Sir,

Eales’ disease, first described by British ophthalmologist, Sir Henry Eales, in 1882,[1] is an idiopathic obliterative retinal periphlebitis, occurring in young adult males with a mean age of onset of 20-30 years (age range 11-40 years). It is more commonly seen in the Indian subcontinent (frequency of 1 in 135-200 ophthalmic patients reported from a referral eye hospital in India).[2]

It starts as an active perivenular inflammation associated with retinal hemorrhages, and hemorrhagic infarctions of the retina, in multiple quadrants, starting at or anterior to the equator and progressing posteriorly. It may also be associated with arteritis, papillitis or uveitis. Recurrent vitreous hemorrhage, tractional retinal detachment, rubeosis iridis, and neovascular glaucoma are its sequelae.[2] Bilateral eye involvement, simultaneous or sequential, may be seen in 70-80% of the cases. The pathophysiology is hitherto unknown, but hypersensitivity to tuberculin protein has been postulated based on epiretinal membrane polymerase chain reaction (PCR) studies.[3] The role of various proteins, retinal autoimmunity, HLA class I and II, oxidative stress, VEGF overexpression has also been studied.[4]

Various neurological manifestations have been described in Eales’ disease including subacute myelopathy, strokes, seizures and nonspecific white matter changes.[5-9] They can present within few days to several years after the onset of the disease and may precede the diagnosis in a few.

We report a 23-year-old male who presented with insidious onset, progressive, asymmetric spastic paraparesis, gait imbalance and bladder dysfunction, in the form of frequency, urgency and urge incontinence of 3 months duration.

A month later, he developed floaters in the right eye which gradually progressed to complete visual blurring in the right eye. It was not associated with painful eye movements or local signs of irritation. He did not report any neck or back pain, fever, cough, breathlessness, loss of weight or appetite, features of connective tissue disease, joint pain, joint swelling, skin rash, oral and genital ulcers, or a high risk behavior. His past and family history was unremarkable.

Examination revealed reduced visual acuity in right eye, (finger counting at 3 meters), hazy media, and a normal pupillary light reflex. He had asymmetric spastic paraparesis (Medical research council grade 4- to 4 in left lower limb, grade 4+ in right lower limb), with brisk deep tendon jerks and extensor plantar response. Joint position and vibration sense were impaired in both lower limbs with a positive Romberg’s sign.

On indirect ophthalmoscopy (IO) perivascular hemorrhages [Figure 1a] and perivascular sheathing [Figure 1b] involving

---

**Figure 1:** Panel (a), (b) Indirect ophthalmoscopy showing perivascular hemorrhages (black arrow head), perivascular sheathing (dashed black arrow). Hard exudates in the macular area (white arrow) and decreased perfusion in the superior and inferotemporal quadrant (black arrow); Panel c- Fluorescein angiography demonstrating abrupt cut off of vessels (curved white arrow), area of retinal ischemia (white arrow head) and dye leakage (dashed white arrow); Panel (d), (e)- MRI dorsolumbar spine (T2 Weighted image) showing two long segment cord hyperintensity extending from D9-D12 and involving conus (dashed white arrows), cross section showing more than 2/3rd cord involvement; Panel (f, g) – MRI Brain (T2 Fluid attenuated inversion recovery image) depicting periventricular hyperintensity (f) and periependymal hyperintensity around the fourth ventricle (g) (black arrow)
both arteries and veins, hard exudates [Figure 1b] and decreased perfusion of the superior and inferotemporal quadrants [Figure 1a and b], were seen which was suggestive of retinal vasculitis. Fundus fluorescein angiography (FFA) demonstrated abrupt cut off of vessels involving both arteries and veins, areas of ischemia and cuffing of vessels, suggesting perivascular inflammation [Figure 1c]. Contrast enhanced magnetic resonance imaging (CEMRI) of dorsolumbar spine revealed two non-enhancing hyperintensities (HI) with cord edema extending from D9 to D12 and involving the conus with more than 2/3rd intramedullary involvement [Figure 1d and e].

Patient was investigated further keeping in mind differentials of Longitudinally extensive transverse myelitis (LETM) [Table 1] with retinal vasculitis [Table 2].

Serum investigations are summarized in Table 3. Cerebrospinal fluid (CSF) was acellular, with 62.4 mg/dl protein and normal CSF: Plasma glucose ratio (0.53). Mantoux was positive (11 mm). Contrast enhanced computed tomography of chest and abdomen was normal. Pathergy was negative. He had positive proliferating cell nuclear antigen (PCNA) and PM-Scl antibodies. *PCNA is detected in low frequency in SLE[2] and PM-Scl is found in overlap syndromes. Clinically he did not have an overlap syndrome. Although Lyme’s antibody titre, serology for rickettsial diseases and PCR for pathogens in ocular specimens, were not done, in the absence of rash and retinal infiltrates or necrosis, clinically these possibilities were less likely.

