Letter to the Editor

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Venous Sinus Thrombosis – Women's Disease?

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Cerebral venous thrombosis (CVT) is a rare disease, representing 0.5 - 1 % of all strokes, with annual incidence ranging from 1 - 2 per 100 000 [1,2]. CVT is more common in females than males (3:1) with the highest incidence in young women [1]. The incidence in women aged between 30 and 50 years is 3 per 100.00 people per year [1]. Gradual increase in the incidence is observed during the last years with increasing incidence by 5 % annually [2].

Guidelines recommend acute treatment of CVT with low molecular weight heparin (LMWH) or unfractionated heparin (UFH), and switching to warfarin as a standard treatment regime [3-6,7,8]. Standard of care treatments are consensus-based, derived mainly from the observational studies. Direct oral anticoagulants (DOACs) were proven to be as effective but safer compared to warfarin in patients with venous thromboembolism, but they are not first line therapy in CVT yet. Data on DOACs usage for CVT in clinical practice is scarce, several prospective multicentre randomized clinical trials (RCTs) are running [9-11]. A recently published meta-analysis on DOACs in CVT by Nepal and associates showed that DOACs in CVT are similarly effective and safe compared to warfarin with better recanalization rates [12]. Enrolment into RCTs on DOACs usage in CVT is slow due to the rarity of the disease. It is not suggested to use DOACs in pregnancy, breastfeeding and in antiphospholipid syndrome. The duration of anticoagulation treatment according to American Health Association/American Stroke Association (AHA/ASA) and European Stroke Organization (ESO) guidelines recommend treatment of provoked CVT for 3-6 months, for un-provoked CVT 6-12 months and if severe thrombophilia or recurrent venous thromboembolism was found for the indefinite duration of time [7,8]. Treatment of CVT during pregnancy is still a big challenge for clinicians.

In women association with pregnancy, puerperium, hormonal contraception or hormone replacement therapy are sex-specific risk factors [13]. CVT accounts approximately 1/3 of pregnancy-associated strokes with an incidence of 9/100.000 pregnancies [13]. Oral contraceptives (OC) are a contributing factor in up to 70 % of cases, additionally it is known that there is a synergistic effect of obesity and OC [14]. Independent risk factors in the puerperium are excessive vomiting, infections, caesarean delivery, increasing maternal age and arterial hypertension [13]. General factors increasing the risk for CTV are genetic thrombophilia (factor V Leiden, prothrombin gene mutation, protein C and S deficiency), anaemia, malignancy, systemic diseases, concomitant infections, smoking, trauma or surgery [13]. Clinical symptoms of CVT usually start subacutelly with headache, epileptic seizures, focal symptoms, visual loss or mental status disorders [13].

Treatment with warfarin is still the recommended therapy [3-6]. DOACs were proven to be as effective but safer compared to warfarin in patients with venous thromboembolism, but they are not first line therapy in CVT yet. Data on DOACs usage in CVT in clinical practice is scarce, several prospective multicentre RCTs are running [9-11]. Latest meta-analysis on DOACs and CVT showed that DOACs have better recanalization rates compared to warfarin [12]. More data is needed to place DOACs as first line therapy in patients with CVT. Due to current known data DOACs could not be the treatment strategy in pregnancy, breastfeeding or in patients with antiphospholipid syndrome [5]. During COVID epidemic some patients suffered CVT due to COVID infection itself and CVT associated

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with vaccination is also a well-known predisposing factor. Vaccine-induced thrombotic thrombocytopenia (VITT) after vaccination against COVID-19 is a rare but devastating adverse event following adenoviral vector-based vaccinations for COVID-19 [15]. VITT treatment include anticoagulation with a non-heparin-based anticoagulant [15]. Supportive therapy in CVT constitutes of hydration, headache and seizure management and treatment of increased intracranial pressure, including decompressive craniectomy when malignant mass effect from oedema or intracranial haemorrhage (ICH) occur [3-6]. The duration of anticoagulation treatment according to AHA/ASA and ESO guidelines is 3-6 months for provoked CVT, 6-12 months for un-provoked and if severe thrombophilia or recurrent venous thromboembolism was found for the indefinite duration of time [7,8].

Mortality rate of CVT has fallen during the last years due to better diagnostic work up and earlier appropriate treatment [13]. 10 - 15 % of patients still have modified Rankin score (mRS) 3-6, but majority have good functional outcome [13]. Worse prognosis is described in older age patients, male, when ICH is present at admission and if patient has depressed level of consciousness at the presentation [14]. The most frequent complication of CVT is arteriovenous fistula. Due to data women have better prognosis [13].

CVT is a rare disease. Women are more often affected than man and there are well known sex-specific risk factors such as pregnancy, puerperium, OC or hormonal replacement therapy. Treatment of CVT consists of anticoagulation therapy and supportive therapy. Prognosis has improved during last years with better outcome in females.

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