

**Case Report**

# Transient Visual Loss Associated with the Factor V Leiden Mutation

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Transient visual loss may be a manifestation of reduced ophthalmic or cortical perfusion or related to migraine or migraine equivalent phenomenon. Although transient and permanent loss of vision has been described in several hypercoagulable states, transient visual loss has not been described in patients with the Factor V Leiden mutation. In this report, we describe two patients this hypercoagulability state that presented to the emergency department with transient visual disturbance. Although headache was also part of the presenting symptoms, the visual disturbance did not consistently precede the headache in the classical migraine aura pattern. Several reports have demonstrated an increased incidence of hypercoagulable states in migraine with aura suffers. It may be that patients with hypercoagulability states have ischemic events that are misclassified as migraine with aura.

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**Key Words:** *transient, visual loss, ophthalmic, cortical, perfusion, hypercoagulability*

## INTRODUCTION

Transient visual loss can occur from arterial occlusion of vessels which supply the central nervous system or the eye. Amaurosis fugax, a sudden monocular transient visual loss or change in vision, usually indicates a lack of internal carotid artery perfusion, although, less often, middle or posterior cerebral artery occlusion can result in such symptoms. Bilateral visual loss of cerebral origin is usually caused by a bilateral posterior cerebral or posterior circulation occlusion. Although bilateral and unilateral visual loss has been reported in several hypercoagulable states, such visual phenomenon have never been reported as a manifestation of the heterozygous Factor V Leiden mutation, except for one case in the setting of pregnancy. In this report we outline two cases of recurrent episodes of visual loss as a neurological symptom related to this hypercoagulable state. In the first case, visual loss was the only new symptom in a previously undiagnosed female adolescent, and in the second case visual disturbance was the primary presenting neurologic symptom in a woman with a known diagnosis who discontinued anti-coagulant medication.

## CASE REPORT

### Case 1

A developmental normal 15-year-old right handed girl presented to the Emergency Department (ED) for a debilitating pressure-type headache lasting several hours duration. The

pain started in the bilateral temporal regions and progressed over the vertex to the occipital region over several minutes. Unlike the patient's usual migraine headaches, this headache was not relieved by sleep and actually became worse with lying down. While waiting for evaluation, the patient experienced sudden bilateral vision loss for several seconds without other associated neurological symptoms. A similar episode occurred three weeks earlier while the patient was sitting at her desk at school. Physical examination and growth parameters were normal. Cranial nerve examination demonstrated a 20/70 visual acuity bilaterally and a mild pupillary asymmetry, with the left pupil decreasing from 5mm to 3.5 mm and the right pupil decreasing from 5mm to 2.5 mm with light stimulation. Fundoscopic examination was unremarkable. Deep tendon reflexes in the left upper and low extremities were slightly brisker than on the right. The remainder of the neurological examination was normal. A magnetic resonance imaging (MRI) scan demonstrated a 5mm hyperintensity in the right anterior putamen on FLAIR and T2 images but no corresponding diffusion abnormality (**Figure 1**). Magnetic resonance angiogram (MRA) scan of the intracranial and neck vessels and CSF examination were normal.

