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MACROHEMATURIA IN THE COURSE OF RIVAROXABAN THERAPY: A CASE OF BLADDER TUMOUR

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Introduction. Rivaroxaban is an oral anti-coagulant that has been approved by the FDA for secondary prevention after acute coronary syndrome [1]. It's a non-vitamin K antagonist that selectively inhibits factor Xa. As it does not require routine check-ups to adjust dosage according to coagulagram monitoring and checking of International Normalised Ratio (INR), it can be more convenient to the patient.Anti-Xa agents rivaroxaban doesn't require laboratory testing for dose adjustment [2, 4].

One of the most common side effects of using this drug is macroscopic hematuria. But there are several other conditions that can present with macroscopic hematuria such as urological malignancies including Bladder Cancer. Recurrent macroscopic hematuria presents with a multitude of differentials. One of the most common causes is urinary tract infection and urinary tract stones but it typically presents with pain. This also may be the only sign of an underlying urological malignancy.It isn't rare for patients on anticoagulant therapy to have visible hematuria Macroscopic hematuria may be present in benign causes such as benign prostatic hyperplasia, urinary tract calculi and urinary tract infections

Bladder cancer is the tenth most common cancer worldwide and the most common cancer of the urinary tract . The most predominant presenting symptom in 80% of patients is hematuria which is usually gross, painless and intermittent in nature. Some of the independent risk factors for the presence of bladder cancer

include; male sex, advanced age or age over 60 years and macrohematuria. Bladder cancer is the most frequent of urological cancer to be diagnosed in patients presenting with visible hematuria.

This report outlines the case of a patient on long term rivaroxaban therapy who developed macroscopic hematuria, not as a consequence of the medication but rather due to bladder cancer. Eventhough anticoagulation therapy induced hematuria is common, this report serves to highlight the importance of considering other urological conditions that may present similarly. Written informed consent was obtained from the patient and the CARE framework was followed in the drafting of this case report[5].

Aim of the study. The aim behind this research is to raise awareness of the increase in bladder cancer and the need for a proper diagnostic algorithm for patients presenting with visible hematuria. Further, to prevent the frequency of misdiagnosis and for better understanding of the pathophysiology.

It is also necessary to conduct more research on the likelihood of rivaroxaban therapy acting as a risk factor in bladder cancer.

Materials and methods. Since the research is based on a clinical case report, the patient's clinical data was obtained from the "4D Client" database of the nephrological department at the Regional Hospital of Grodno. Prior to accessing patient's information, consent was taken in a written form.

Results and discussion. A 69-year old man presented to the nephrological department with fluctuations in blood pressure, frequent urination and brown urine. Deterioration of health had started three days ago. The patient has a past medical history of type 2 Diabetes Mellitus, Arterial Hypertension, Coronary Artery Disease complicated by Myocardial Infarction (in 2018) for which he has undergone coronary artery bypass grafting as well as stenting of coronary artery. Family history for oncological diseases were absent. The patient has no relevant psychosocial history.

On a daily basis, he takes Valsartan 80/12.5mg two times a day and Bisoprolol 2.5mg once a day as antihypertensive medication. Metformin 1500mg per day for control of Diabetes, Rosuvastatin 20mg per day as a lipid lowering agent and Molsidomine 2mg a day for stenocardia is also taken. Rivaroxaban 20mg per day has been taken for anti-coagulation purposes for about 7 months at the time of admission.

Upon examination of the patient, he was conscious and alert, with a rhythmic pulse of 78 beats per minute. Respiratory rate was 17 breaths per minute, blood pressure was measured as 130/80 mmHg, oxygen saturation of 97% on room air. He has a hypersthenic body constitution with a BMI of 38.7 (Obese class II). No lymphadenopathy was noted. Lung sounds were clear and heart sounds were muted and rhythmic upon auscultation. Renal angle tenderness was absent. The rest of the examination yielded no significant findings.

Haematological investigations were performed, revealing increased Erythrocyte Sedimentation Rate (ESR) and Normocytic Normochromic Anaemia. Biochemical Analysis showed a markedly elevated C-Reactive Protein and Increased Uric acid. Urine analysis revealed dark yellow colour, decreased pH and presence of epithelial

cells. Coagulogram results were within normal limits. Although the patient complained of frequent urination, his diuresis was within normal limits.

Relevant Instrumental investigations included Ultrasound which showed the presence of a hypoechoic formation (41x37x40mm) with clear, uneven contours along the posterior wall of the bladder. Slight prostate enlargement was also noted and was confirmed to be Benign Prostatic Hyperplasia (BPH) Grade II. Further investigation using Multi-Slice Computer Tomography (MSCT) visualised a hyperdense structure with uneven contours in the lumen of bladder along the posterior wall that did not accumulate a contrast agent.

Other differential diagnoses considered were macroscopic hematuria caused by BPH but as Prostate Specific Antigen was within normal levels (1.1 ng/ml; normal levels should be 4.0 ng/ml and lower), this diagnosis was excluded.

Upon admission, rivaroxaban was discontinued and was replaced by aspirin. Aspirin,an antiplatelet agent was recommended as studies show lesser complication related hematuria The patient was recommended to undergo Transurethral resection (TUR) of bladder as both a diagnostic and therapeutic intervention. The formation confirmed by imaging studies was resected and sent for histopathological analysis and the result revealed the presence of a papillary urothelial carcinoma with low malignant potential (T1N0M0). The patient had no post operative complications and his condition was satisfactory. The patient was discharged with recommendations to a follow up with oncologist and instrumental testing in a month.

Conclusion. Patients on long-term anticoagulant therapy, presenting with bleeding from the urinary system is very common. Regardless, it's always necessary to eliminate other possible, more dangerous causes by performing proper diagnostic assessment of hematuria before arriving at the conclusion of it being medication-induced. Also, not all patients will have typical risk factors for bladder cancer, much like this patient. It is important to always consider the possibility of such situations and careful evaluation of all patients is necessary.

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