Brain CEMRI revealed white matter hyperintensities along fourth ventricle and the posterior horn of the lateral ventricle [Figure 1f and g]. Serum and CSF was negative for anti-aquaporin 4 antibodies and our patient did not fulfill the international consensus diagnostic criteria for Neuromyelitis optica spectrum disorders. The pattern of cord and brain involvement with presence of hemorrhages in the fundus and absence of optic disc pallor did not favor a diagnosis of Multiple Sclerosis. Conus involvement in young males can occur in MOG-related diseases, but retinal vasculitis is not a feature of MOG. Susac syndrome characterized by encephalopathy, hearing loss and vision loss is a close differential of Eales disease but it shows branched retinal artery occlusion whereas Eales shows predilection for retinal veins, which was seen in our case.

With a negative work up for various etiologies of LETM and retinal vasculitis, Eales’ disease was considered as the probable diagnosis, and the patient given a 5-day course of 1 gram intravenous methylprednisolone, followed by slow oral taper of prednisone over 6 months. He also underwent laser photocoagulation in the right eye twice. At one year follow-up, his visual acuity was 6/12 in the affected eye and his power in his both lower limbs was MRC grade 5/5 and he was off corticosteroids.

Neurological involvement in Eales’ disease was first reported by Silverskoid in 1947[5] in three patients who presented with

| Table 1: Differential Diagnosis of Longitudinally extensive transverse myelitis |
|-----------------------------------|-------------------------------------------|
| 1. Demyelinating Disorders         | Neuromyelitis Optica                      |
| 2. Infectious Causes              | Acute disseminated encephalomyelitis       |
| 3. Paraneoplastic Disorders       | Multiple sclerosis                         |
| 4. Autoimmune didorsers           | Anti MOG associated encephalomyelitis      |
| 5. Vascular causes                | DNA Viruses                               |
|                                   | Herpes Simplex virus-1 (HSV-1)             |
|                                   | Herpes simplex virus-2 (HSV-2)             |
|                                   | Varicella-Zoster virus (VZV)               |
|                                   | Cytomegalovirus (CMV)                      |
|                                   | Human herpes viruses 6 and 7 (HHV 6 and 7) |
|                                   | Epstein-Barr virus (EBV)                   |
|                                   | RNA Viruses                               |
|                                   | Dengue virus                              |
|                                   | Influenza A virus                         |
|                                   | Human T-lymphotropic virus (HTLV)          |
|                                   | Hepatitis A and C virus                    |
|                                   | Bacteria                                  |
|                                   | Mycoplasma                                |
|                                   | Treponema pallidum                        |
|                                   | Mycobacterium tuberculosis                |
|                                   | Brucella                                  |
|                                   | Borrelia                                  |
|                                   | Actinomycenes                             |
|                                   | Fungal infections                         |
|                                   | Blastomyces dermatitidis                 |
|                                   | Coccidioides                              |
|                                   | Apergillus                                |
|                                   | Parasitic infections                      |
|                                   | Schistosoma                               |
|                                   | Toxoplasma                                |
|                                   | Cysticercus                               |
|                                   | Echinococcus                              |
| 6. Metabolic causes               | Systemic Lupus Erythematosus             |
|                                   | Sjogrens syndrome                        |
|                                   | Behcets                                   |
|                                   | Neurosarcoidosis                          |
|                                   | Antiphospholipid syndrome                 |
| 7. Radiation Myelopathy           | Spinal cord infarction                    |
|                                   | Dural Arteriovenous fistula               |
| 8. Postvaccination                | Vascular causes                           |
|                                   | Spinal cord infarction                    |
|                                   | Dural Arteriovenous fistula               |
| 9. Idiopathic                    | Metabolic causes                          |
|                                   | Vitamin B12 deficiency                    |
|                                   | Copper deficiency                         |
|                                   | 7. Radiation Myelopathy                   |
|                                   | 8. Postvaccination                        |
|                                   | 9. Idiopathic                             |
Letters to the Editor

Table 2: Differential diagnosis of fundus findings of retinal vasculitis

| Systemic causes            | Infections                  |
|----------------------------|-----------------------------|
|                             | Bacterial                   |
|                             | Viral                       |
|                             | Parasitic                   |
|                            | Rickettsial                 |
| Systemic inflammatory disorders |                           |
|                             | Behcet’s disease            |
|                             | Sarcoidosis                 |
|                             | Systemic lupus erythematosus|
|                             | Rheumatoid arthritis        |
|                             | Relapsing polychondritis    |
|                             | Sjogren’s                   |
|                             | Vasculitis                  |
|                             | Takayasu arteritis          |
|                             | Crohn’s disease             |
|                             | Buerger’s disease           |
|                             | Inflammatory myopathies     |
| Malignancies                |                             |
|                             | Leukemia                    |
|                             | Ocular lymphoma             |
| Others                     |                             |
|                             | Diabetes                    |
|                             | Sickle Cell Disease         |
|                             | Post vaccination            |
|                             | Multiple sclerosis          |
| Ocular causes               |                             |
|                             | Branch Retinal Ven Occlusion|
|                             | CRVO                        |
|                             | Dragged Disk Syndrome       |
|                             | Bird shot choroidopathy     |
|                             | Coat’s disease              |
|                             | Parsplanitis                |
|                             | IRVAN (Idiopathic retinal vasculitis, aneurysms, and neuroretinitis) |
|                             | Idiopathic central serous chorioretinopathy |
|                             | Retinal macroaneurysms     |
|                             | Idiopathic recurrent branch retinal arterial occlusion |
|                             | Acute multifocal hemorrhagic retinal vasculitis |
|                             | Frosted branch angiitis     |

