EDİTÖRE MEKTUP LETTER TO THE EDITOR

A CASE OF SNEDDON'S SYNDROME WITH FACTOR V LEIDEN MUTATION AND PROTEIN S DEFICIENCY-LETTER TO THE EDITOR.

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Sir,

A 31 year-old woman was applied to our University hospital neurology outpatient clinic with the complaint of expressive aphasia and gait ataxia while using acetylsalicylic acid: 300 mg/day regularly. Expressive aphasia, left 12th cranial nerve involvement and gait ataxia to the left side were found in her neurological examination and had diagnosed transient ischemic attack (TİA). In her physical examination Raynaud's phenomena and patches of livedo reticularis, which extended across her lower back, thighs and bilaterally dorsal hands (Fig 1) were seen. Her medical story was notable for previous TİA attacks, hypertension (HT), and pregnancy with intrauterine growth restriction child and dead born. She had a 10 years old healthy boy. Her father had died with myocardial infarction when he was 35 years old.

Her brain Magnetic Resonance Imagine (MRI) detected numerous, scattered cortical, subcortical ischemic lesions and lacunar infarctions in centrum semiovale (Fig2). Doppler and cardioechographical findings were not indicate any etiologic factor for cardiac or cervical vascular embolus.

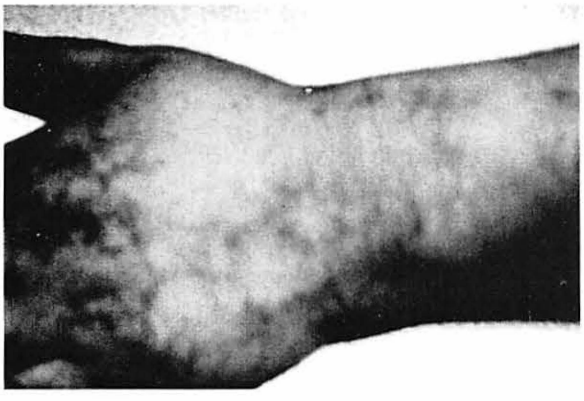

Figure 1: Patches of livedo reticularis on dorsal hand.

In laboratory examination; Cell Blood Cell count (CBC), sedimentation rate, and routine biochemistry values and blood homocysteine level were all in their normal ranges. Coagulation tests

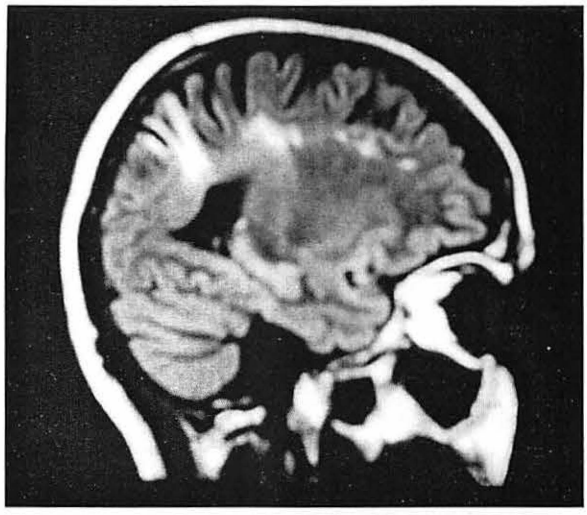

Figure 2: MRI: Subcortical ischemic lesions.

including detection of antithrombin III, rheumatoid factor, Anti Nuclear Antibody (ANA), Anti-ds DNA, Anticardiolipin antibody (ACA) IgM and IgG, p and c-antineutrophil cytoplasmic antibodies (p ANCA, c ANCA) and Lupus anticoagulant were all negative. Protein C: 75 (N: 70-130) and Antithrombine III: % 89 (N: 86%-120%) both were in normal range but Protein S: 57 (N: 60-140); Activated protein C resistance (APC- resistance): 103 (N: 120-130) were both reduced. She had no gene mutations including PT 20210 G-A: G/G (N: G/G) and MTHF2 677C-T: C/C (N: C/C) but DNA analysis with micro-array showed Factor V Leiden hetereozygot mutation: [FV 1691 G-A: G/A (N: G/G)].

The diagnosis of the patient was Sneddon's syndrome (SS) with the etiologic factors of Factor V Leiden mutation, Protein S deficiency and APC-resistance. Anticoagulation therapy with warfarin was added her treatment. Yet, she has been using warfarin and acetylsalicylic acid with no further neurological problems in 2 years. SS is associated with cerebral ischemic events, livedo and is caused by vascular thrombosis (1). Despite several thrombophilic conditions have been implicated, it

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is often associated with primitive antiphospholipid syndrome (2). Isolated or multiple infarcts can be seen in computerized tomography (3). Thrombosis of cerebral vessels has been noticed in few cases reaching autopsy so a thrombotic process is thought likely even in the absence of antiphospholipid (aPL) (4,5).

Miscellaneous clotting abnormalities have been previously reported in isolated cases of aPL- negative patients such as homozygous factor V leiden mutation (4,6,7), increased platelet aggregability (8), increased b- thromboglobulin levels (9), modifications of the tissue plasminogen activator/inhibitor ratio (10), familial deficiency in antithrombin III (11), increased amounts of antithrombin III (3), dysfibrinogenemia (2), activated protein C resistance (7), impairment of coagulation factor VII and free protein S (12).

Patients with factor V leiden mutation have a single point mutation of factor V gene Arg506Gln or R506Q leading to activated protein C resistance and reduced anticoagulant effect of the protein C/ S natural inhibitor system (4).

The prevalence of heterozygous factor V Leiden mutation in aPL negative patients with sneddon syndrome was 19 % in Besnier R et al. series (4).

Normally, the protein C system becomes activated when thrombin binds to thrombomodulin. This pathway regulates the activity of clotting factors Va and VIIIa. Disruption of this pathway results in a potentially hypercoagulable state (13). Furthermore association between APC resistance and venous or arterial disease have been reported recently (14,15). In addition Schellong et al. (12) reported protein S deficiency in four Sneddon's syndrome patients, protein C deficiency in two patients and factor V Leiden mutation in two patients in their series.

In the light of our case and other cases we could say that coagulation disorders have been proposed as an etiologic factor of Sneddon's syndrome.

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