or are unknown etiology. However, the most common cause of RATE and RI is AF - 64% of published cases [1]. Our patient also has cancer and is taking hormone therapy with tamoxifen, which is known that can lead to hypercoagulation in circulation system [9]. Thromboembolic events are common side effects (including deep vein thrombosis, microvascular thrombosis and pulmonary embolism) [10]. It was observed, that patients who received adjuvant therapy with nonsteroid estrogen antagonists for breast cancer had a 5.4% frequency of thromboembolic complications more than those who have not. The combination of chemotherapy with tamoxifen was associated with more venous and arterial thromboembolic complications than using only a chemotherapy in premenopausal patients [11]. Other risk factors includes rheumatic heart disease, dilated cardiomyopathy, endocarditis [8]. Our patient had chronic AF and hypercoagulable state, treated by warfarin. However, patient had not reached therapeutic INR interval several times before, so ischaemic stroke years ago and RATE this time could be resulted by subtherapeutic INR.

Renal infarction, as a result of RATE, based on clinical view in imaging tools, can be divided in total and partial. [5]. According to fourty - four cases study - the most accurate diagnostic methods of RI are angiography (100% accuracy), renal isotope scan (97% accuracy), contrast-enhanced computed tomography (CT scan) (80% accuracy). Ultrasound was the least informative (11% accuracy) [12]. Ultrasound and contrast enhanced CT scan was used in our patient. The first diagnostic method showed inflammation signs in the right lower quadrant, near appendix. But appendix was not visualised. Eventually CT scan was performed. It showed

right renal artery contrasting defect followed by right renal lower pole hipodensity – ischaemia sign. Contrast enhanced CT scan was the most popular diagnostic tool in most RI cases [8]. According to literature, wedge – shaped non-contrasting, lower density peripheral areas with cortical rim sign was seen in most CT scans [12,13].

RATE treatment can be divided into intravenous, oral anticoagulation, thrombolytic therapy, thrombectomy or renal angioplasty [8,12]. However, the most common treatment options for RATE followed by RI were unfractionated and low molecule mass heparins, warfarin (82.2% cases). Conservative treatment methods is thought to be much safer than invasive techniques in some cases. It is due to greater risk of contrast nephrotoxicity or additional invasive methods during the procedure. Invasive techniques are proper in situations, when urgent and aggressive intervention is needed to ensure residual renal function in patients with function impairment or if only one kidney is left [8]. The treatment strategy mostly depends on the scale of affection and renal function impairment. In our case, the risk of invasive treatment strategy was evaluated and patient received anticoagulation therapy with unfractionated heparin, which, was replaced by fraxiparine and later by rivaroxaban. During the treatment with anticoagulants, the patient bled from gastrointestinal tract, so erythrocyte mass transfusion was done in order to correct blood loss. According to literature, the major complication of anticoagulation therapy is bleeding. It is known, that low mass weight heparin is associated with fewer bleeding risks in compare to unfractionated heparin [14]. Metaanalyses support the inference that low mass weight heparin does not result in an increased risk of major bleeding compared with unfractionated heparin [15].

RATE and RI prevention is closely associated with adequate treatment strategy. There is evidence, that not reaching therapeutic INR interval can lead to thromboembolic events or even death. According to danish nationwide cohort study, the majority of thromboembolic events occurred during subtherapeutic INR and after warfarin interruption, independently of reasons for interruption [16]. For better and much comfortable anticoagulation therapy control, rivaroxaban is much more recommended to use than warfarin [17].

## Conclusions

Renal artery thromboembolism is a rare condition, that can mimic any other acute abdomen cause with nonspecific clinical manifestation. In a presence of symptoms triad - localised flank pain, nausea, vomiting and elevated C-reactive protein, white blood cells, creatinine, d-dimers - contrast enhanced CT scan should be performed as soon as possible. Treatment option should be chosen depending on renal function and patient overall health status: for elder and non-

complicated patients - anticoagulation therapy is thought to be the safest treatment strategy. Unfractionated heparine, if possible, could be replaced by low mass weight heparin in order to prevent anticoagulation therapy complications. To prevent embolic complications of AF – warfarine therapy can be replaced by rivaroxaban therapy. In our clinical case rivaroxaban was chosen because of bleeding from gastrointestinal tract. This choice was much more safer and comfortable to control for our patient.

*Conflicts of Interest:* the authors declare no conflict of interest.

