

PRESUMED EALES' DISEASE WITH NEUROLOGIC INVOLVEMENT

Report of Three Cases

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Purpose: To report three cases of presumed Eales' disease with neurologic lesions.

Methods: Case reports, systemic and neurologic evaluation, and magnetic resonance imaging.

Results: All three patients were young men who had seizures in the past; two had migrainous headache. Magnetic resonance imaging showed putaminal infarct in two cases and edema in the white matter of temporal cortex was noticed in one case. Clinical features in all these patients were suggestive of Eales' disease.

Conclusion: Ischemic infarction of the brain can be seen in clinically suspected cases of Eales' disease.

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Eales' disease is an idiopathic inflammatory venous occlusive disease primarily affecting the peripheral retina of young adult men. The essential features of Eales' disease are retinal periphlebitis, peripheral capillary nonperfusion, and retinal neovascularization. Etiopathogenesis of Eales' disease is unknown. No systemic disease has been found to be associated.¹ However, association of neurologic diseases such as multiple sclerosis,^{2,3} acute or subacute myelopathy,⁴ multifocal white matter abnormality,⁵ cerebral stroke,⁶ and chronic progressive noncompressive myelopathy⁷ has been reported. We now report on three patients whose clinical features mimicked Eales' disease and who had associated neurologic lesions. Two of them had seizures before ocular symptoms and the other after diagnosis of Eales' disease. In addition, two of them had migrainous headaches and one had isolated partial third nerve palsy. Magnetic resonance imaging

(MRI) of the brain showed putaminal infarct in two cases. In the third, MRI showed edema in the white matter and cortex in the left temporal lobe and in left insular cortex. The lesion was thought to be due to an ischemic insult.

Subjects and Methods

A total of 2569 charts of patients with Eales' disease seen in the outpatient department of Sankara Nethralaya, Chennai, between 1989 and 1998 were reviewed. Diagnosis of Eales' disease was made in patients between 15 and 40 years of age with evidence of one of three criteria: 1) peripheral retinal perivasculitis in either eye, 2) neovascular or fibrovascular proliferation at the level of retina or elevated into the vitreous cavity with or without tractional retinal detachment with perivasculitis in the same and/or the other eye, and 3) vitreous hemorrhage with perivasculitis in the same or the other eye. Laboratory and radiologic investigations were carried out to rule out tuberculosis, sarcoidosis, syphilis, sickle cell hemoglobinopathy, and collagen diseases. None of the pa-

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tients with systemic features suggestive of Behçet disease was labeled with Eales'. Patients with associated active or healed choroiditis, diabetes mellitus, or central or branch retinal vein occlusion were excluded. Criteria for diagnosis of Eales' disease have been described in our previous report.¹ Three patients were found to have a history of associated neurologic disease and were evaluated by a neurologist. A summary of the three cases is given below.

Case Reports

Case 1

A 30-year-old man presented to us with sudden blurring of vision in the right eye. He was seen earlier by an ophthalmologist who diagnosed vitreous hemorrhage and referred the patient to us. The patient had a history of an acute episode of left frontal headache, diplopia, and fever 3 years ago. Neurologic examination had revealed an isolated partial third nerve palsy on the left side with no other deficits. Computed tomographic scan of the brain, cerebrospinal fluid analysis, routine biochemical analysis, and work up for vasculitis were normal. He recovered completely after a 2-week course of systemic steroids. A month later he developed a solitary left partial motor seizure with secondary generalization and fever. Electroencephalography revealed normal resting and sleep record and isolated generalized sharp wave during hyperventilation.

Two years later he had a severe attack of vertigo, right temporal headache, and unsteadiness during walking. Results of Doppler and magnetic resonance angiography were normal. Magnetic resonance imaging revealed a lacunar infarct of the right caudate nucleus and putamen (Figure 1). He responded well to cinnarizine 75 mg per day. Serum lipid profile and results of investigations for collagen diseases were normal. The patient was advised to take 325 mg of aspirin and 200 mg of phenytoin per day.

