Hereditary hemorrhagic telangiectasis (Rendu-Osler-Weber syndrome) and atrial fibrillation – is it ever too late to do something?!

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Introduction: Hereditary hemorrhagic telangiectasia (HHT), also known as Rendu-Osler-Weber disease, is an autosomal dominant inherited disorder, the second-most-common inherited bleeding disorder. Mutations in three genes involved in the TGF-β signaling pathway may occur, leading to disrupted angiogenesis and the formation of fragile and tortuously dilated capillaries and postcapillary venules. The resulting vascular lesions are classified into two groups: arteriovenous malformations (AVM) and telangiectasias. Anticoagulant therapy in patients with permanent atrial fibrillation (AF) and this syndrome presents a challenge in clinical practice and requires a multidisciplinary approach.[1-10]

Case report: We present the case of a 70-year-old female patient who has had recurrent epistaxis since childhood and, since the age of 50, has been evaluated at the University Hospital Centre Zagreb due to frequent gastrointestinal bleeding-undergoing multiple thermocoagulation of gastrointestinal angiodysplasias. In 2013 AF was diagnosed, but she was not referred for ablation therapy and anticoagulant therapy was not introduced due to frequent bleeding. Family history reveals that the patient's mother, brother, niece and younger daughter also have telangiectasias. The first hospitalization was in January 2023 with symptoms of heart failure (HF) due to anemia with clearly visible telangiectasias which were noted (**Figures 1** and **2**). Echocardiography results were consistent with dilated cardiomyopathy, volume overload of the left ventricle with signs of high-output syndrome, a significantly dilated left atrium, and dilation of the right heart chambers with significant tricuspid and moderate mitral regurgitation as hemodynamic manifestations of hereditary hemorrhagic angiodysplasia. MSCT confirmed multiple arteriovenous malformations in the liver (**Figure 3**), as well in the lower right lung lobe, measuring 25x21x26 mm (**Figure 4**). No such malformations were found in the brain. After optimizing HF therapy and correcting chronic iron deficiency with parenteral iron, given the high ischemic risk and high bleeding risk, the patient was referred to a hematologist at the Dubrava University Hospital, where treatment with bevacizumab was initiated (April to September 2023), achieving a good therapeutic response. A subsequent reevaluation was conducted to assess the possibility

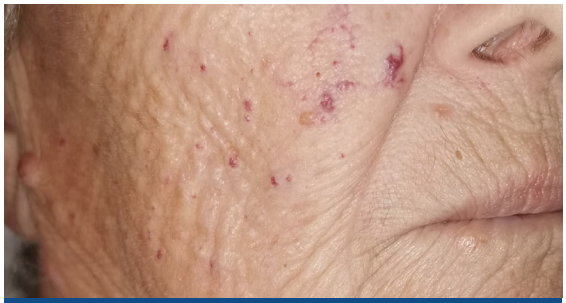

FIGURE 1. Face telangiectasias.

FIGURE 2. Fingertips angiodysplasias.

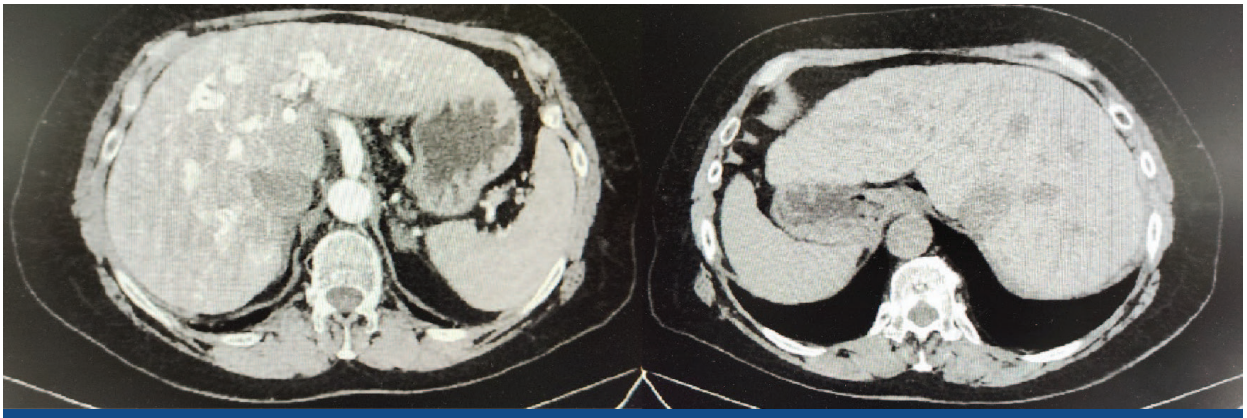

FIGURE 3. Multiple liver arteriovenous malformations.

of left atrial appendage occlusion, which was performed in December 2023, with the implantation of an Amplatzer Amulet 22 mm device. Post-procedurally, the patient received dual antiplatelet therapy for six weeks. Due to frequent episodes of epistaxis and the need for red blood cell transfusions, a follow-up transesophageal echocardiography was performed in January 2024, which ruled out leakage and thrombosis, so dual antiplatelet therapy was discontinued. The patient has remained clinically stable in terms of HF, with no thromboembolic complications. Continuous follow-up with a hematologist and cardiologist is ongoing, alongside optimized HF therapy. Further therapeutic options for AVM will be reevaluated.

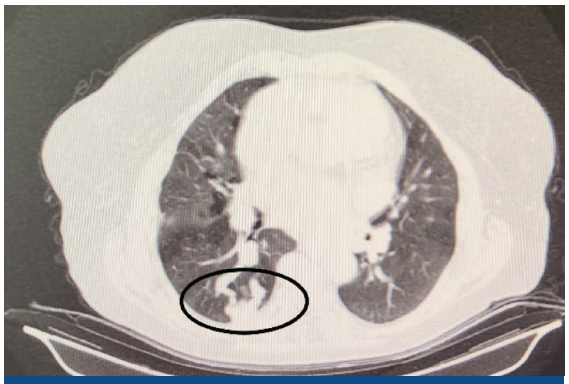

FIGURE 4. Large lung arteriovenous malformation.

Conclusion: In a female patient with permanent AF who has developed symptoms of HF - both as part of permanent AF with a clinical presentation of HF with preserved ejection fraction and as part of chronic anemic syndrome, along with multiple arteriovenous malformations and developed high-output syndrome - it is challenging to choose the optimal treatment strategy for stroke prevention while simultaneously managing bleeding. According to two studies conducted on patients with HHT, the use of bevacizumab (a monoclonal IgG antibody that inhibits vascular endothelial growth factor – VEGF) has yielded excellent results in reducing epistaxis. Similar experiences have been reported in Croatia. Despite potential benefits, data regarding the use of left atrial appendage occlusion (LAAO) in HHT patients with non-valvular atrial fibrillation (NVAF) is scarce and need further investigation, but LAAO might represent a promising non-pharmacological alternative to prevent thromboembolic events in patients with HHT and NVAF.

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