Arterial Thrombosis in “Protein C Deficiency”- A Rare Event

Arvind Mishra¹, MR Patil²

Abstract
We report here a case of a 35 year old male with protein C deficiency who presented with acute right sided hemiparesis with right sided facial palsy due to cerebral arterial thrombosis. He was treated with anticoagulation therapy and improved. This case is interesting as arterial thrombosis is rarely observed event in protein C deficiency.

Introduction
We report here a case of protein C deficiency presenting as right sided hemiparesis due to arterial thrombosis. Review of world literature revealed only few cases of arterial thrombosis due to protein C deficiency. Protein C is one of the vitamin K-dependent proteins that is synthesised in the liver and circulates in plasma as a serine protease zymogen.¹ It has an important role in the regulation of blood coagulation and fibrinolysis. Heterozygous protein C deficiency occurs in 0.2 to 0.4 percent of normal individuals, and is found in approximately 4 to 5 percent of consecutive outpatients with objectively confirmed deep venous thrombosis¹. Deep vein thrombosis (DVT) of the lower extremities and pulmonary embolism are the most frequent clinical manifestations.²,³ Arterial thrombosis seems to be uncommon, although ischaemic stroke and other arterial occlusive events have been reported.¹

Case Report
A 35 year old Male, farmer by occupation was admitted in the medical wards with complaints of weakness of right side of the body with facial deviation for 2 days. He noticed weakness in his right half of the body when he got up from the bed in the morning two days prior to the hospitalisation. During this 2 days period, he could carry out routine activities on 1st day and till afternoon of the 2nd day but his movements gradually got restricted by evening making him bed ridden by the end of 2nd day. In the mean time his wife also noticed facial deviation to left side. There was no history of fever, seizures, headache or trauma. He was not a known hypertensive or diabetic. Family history was not significant. He was non obese, non smoker and non alcoholic.

On Examination
He was fully conscious and oriented. Anaemia, jaundice and lymphadenopathy were absent. Pulse rate was 76 per minute, regular with no special character and all peripheral pulses were adequately palpable. BP 110/70 mm of Hg. Fundus examination was normal. CNS examination revealed right sided hemi paresis (power right upper limb grade 1/5, right lower limb grade 1/5) along with right sided supranuclear facial nerve palsy. Speech was slurred. No findings on sensory examination. Rest of the systemic examination was within normal limits.

Investigations
On investigations, routine parameters, Hb, total leucocyte count, platelet count, serum sodium, potassium, random blood sugar and serum creatinine were within normal limits. Liver function tests were also normal. Serum lipid profile did not reveal any abnormality. Trans-oesophageal echocardiography was also normal. Cerebrospinal fluid examination did not reveal any abnormality. Magnetic resonance imaging of cranium revealed isointense signals on T₁ weighted images and hyperintense signals on T₂ weighted along with FLAIR images which showed restriction on diffusion weighted imaging and with low ADC values in left temporal, basal ganglia, corona
radiata and central semiovule regions suggestive of acute infarcts (Figures 1 and 2). Vasculitic profile (ANA, P-ANCA, C-ANCA, RF) was done and it showed normal results. Thrombophilia profile revealed protein C functional -15.10% of normal (70.0-140.00), Protein S functional 82.00% of normal (70.00-150.00) and serum homocysteine was 10.4 µmol/l (0.0-15.0). Repeat thrombophilic profile after one month revealed protein C functional- 20% of normal (70.00-140.00). Patient was diagnosed as case of hypercoagulable state due to protein C deficiency leading to present vascular event. He was kept on anticoagulation therapy with warfarin and showed improvement with regaining of power of about 3/5 in both upper and lower limbs after 30 days of follow up.

Discussion

Hypercoagulable state is a condition in which a clearly identified alteration of the blood tends to shift the haemostatic balance to excess platelets/fibrin deposition and lead to arterial and venous thrombosis in response to vascular injury that would not trigger thrombosis under normal circumstances.1

The prevalence of protein C deficiency in healthy population is 0.2-0.4%, while in patients with DVT it is 3.7% and in patients with thrombophilia it is 4.8%.3 Protein C deficiency is an uncommon genetic abnormality that may be a contributory cause for thrombophilia, often in conjunction with other genetic or acquired risk factors. Protein C levels of less than 55 percent of normal (in the absence of oral anticoagulant therapy, vitamin K deficiency, or overt liver disease) suggest protein C deficiency.1 Deep and superficial venous thromboses are the most common clinical presentations of protein C deficiency. By age 45 years, up to 50 percent of heterozygous subjects in clinically affected families will have venous thromboembolism, and half of the episodes will be spontaneous2. Protein C deficiency has been linked to unusual sites of venous thrombosis, including the cerebral and mesenteric veins. Arterial thrombosis seems to be quite uncommon.1 The other genetic factors causing thrombophilia are factor V leiden mutation, Prothrombin G20210A, protein S and AT-III deficiency. Raised plasma homocysteine with methyl tetrahydrofolate reductase (MTHFR) mutations, ACA and LA are the other common risk factors for thrombophilia.1

Hereditary thrombophilia should be suspected mostly in venous and rarely in arterial vasculature in following conditions:3
1. Age < 45 years
2. Spontaneous/unprovoked thrombotic episodes
3. Recurrent thrombotic episodes without any obvious cause
4. Trivial trigger factors leading to life-endangering thrombotic episodes
5. Thrombosis at unusual sites, such as cerebral, mesenteric and upper limb venous thrombosis
6. Family history of thrombosis

Prior to labelling a patient with inherited protein C deficiency it is mandatory to rule out acquired causes of protein C deficiency like liver disease, vitamin K deficiency, renal insufficiency, disseminated intravascular coagulation (DIC), postoperative states with ARDS and patients on oral anticoagulants, all of which can cause low levels of these factors1. A thorough search for these acquired causes was made in our patient but none were detected. Multiple deficiencies are seen following acute thrombosis, hence, whenever more than one natural anticoagulant (protein C, protein S, AT-III, FVL, APCR) is found deficient it is essential to repeat an assay after 4-6 weeks to reconfirm the deficiency. If the patient is on oral anticoagulant therapy, the same should be withheld for at least two weeks and patient put on bridging heparin therapy prior to repeating an assay for all mentioned defects except AT, which is interfered with heparin therapy.4
He was managed by oral anticoagulation targeting INR at 2.5. He gradually improved and regained power in both limbs as mentioned above after 30 days after admission. At present he is under our constant observation and regular follow up and not showing any deterioration.

References