His eyes were examined 4 months later. His vision was 20/100 in the right eye and 20/30 in the left eye. Anterior segment, ocular movements, and intraocular pressures were normal. Fundus examination of the right eye showed vitreous hemorrhage obscuring the central portion of the retina. Periphlebitis was seen along the superotemporal quadrant of the retina. Left eye fundus showed sheathing of retinal veins in the periphery. A clinical diagnosis of Eales' disease was made. Ultrasonogram of the right eye revealed posterior vitreous detachment and an attached retina throughout. Investigations revealed normal hemogram, erythrocyte sedimentation rate, blood sugar, and coagulation profile, and a nonreactive treponemal hemagglutination assay. Rheumatoid arthritis factor was negative. Antinuclear antibody was not detected. Sickle cell preparation was normal. Mantoux test was positive with induration of 25 mm × 25 mm. Fundus fluorescein angiogram revealed areas of neovascularization in the inferotemporal quadrant and an area of capillary nonperfusion with blocked fluorescence in the temporal quadrant of the right eye. Argon laser photocoagulation was done in the right eye. The patient was given prednisolone 60 mg per day orally. This was gradually tapered off by 10 mg per week. After 20 days, his vision improved to 20/30 in the right eye. On last follow-up a year later, his vision was 20/20 in both eyes. Right eye showed old vitreous hemorrhage inferiorly with sheathing of retinal vessels. He underwent another session of argon laser photocoagulation in the right eye. His latest neurologic examination did not reveal any abnormality.

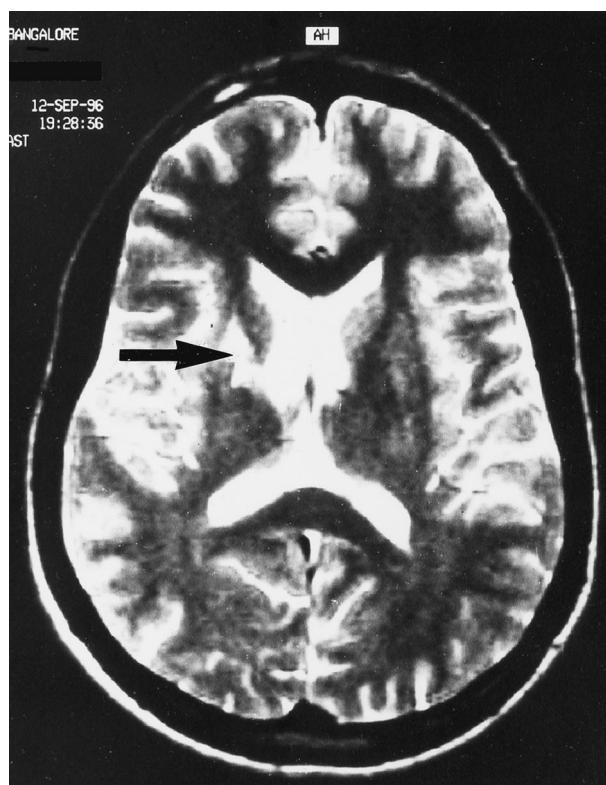


Fig. 1. Magnetic resonance imaging T2 sequence reveals infarct in right caudate nucleus and putamen (Case 1).

Case 2

A 23-year-old man presented with complaints of severe redness, floaters of 1-month duration, and blurred vision for 15 days in the left eye. He had a history of enucleation of the right eye 10 years earlier, but details were not available. He had consulted a local ophthalmologist 10 days earlier and was diagnosed with retinal vasculitis in the left eye. The patient had been treated with a single dose of intramuscular methylprednisolone 500 mg and had improvement of vision. The patient gave a history of an episode of altered speech, which spontaneously recovered 1 and a half years before the ocular problem. Evaluation by a neurologist at that time had revealed no other clinical neurologic deficits. A year earlier he had developed right facial seizures, which progressed to generalized seizures. Computed tomography scan showed multiple infarcts and calcified granuloma in the left frontal region. An MRI scan showed chronic left putaminal infarct with gliosis, dilatation of the left frontal horn, and areas of ischemia in both periventricular white matter and right basal ganglia with mild atrophic changes (Figure 2). The patient was treated with tablet phenytoin 300 mg per day.