## References

- Bourgault M, Grimbert P, Verret C, Pourrat J, Herody M, Halimi J. et al. Acute renal infarction: a case series. *Clinical Journal of the American Society of Nephrology* 2012; 8(3):392-398. <https://doi.org/10.2215/CJN.05570612>
- Huang C, Lo H, Huang H, Kao W, Yen D, Wang L. et al. ED presentations of acute renal infarction. *The American Journal of Emergency Medicine* 2007; 25(2), 164-169. <https://doi.org/10.1016/j.ajem.2006.06.010>
- Domanovits H, Paulis M, Nikfardjam M, Meron G, Kürkciyan I, Bankier A. et al. Acute renal infarction: clinical characteristics of 17 patients. *Medicine* 1999; 78(6):386-394. <https://doi.org/10.1097/00005792-199911000-00004>
- Jurubita R, Obrisca B, Ismail G. A rare cause of acute kidney injury in a female patient with breast cancer presenting as renal colic. *Case Reports in Nephrology* 2016; 2016(9565873):4. <https://doi.org/10.1155/2016/9565873>
- Chu P, Wei Y, Huang J, Chen S, Chu T, Wu K. Clinical characteristics of patients with segmental renal infarction. *Nephrology* 2006; 11(4):336-340. <https://doi.org/10.1111/j.1440-1797.2006.00586.x>
- Van de Velde C, Rea D, Seynaeve C, Putter H, Hasenburg A, Vannetzel J. et al. Adjuvant tamoxifen and exemestane in early breast cancer (TEAM): a randomised phase 3 trial. *Lancet* 2011; 377(9762):321-331. [https://doi.org/10.1016/S0140-6736\(10\)62312-4](https://doi.org/10.1016/S0140-6736(10)62312-4)
- Frost L, Engholm G, Johnsen S. et al. Incident thromboembolism in the aorta and the renal, mesenteric, pelvic, and extremity arteries after discharge from the hospital with a diagnosis of atrial fibrillation. *Arch Intern Med* 2001; 161(2): 272-276. <https://doi.org/10.1001/archinte.161.2.272>
- Huang H, Hsu C, Chen K. Acute renal artery embolism: a case report and literature review. *General Medicine: Open Access* 2016; 04(03):1-4. <https://doi.org/10.4172/2327-5146.1000245>
- Caine G, Stonelake P, Lip G, Kehoe S. The hypercoagulable state of malignancy: pathogenesis and current debate. *Neoplasia* 2002; 4(6):465-473. <https://doi.org/10.1038/sj.neo.7900263>
- Tamoxifen 20mg Film-Coated Tablets - Summary of Product Characteristics (SmPC) - (eMC). *Medicines.org.uk*. Available online: <https://www.medicines.org.uk/emc/product/2248/smpc> (accessed on 19 February 2019).
- Saphner T, Tormey D, Gray R. Venous and arterial thrombosis in patients who received adjuvant therapy for breast cancer. *Journal of Clinical Oncology* 1991; 9(2):286-294. <https://doi.org/10.1200/JCO.1991.9.2.286>
- Hazanov N, Somin M, Attali M, Beilinson N, Thaler M, Mouallem M. et al. Acute renal embolism. *Medicine* 2004; 83(5):292-299. <https://doi.org/10.1097/01.md.0000141097.08000.99>
- Suzer O, Shirkhoda A, Jafri S, Madrazo B, Bis K, Mastromatteo J. CT features of renal infarction. *European Journal of Radiology* 2002; 44(1):59-64. [https://doi.org/10.1016/S0720-048X\(01\)00476-4](https://doi.org/10.1016/S0720-048X(01)00476-4)
- Mulloy B, Barrowcliffe T, Gray E. Heparin and low-molecular-weight heparin. *Thrombosis and Haemostasis* 2008; 99(11):807-818. <https://doi.org/10.1160/TH08-01-0032>
- Levine MN, Raskob G, Landefeld S, Kearon C. Hemorrhagic complications of anticoagulant treatment. *Chest* 2001; 119(1):108-21. [https://doi.org/10.1378/chest.119.1\\_suppl.108S](https://doi.org/10.1378/chest.119.1_suppl.108S)
- Raunso, J, Selmer C, Olesen JB, Charlot MG, Olsen A-MS, Bretler D-M. et al. Increased short-term risk of thromboembolism or death after interruption of warfarin treatment in patients with atrial fibrillation. *European Heart Journal* 2011; 33(15):1886-92. <https://doi.org/10.1093/eurheartj/ehr454>
- Coleman CI, Haas S, Turpie AG, Kuhls S, Hess S, Evers T. et al. Impact of switching from a vitamin K antagonist to rivaroxaban on satisfaction with anticoagulation therapy: the XANTUS-ACTS substudy. *Clinical Cardiology* 2016; 39(10):565-9. <https://doi.org/10.1002/clc.22565>

## INKSTŲ ARTERIJOS TROMBOEMBOLIJA IR JOS SUKELTAS INKSTO INFARKTAS: APENDICITĀ IMITUOJANTIS ŠONO SKAUSMAS I.Šidiškienė, Ž.Barauskas, L.Minkevičiūtė

Raktažodžiai: inkstų arterijos tromboembolija, prieširdžių virpėjimas, šono skausmas, apendicitas.

Santrauka

Inkstų arterijos tromboembolija (IATE) – reta ir rimta būklė, dažnai sukelianti diagnostinių problemų. Kiekvienas gydytojas, savo darbe susidūręs su sunkiai paaiškinamu šono skausmu, ypač esant rizikos veiksniams, turėtų prisiminti šią patologiją. IATE gali sukelti dalinį arba visišką inkstų infarktą, todėl būtina ankstyva diagnostika bei adekvatus gydymas. Šiuo tikslu pristatome klinikinį atvejį bei literatūros apžvalgą, apimančią dažniausius IATE simptomus, rizikos veiksnius, diagnostikos bei gydymo ypatumus, prevenciją.

Adresas susirašinti: bar.zilvinas@gmail.com