Table 3: Serum Investigations

| Serum Investigations                          | Results          |
|-----------------------------------------------|------------------|
| Hemogram                                      | Normal           |
| Liver function test                           | Normal           |
| Kidney function test                          | Normal           |
| Erythrocyte sedimentation rate                | 10 mm/h          |
| Rheumatoid factor                            | Negative         |
| C reactive protein                            | Negative         |
| Creatine Phosphokinase levels                 | 292 IU/l         |
| Serum Angiotensin converting enzyme level     | Normal           |
| Hepatitis B virus surface antigen             | Negative         |
| Hepatitis C virus Antibody                    | Negative         |
| Human immunodeficiency virus test             | Negative         |
| Venereal Disease Research Laboratory test      | Negative         |
| Antinuclear Antibody                          | Negative         |
| Lupus anticoagulant, anticardiolipin antibodies and beta 2 glycoprotein 1 | Negative |
| anti-double stranded deoxyribonucleic acid (dsDNA) | Negative       |
| Anti-neutrophilic cytoplasmic antibodies (ANCA)| Negative        |
| U1SnRNP                                       | Negative         |
| Proliferating cell nuclear antigen (PCNA)     | Positive         |
| PM-Scl (Polymyositis- scleroderma)            | Positive         |

To conclude, Eales’ is an uncommon, idiopathic ophthalmological disease, and an important treatable cause of myelopathy with retinitis. Simultaneously, bearing in mind that it is a diagnosis of exclusion, an exhaustive workup is prerequisite before clinching on to its diagnosis.

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.

Financial support and sponsorship

Nil.

Conflicts of interest

There are no conflicts of interest.

Tanushree Chawla, Anu Gupta*, Kamakshi Dhamija*, Debashish Chowdhury
Department of Neurology, Govind Ballabh Pant Institute of Post Graduate Medical Education and Research (GIPMER), New Delhi, India
*Present address: Department of Neurology, All India Institute of Medical Sciences, New Delhi, India.

Address for correspondence: Dr. Tanushree Chawla, Department of Neurology, Govind Ballabh Pant Institute of Post Graduate Medical Education and Research (GIPMER), New Delhi, India.
E-mail: drtnshr.chaw@gmail.com

fairly rapidly progressive myelopathy along with pleocytosis in acute phase of Eales’ disease. White and Singhal and Dastur have also reported neurological involvement in Eales’ disease in their respective case series.

The development of myelopathy was found to be acute to subacute and dorsal spine was the most common site of involvement. Not much is known about the pathological findings in Eales’. Singhal and Dastur performed autopsy of one of their cases and postulated that Eales’ is a syndrome of “vasculopathy with episodic demyelinating retino-encephalo-myelopathy”, which develops as a result of hypersensitivity of retinal tissues to an unknown infective agent.
Letters to the Editor

REFERENCES
1. Eales H. Retinal haemorrhages associated with epistaxis and constipation. Brim Med 1880;9:262.
2. Biswas DJ, Verma DA. An update on Eales’ disease. Kerala J Ophthalmol 2007;19:8.
3. Madhavan HN, Therese KL, Gunisha P, Jayanthi U, Biswas J. Polymerase chain reaction for detection of Mycobacterium tuberculosis in epiretinal membrane in eales’ disease. Invest Ophthalmol Vis Sci 2000;41:822-5.
4. Biswas J, Ravi RK, Naryanasamy A, Kulanadi LT, Madhavan HN. Eales’ disease-current concepts in diagnosis and management. J Ophthalmic Inflamm Infect 2013;3:11.
5. Silfverskiold BP. Retinal periphlebitis associated with paraplegia. Arch Neurol Psychiatry 1947;57:351-7.
6. White RHR. The aetiology and neurological complications of retinal vasculitis. Brain 1961;84:262-73.
7. Singhal BS, Dastur DK. Eales’ disease with neurological involvement Part 1. Clinical features in 9 patients. J Neurol Sci 1976;27:3-21.
8. Anand SS, Das G, Chakraborty DP, Saha SP, Bose B. Eales’ disease with neurological complications. Neurol India 2013;61:428-9.
9. Irkec C, Capraz Yildirim I, Batur Caglayan HZ, Atmaca L, Karakus A. Eales disease with white matter lesions Open Access Sci Rep 2012;1:182.

Submitted: 09-Nov-2019   Revised: 19-Nov-2019   Accepted: 15-Dec-2019
Published: 29-Jun-2020

This is an open access journal, and articles are distributed under the terms of the Creative Commons Attribution-NonCommercial-ShareAlike 4.0 License, which allows others to remix, tweak, and build upon the work non-commercially, as long as appropriate credit is given and the new creations are licensed under the identical terms.

DOI: 10.4103/aian.AIAN_573_19