On examination his visual acuity was 20/40 in the left eye. Slit-lamp examination of the left eye was normal and fundus examination showed multiple superficial hemorrhages and sheathing of retinal vessels with peripheral chorioretinal atrophic patches in the superior and inferior areas. Macular edema was noted. Investigations revealed Venereal Disease Research Laboratory (VDRL) test, *Treponema pallidum* hemagglutinin test, antinuclear antibody, rheumatoid factor, brucella agglutination test, anti-*Toxoplasma gondii* immunoglobulin G and immunoglobulin M anti-

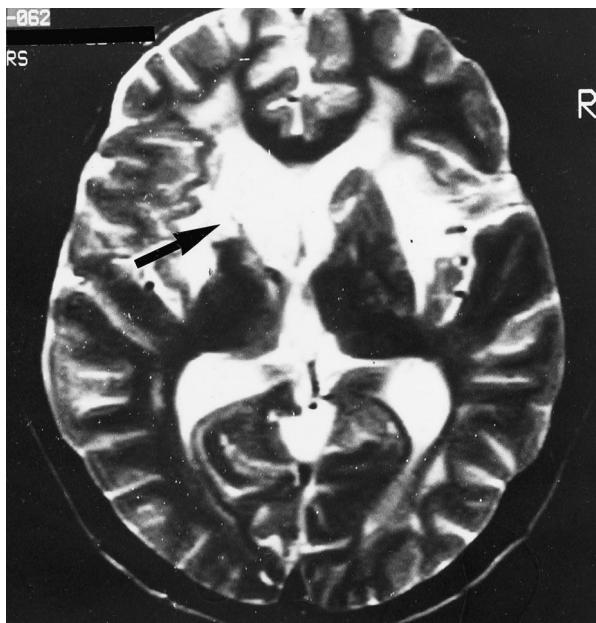


Fig. 2. Magnetic resonance imaging T2 sequence reveals left putamen infarct with atrophic dilatation of left frontal horn (arrow). Ischemic zones in periventricular white matter are seen (arrow) (Case 2).

bodies, and urine culture as negative. Coagulation profile was normal. Sickle cell preparation was negative. Mantoux test was positive with $20\text{ mm} \times 20\text{ mm}$. Chest X-ray was normal. Systemic evaluation did not reveal any evidence of Behcet disease.

He was put on oral prednisolone 60 mg per day for 1 week and tapered by 10 mg per week. A posterior sub-Tenon injection of triamcinolone acetonide 40 mg was also given in the left eye.

On follow-up after 2 months the patient's visual acuity improved to 20/20 in the left eye. Intraocular pressure was normal. Fundus examination revealed resolving perivasculitis and star exudates at the macula. No clinical evidence of neurologic lesions was found.

Three months later his best-corrected visual acuity was 20/30 in the left eye. Fundus examination of the left eye showed fresh vitreous hemorrhage, exudates at the macular area, and periphlebitis. Fundus fluorescein angiography showed no neovascularization, but areas of capillary nonperfusion in the superotemporal quadrant. The patient underwent a sector photocoagulation. As there was active periphlebitis, he was put on oral prednisolone again at 60 mg per day, to be gradually tapered off. On final follow-up 2 months later, his vision was 20/15 in the left eye. His retina showed no evidence of active inflammation.

