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UNUSUAL CLINICAL SCENARIO - FACTOR VII DEFICIENCY PRESENTING AS ACUTE ISCHEMIC STROKE

Neurology

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ABSTRACT

We report a case of 77 year old female who presented with left MCA territory infarct within the window period. IV tPA was deferred in view of elevated INR and patient underwent DSA which revealed distal branch occlusion of the left MCA superior division. Persistently deranged INR was further evaluated for coagulation factor deficiencies which revealed factor VII deficiency. Inherited factor VII deficiency is a rare inheritable haemorrhagic disease affecting 1/500,000 individuals. Thrombosis in patients with hereditary bleeding disorders are uncommon. We report a case of unusual and rare thrombotic presentation of inherited bleeding disorder and review its treatment and prevention guidelines.

KEYWORDS

Factor VII deficiency, Acute ischemic stroke, Hereditary haemorrhagic disease.

INTRODUCTION:

Factor VII deficiency is an uncommon coagulation disorder that could be inherited as an autosomal recessive trait or be acquired because of cirrhosis of liver or drugs (antibiotics, warfarin, Anti Thymocyte Globulin etc.). Inherited disorders of blood coagulation factors are usually present with bleeding diathesis in the form of multiple petechiae, ecchymosis and excessive bleeding during menses or prolonged bleeding after any injury. However thrombotic events in this disorder are exceedingly rare.

CASE REPORT:

A 77 year old female had medical history of Parkinson plus, Hypertension, diabetes, hypothyroidism, CAD-post angioplasty, Sick Sinus Syndrome - post-Permanent Pacemaker Implant in situ and longstanding NVAF had presented to the emergency with abrupt onset weakness of right upper and lower limb with inability to speak since 3hrs. Examination revealed a conscious, alert patient with global aphasia . B/L pupil were 2mm symmetrical with normal reaction to light. Motor power in right upper limb and right lower limb was 0/5. Right plantar response was extensor. Mild cog-wheeling and hypomimia was also observed. NIHSS at admission -20/42. Patient had long standing history of NVAF for which patient was on warfarin, which was withheld in view of INRs being in ranges from 1.5 – 6 even on low doses of warfarin and subsequently patient was managed with apixaban. Apixaban was withheld 1 week prior to the episode due to a trivial fall and facial injury (INR- 2.7). Urgent NCCT head performed which revealed left MCA hyperacute infarct with ASPECT score of 7/10 (Figure. 1).PT-INR was sent prior to decision for IV tPA due to longstanding deranged PT-INRs. INR was 2.1, hence IVtPA was deferred. Urgent CT angio brain and neck vessels revealed short segment thrombosis in distal M2 segment of left MCA territory. Urgent DSA (Figure. 2) was performed which revealed distal occlusion of branch of superior division of left MCA. Mechanical thrombectomy was also deferred in view of distal vessel occlusion with deranged INR with recanalization of MCA.

2D Echo revealed dilated left atrium (4cm) and left ventricle with global hypokinesia with LVEF 38%. Carotid Doppler was normal. Repeat NCCT head revealed evolutionary changes in acute infarct in left MCA territory involving the parasylvian and left frontal cortex with loss of grey-white matter differentiation. USG and Fibroscan excluded any possibility of cirrhosis of liver with negative viral markers. Perusal of her reports of PT-INR had revealed elevated INR in range of 1.5- 6 since last few years while she was on apixaban. Further evaluation with coagulation profile revealed normal Factor IX assay (>150). Factor VII was low (8%).Serum Procalcitonin was 0.08. ntPro-BNP was 1444. Patient showed improvement in her neurological status to a conscious state with fair comprehension to speech with improvement in her motor power of right upper limb and right lower limb 3-/5. CT angio head and neck revealed left MCA territory infarct without any significant luminal narrowing of circle of Willis, CCA, ICA, ECA with mild atherosclerotic changes with possible recanalization of short segment thrombosis in M2 branch of left MCA was seen as compared to the previous scan (Figure. 3a;3b). She was managed with aspirin, LMWH in DVT preventive dosage, statins, anti-arrhythmics, thyroxine.

No history of excessive bleeding was reported and there was no reported family history of coagulation disorder. Apixaban was started for NVAF. She remains well with no recurrence of stroke or clinical bleeding during the follow up in past 3 months with NIHSS of 6/42.

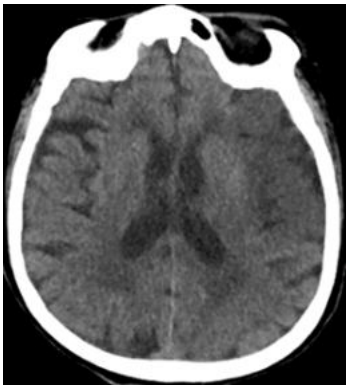

FIGURE 1. Left MCA territory infarct with early ischemic changes.

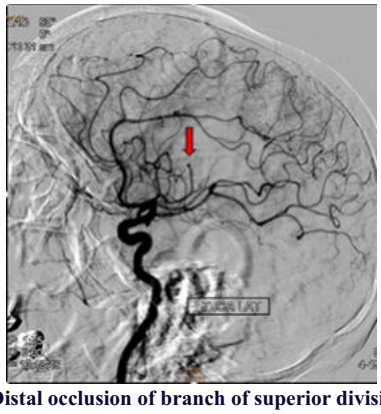

FIGURE 2. Distal occlusion of branch of superior division of left MCA.

DISCUSSION:

- Factor VII deficiency affects 1/500,000 individuals.(1,2) It usually presents with excessive bleeding during menses, surgeries or tooth extraction and has also been rarely reported to be associated with thrombotic events. Factor VII is reported as Factor VII activity, expressed as percentage, with normal activity being 50-150%.
- Common locations of thrombosis involve deep veins of lower limbs and pulmonary vasculature.(3,4,5) The exact mechanism of triggering thrombosis is unknown. Previous case series have

suggested that thrombogenicity was associated with old age, surgery, bed immobilization and replacement or substantial therapy, but conventional risk factors with an increased risk for thrombosis were found among all these patients.

- Haemorrhagic episodes are managed with the replacement of Factor VII or FFP supplementation, however therapy must be individualized and should take into account the past history of haemostatic challenges, family history of bleeding and thrombosis, just like the level of factor.
- The dilemma arises when patient with Factor VII deficiency presenting with ischemic stroke and requires anticoagulation.
- There are no recognized clinical management guidelines for managing these patients owing to the limited number of cases and undetermined pathophysiology for the thrombotic events. Following are the general consensus for the management of thrombotic episodes in patient with Factor VII deficiency.(6,7,8)
- Single/dual antiplatelets
- Anticoagulants that do not directly affect Factor VII such as direct oral anticoagulants, would carry less risk of bleeding complications and may be safer alternatives to warfarin to reduce the risk of thrombotic stroke in patients with atrial fibrillation and Factor VII deficiency Eg.dabigatran, rivaroxaban, apixaban and edoxaban .
- Thrombophilia screening to exclude co-existing pro-thrombotic defects and for all patients it is recommended to control known cardiovascular disease risk factors.

For mild deficiencies when patients are asymptomatic the use of antithrombotic prophylaxis must be considered with or without concomitant use of replacement therapy.

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