Hypereosinophilia as a Cause of Recurrent Stroke

Sir,

Hypereosinophilia is reported in the literature as an uncommon cause of stroke. It's neurological manifestations include encephalopathy and neuropathy.[1,2] As strokes can cause significant residual impairments, some of which are refractory to medical management, it is imperative for clinicians to be aware of this uncommon but treatable etiological factor for stroke.

Hypereosinophilia is defined as an absolute eosinophil count greater than 500 cells per cc [Figure 1]. It is further classified as mild, moderate and severe – with levels between 500-1500 cells/cc being mild, 1500-5000/cc being moderate and >5000/cc classified as severe hypereosinophilia. The criteria for hypereosinophilic syndrome include elevated eosinophil count greater than 500 cells/cc, in the absence of other secondary causes. An earlier requirement of persistent elevation of eosinophil count above 500 cells/cc for more than 6 months is no longer followed.[3]

The mechanisms by which eosinophilia can cause neurological dysfunction are multi-factorial, due to embolism from a focus of endomyocardial fibrosis or through endothelial dysfunction mediated by hypereosinophilia.[1,2,4,] In addition, hypereosinophilia may promote thrombus formation by the action of eosinophils through Major Basic Protein, Eosinophil Peroxidase (EPOX), Eosinophil Cationic Protein (ECP) and Eosinophil Derived Neurotoxin (EDN). Major Basic Protein affects activity of Heparin, EPOX reduces activity of Tryptase and Heparin and ECP reduces activity of Heparin and glycosylated forms of thrombomodulin.[4-6] Some other mechanisms also operate to cause a likely prothrombotic effect of hypereosinophilia.

We present a case of 41-year-old right-handed male, farmer by profession, without known co-morbidities (diagnosed as having hypertension upon admission in our unit), smoker (4-5 beedis/day for the last 15 years), non-alcoholic, presented to the rehabilitation out-patient services with weakness of right upper limb-RUL more than lower limb, slurring of speech and deviation of the angle of mouth to the left of 24 days' duration. The symptoms were sudden in onset with gradual motor recovery in the affected lower limb and no motor recovery in the RUL over the next three weeks post stroke. There were no symptoms or signs of sensory deficits, dysphagia, headache, vomiting, dizziness, chest pain, palpitations or dyspnea. No past history of respiratory illness or any skin condition was present. Detailed clinical examination revealed mild dysarthria, right sided facial palsy, spasticity in the right upper and lower limbs (Modified Ashworth Scale-1), 0/5 power in RUL (Medical Research Council-MRC scale), 3/5 power of right hip and knee extensors, 0/5 power of right ankle dorsiflexors and plantar flexors, brisk deep tendon jerks and Babinski 'upgoing' on the right side.

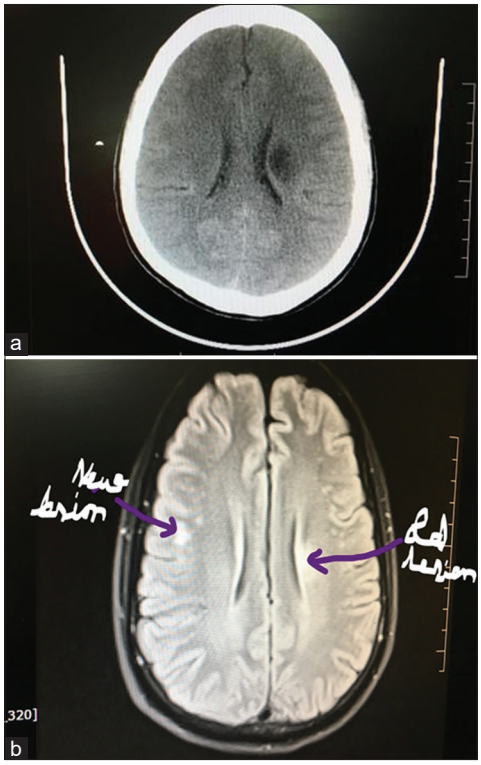

Figure 1: (a) MRI Brain showing left centrum semi ovale infarct. (b) MRI Brain T2 flair showing new lesion in right frontal lobe

Diagnostic work up revealed. Hemoglobin-11.5g/dl, Packed Cell Volume-38%, Total Count-7500 cells/cc, Differential Leucocyte Count-Neutrophils- 57%, Eosinophils-23%., Serum Homocysteine-10.5 micromoles/L, Vitamin B12->1500 ng/ml. Fasting Blood Sugar-95mg/dl, HbA_1C-5.5, Serum Aspartate aminotransferase (AST)-57 IU/L, Alanine aminotransferase (ALP)-71 IU/L, Blood urea 25 mg/dl, Serum Creatinine- 0.99 mg/dl. Anti-Nuclear Antibody, Anti Neutrophil Cytoplasmic Antibody profile- negative, Protein C, S levels and Antithrombin 3 levels showed no abnormality. Computed Tomogram (CT) Brain showed Left Centrum semi-ovale hypodensity. CT angiogram suggested normal study. Carotid Doppler was normal and two-dimensional Echocardiography suggested normal study.