Case 3

A 34-year-old man was seen with complaints of decreased vision in the left eye for 15 months. Seven years ago, he was diagnosed with Eales' disease with vitreous hemorrhage in the right eye, and treated with oral steroids, argon laser photocoagulation, vitrectomy, and anterior retinal cryopexy. His vision returned to 20/20 in both eyes. Laboratory investigations including hemogram, rheumatoid factor, antinuclear antibody, VDRL, and *Treponema pallidum* hemagglutinin test were negative. Mantoux test was positive. Chest X-ray was normal. A year after the ocular complaints, the patient had an episode of a tingling sensation in the left hand

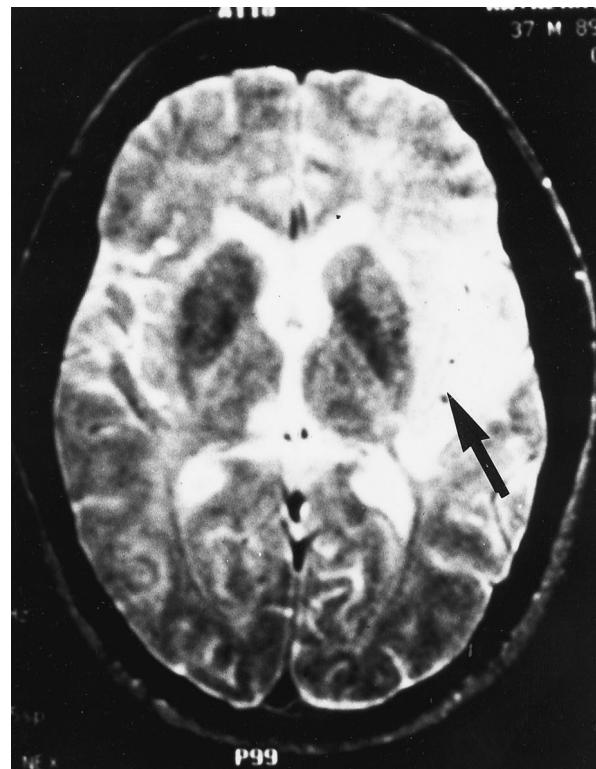


Fig. 3. Magnetic resonance imaging T2 sequence shows white matter and cortical edema involving the left temporal lobe (Case 5).

and weakness of left facial muscles with loss of articulation for about 4 hours at a stretch. Results of an electroencephalogram and computerized axial tomography scan were normal. He was seen by a neurologist in the United States and diagnosed with complicated migraine. A similar episode but of lesser magnitude occurred 3 years later. Results of a repeat electroencephalogram and computerized tomography scan were normal. A month before his current presentation, he had generalized seizures, which lasted for 8 hours. An MRI showed white matter and cortical edema in the superior aspect of the left temporal lobe, in the temporal operculum and the left insular cortex. A radiologic diagnosis of infarction or infectious process was considered (Figure 3).

On examination at the time of presentation, the patient's visual acuity was 20/15 in the right eye and inaccurate perception of light in the left eye. He had moderate left exotropia. Slit-lamp examination was normal in the right eye, whereas the left eye showed relative afferent pupillary defect. Intraocular pressures were normal. Indirect ophthalmoscopy showed mild lenticular changes, clear vitreous cavity, and extensive panretinal photocoagulation and cryocoagulation marks in the extreme and mid periphery of the right eye. No neovascularization over the disk or elsewhere or tractional retinal detachment was noticed. The left eye showed optic atrophy, macular scar, and extensive photocoagulation and cryoablation scars. No treatment was advised, as there was no active lesion noted in the eyes.

Neurologic examination showed residual pyramidal signs in the form of mild drift in the left upper limb and an upgoing plantar response. Pre- and postexercise lactate were 3.3 mmol/L and 7.2 mmol/L, respectively. No treatment was advised.

Discussion

In our three cases of Eales' disease with neurologic lesions, two (Cases 1 and 2) developed seizures before ocular disease. One patient (Case 3) had seizures 7 years after the ocular problem. All three were young men. They did not have diabetes or hypertension. They exhibited characteristic clinical features of Eales' disease. Extensive investigation did not reveal any evidence of systemic disease. In their neurologic presentation, seizures were common features. In addition, the first and the third patients had a migrainous headache during the course of the disease. Brain MRI showed features of infarction. Such infarction in the brain likely occurred as a result of an episode of inflammation in the cerebral vessels. These neurologic lesions were known to be self-limiting.

