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Warfarin for Headaches?!

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Warfarin for Migraines?!

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Introduction

- Headaches, esp. Migraines have been extensively reported in Antiphospholipid syndrome (APS)/ Antiphospholipid antibodies (aPL)-positive patients.
- APS associated headaches are often untreatable, poorly responding to analgesics or narcotics and occur for years before the diagnosis of APS. (1)
- Many therapeutic agents/strategies such as hydroxychloroquine, B-cell inhibition, complement inhibition and peptide therapy have been proposed to manage thrombotic APS.
- Heparin followed by Long-term anticoagulation with warfarin remains the cornerstone of treatment. (2)

Case Report

- 36-year-old Caucasian female with past medical history significant for Tumid Lupus Erythematosus treated with Hydroxychloroquine, Fibromyalgia and remote history of Irritable Bowel Syndrome with no history of Thrombosis, miscarriages, fetal death or preeclampsia.
- Presented with Severe headaches, 8/10 intensity for the last 4 years. Headaches reported as migraines with stabbing pain, occasionally localizing to right side.
- Patient had undergone extensive workup by Neurology as well as Rheumatology including a normal Lumbar Puncture and multiple normal MRI brain. Blood work showed Lupus Anticoagulant positivity.
- Various treatments for symptomatic Headaches without any significant improvement were tried. The patient was then started on Warfarin Therapy by Rheumatology which significantly relieved the symptoms.
- Later, when warfarin was discontinued by the neurologist, who the patient saw for a follow up, it resulted in worsening of the headaches.
- The headaches resolved again on restarting the Warfarin Therapy.

Pathogenesis

- Alteration in platelet function during a migraine attack with the binding of aPL on platelet membrane phospholipids, namely phosphatidylserine, phosphatidylcholine, and sphingomyelin, leads to Platelet activation. (3)
- The lipid composition of platelet plasma membrane is abnormal in migraine patients. An increase in membrane cholesterol-to-phospholipid ratio is associated with platelet activation. (4)
- LA may be involved in migraine pathogenesis by interacting with neuronal phospholipids such as sphingomyelin. (5)
- Presence of aCL (Anticardiolipin) IgM or LA (Lupus Anticoagulant) was significantly associated with migraine in PAPS (Primary APS) patients. (6)

Imaging

- Patients with hemiplegic migraine or those with known history of migraine presenting with signs of stroke may demonstrate areas of infarction.
- Migraine sufferers with elevated aPL but without hemiplegia or signs of infarction rarely show findings on imaging studies such as computerized tomography (CT), magnetic resonance imaging (MRI) or cerebral angiogram.

Associated clinical features

- Many non-thrombotic neurologic diseases are related to APS and may range from focal lesions to diffuse dysfunction, part of which are migraine, cognitive and memory deficits, extrapyramidal symptoms behavioral and seizures.
- Authors suggest that aPL may be associated with migraine that is commonly followed by an ischemic stroke. (9)

Management

- One of the most prominent clinical considerations is the complete resolution of headaches after anticoagulation with heparin or warfarin for thrombosis treatment.
- A 2- to 3-week therapeutic trial of low molecular weight (LMW) heparin has been used in many APS cases where severe headaches were prominent.
- Multiple studies reported that heparin therapy reduced the frequency and severity of migraine attacks. (7, 8)

Highlights

- Headaches and **Migraines** in particular are common in **APS** and aPL-positive patients.
- The pathogenesis of APS headaches is unclear, but it could be related to **Platelet dysfunction**.
- APS patients with severe refractory migraine show very good response to **Warfarin therapy with INR goal of 2.5-3.5** (9)

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