He was admitted for in-patient rehabilitation with goals of achieving independence in ambulation and improving activities of daily living-ADL. He was continued on secondary stroke prophylaxis and started with anti-hypertensive medication (Amlodipine 5mg/day). On admission, his Scandinavian stroke scale score was 45 (maximum 58) and Barthel Index score was 50 (maximum 100).

After one week of admission, patient reported deterioration in the form of inability to walk without support. On examination, we observed deterioration in motor power of knee extensor (reduced to 2/5 from 3/5 on the MRC scale) and hypotonia in RUL. He was immediately referred to the department of Neurology. CT Brain was repeated which showed no new lesion. He regained lost strength within 24 hours and was transferred back to the rehabilitation unit. Four days after this episode, patient experienced new onset bilateral hearing loss, tinnitus, vertigo and incoordination while walking. Magnetic Resonance Angiography (MRA) showed no vascular anomaly but repeat Magnetic Resonance Imaging (MRI) of the brain with T2 weighted images showed hyperintensities in right high frontal lobe and left centrum semi ovale. Audiometry revealed moderate to severe bilateral sensorineural hearing loss. Repeat laboratory work up revealed an absolute eosinophil count of 2100 cells/cc.

Hematologist opinion was sought to consider eosinophilia as an etiologic factor for the recurrent episodes of neurological deterioration and onset of new symptoms. On his advice, peripheral blood smear (for malignant cells and hemoparasites) and stool (for cysts/ova and parasites) samples were sent. Ultrasound of abdomen (to look for possible organomegaly) was performed. No malignant cells or hemoparasites were identified on peripheral smear, no organomegaly on ultrasound of the abdomen and stool routine evaluation was negative for parasites. There were no skin lesions, respiratory symptoms or chest X-Ray findings to suggest Churg-Strauss syndrome.

Eosinophilia was managed with intravenous dexamethasone 4mg thrice daily for 3 days and empirical course of albendazole. Repeat eosinophil count after 3 days showed 0 cells/cc, Repeat audiometry showed improved hearing sensitivity and clinically patient regained lost power of the right lower limb, and was able to walk with improved coordination. His auditory complaints resolved completely. He was able to participate in the rehabilitation program. His discharge Scandinavian stroke scale score was 48, Barthel Index score-65. He was discharged with a maintenance dose of Prednisolone 60mg/day to be tapered gradually and maintained at 10mg/day pending repeat eosinophil count at 1 month. He was advised to continue with tablets ecospirin, atorvastatin and amlodipine. He reported back in the follow-up after 3 months. Repeat hemogram showed total leucocyte count of 7900 cells/cc and 9% eosinophils on the differential leucocyte count. He showed improvement in motor power of RUL as well, with recovery of grasp and release function of right hand. He was independent ambulator in the community.

Stroke is the most common neurological manifestation of hypereosinophilic syndrome, with favorable outcomes in those with focal deficits and good response to corticosteroids. Unfavorable outcomes are reported with altered mental status, cardiac abnormalities and persistent higher eosinophil counts.[2] The case we have described puts into perspective a patient with a normal routine 'stroke in young' work up with isolated moderate hypereosinophilia. He showed clinical recovery with corticosteroid and evidence of resolving nerve involvement with improved hearing sensitivity in both ears on audiometry as compared to the baseline test. This is consistent with the published literature. Physicians must be aware of this rare and treatable potential cause of stroke.

Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent forms. In the form the patient(s) has/have given his/her/their consent for his/her/their images and other clinical information to be reported in the journal. The patients understand that their names and initials will not be published and due efforts will be made to conceal their identity, but anonymity cannot be guaranteed.

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Conflicts of interest

There are no conflicts of interest.

Srikant Venkatakrishnan, Anupam Gupta, Meeka Khanna, Madhu Nagappa[1], Cecil Ross[2]

Departments of Neurological Rehabilitation and [1]Neurology, NIMHANS, Bangalore, Karnataka, [2]Department of Medicine, St. John's Medical College, Bengaluru, Karnataka, India

Address for correspondence: Dr. Anupam Gupta, Department of Neurological Rehabilitation, NIMHANS, Bangalore, Karnataka, India.
E-mail: drgupta159@yahoo.co.in

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