Association of Eales' disease with multiple sclerosis has been described by Fielo and Foster² and Opala et al.³ Singhal and Dastur⁴ have described acute or subacute myelopathy to be associated with Eales'. Garg and coworkers reported on a 27-year-old man with Eales' disease and neurologic involvement in the form of chronic progressive noncompressive motor myelopathy.⁷ Masson et al⁵ have reported two cases of Eales' disease with neurologic involvement. In their first case neurologic symptoms of cerebellar ataxia were seen 10 years after Eales' disease was diagnosed. In the second case neurologic symptoms and signs of myelopathy followed ocular symptoms by 8 years. Two of our patients had neurologic disease, which was followed by ocular complaints. There was no time relationship observed between the onset of ocular manifestations and neurologic symptoms. Magnetic resonance imaging showed multifocal white matter abnormality.⁵ Kutsal and others⁸ reported right hemiparesis and a left hemiplegia in a patient with Eales' disease. The computed tomographic scan of the patient showed multiple hypodense lesions in the right and left hemispheres. Digital subtraction angiography showed bilateral occlusion of anterior cerebral arteries.

Gordon et al⁶ have reported cerebral stroke in a case of Eales' disease. Antiguedad and Zarraz⁹ described a 34-year-old man with Eales' disease and central nervous system involvement. Magnetic resonance imaging in this patient was suggestive of demyelination. Cerebrospinal fluid showed moderate pleocytosis with intrathecal production of immunoglobulins with oligoclonal bands whereas other values were normal.

The basic pathology involved in Eales' disease is inflammation, ischemia, neovascularization, and its sequelae. The site of involvement is predominantly in the peripheral retinal vessels. Histopathologic studies

have uniformly demonstrated infiltration of chronic inflammatory cells, especially lymphocytes. Stock¹⁰ and Gilbert¹¹ have demonstrated acid fast bacilli in the pathologic specimens of presumed Eales' disease with miliary tuberculosis and periphlebitis and endovasculitis. The association of Eales' with tuberculosis has been debatable. Although tuberculosis is an infective disease with propensity for multisystem involvement, there were no signs or symptoms of systemic tuberculosis in any of these patients to explain the neurologic symptoms. Primary involvement of the central nervous system and the eye due to tuberculosis without systemic disease is extremely rare. Moreover, imaging findings in these three cases were not suggestive of a space occupying tuberculoma that could present as focal fits or thickening of the meninges, which is characteristic of basal meningitis, which could lead to isolated nerve palsies as in the case of our first patient. Renie and coworkers reported sensorineural hearing loss in a subset of patients with Eales' disease in the United States.¹² However, studies in patients with Eales' disease in India did not show any sensorineural hearing abnormalities.¹³

Neurologic symptoms have been described to occur in association with a few uveitic entities such as Vogt-Koyanagi-Harada syndrome, sympathetic ophthalmia, Behcet disease, and acute posterior multifocal placoid pigment epitheliopathy. The features of meningismus, headache, and cerebrospinal fluid pleocytosis have been described as central nervous system manifestations of Vogt-Koyanagi-Harada syndrome.¹⁴ Neurologic involvement in Behcet disease occurs as headache, cerebrovascular accidents with hemiplegia (computed tomographic and MRI), syncopal attacks, and epileptiform fits. These are more common than the reported recurrent facial palsy, diabetes insipidus, paranoid schizophrenia, and behavioral changes.¹⁵ As neurologic evaluation and imaging was not done routinely in Eales' disease cases seen by us, it is possible that our three cases could have combined idiopathic retinal and cerebral vasculitis. Ischemic changes in the brain could be due to prior cerebral vasculitis.

Neurologic history should be obtained in all cases of Eales' disease. If positive, complete neurologic evaluation should be done.

Acknowledgments

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Key words: Eales' disease, seizures, putaminal infarct, cerebral edema.

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