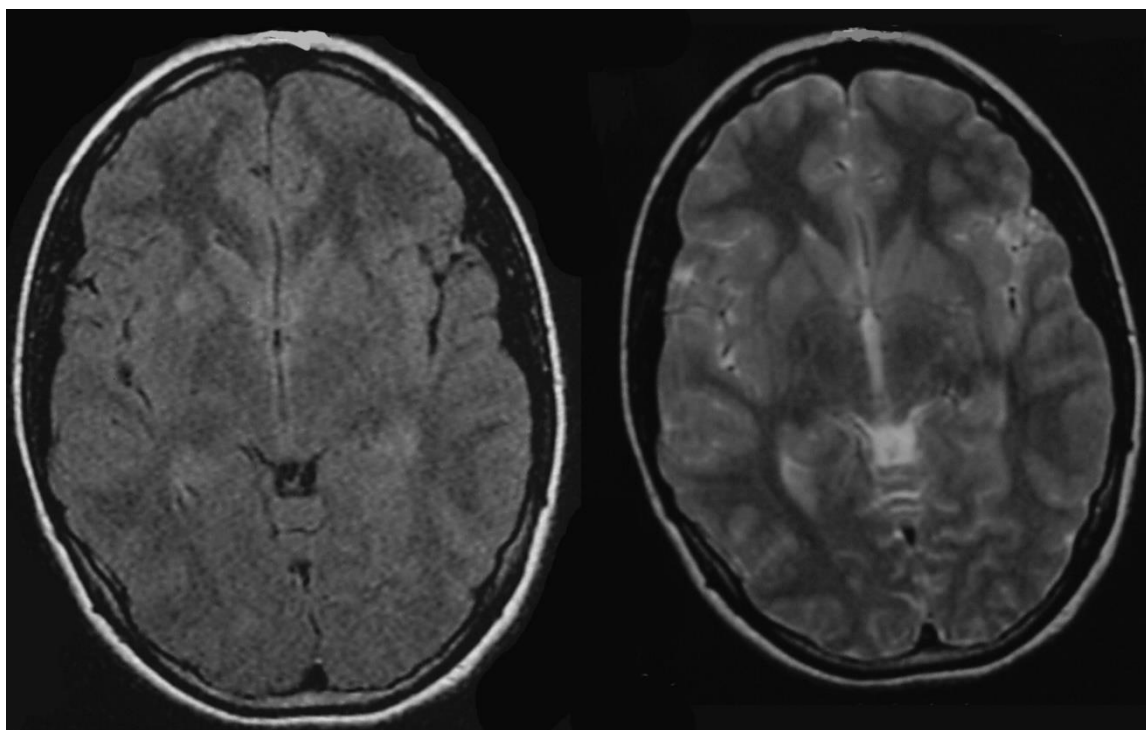
For the three previous years the patient suffered from migraines with a frequency of less than once a month. The migraines were characterized by supraorbital pain with the subsequent development of photophobia and nausea; they were relieved by sleep or NSAIDs and worsened by stress. Family history was positive for a maternal history of migraines, a paternal history of hypertension, a younger

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brother with generalized developmental delay, a paternal aunt who developed a deep venous thrombosis at 32 years of age and a paternal grandfather who developed bilateral strokes

during a mechanical valve replacement operation at the age of 72 years.



**Figure 1.** Axial FLAIR and T2 Images demonstrating the hyperintensity in the right anterior putamen.

**Table 1.** Coagulation Laboratory Values.

Laboratory Value	Case 1	Case 2
Protein S Function	76%	159%
Protein C Function	81%	131%
Anti-Thrombin III Function	90%	121%
Lupus Anti-Coagulant	Negative	Negative
Homocysteine	Normal	Normal
Factor V Leiden	Heterozygous Mutation	Heterozygous Mutation
Prothrombin 20210	Heterozygous Mutation	No Mutation

The patient's headache was relieved by IV fluids and Compazine. Neurontin was increased up to 600mg TID over 2 weeks, but was discontinued after three months due to side effects and a lack of recurrences. Over a two-year period, the patient remained symptom free. Repeated MRIs and neurological evaluations remained unchanged. Then, two days into a viral gastroenteritis, the patient awoke from a nap and developed an episode of headache and visual loss almost identical to the one described above. Approximately 1 hour later, the patient developed left hemibody sensory loss without dysesthesias lasting several hours. As seen in **Table 1**, a hypercoagulation work-up demonstrated a heterozygous R506Q mutation in Exon 10 of the Factor V Leiden gene as identified by restriction enzyme cleavage of PCR amplified DNA.

The patient was started on ASA 81mg PO QD and encouraged to remain well hydrated. After 10 months, the patient has not had any recurrent episodes of migraines or transient neurological symptoms.

### Case 2

Patient 2 was a 38-year-old right-handed female with a history of heterozygous Factor V Leiden and Prothrombin 20210 mutation. The patient was non-compliant with Lovenox over the previous two days during which she had four episodes of visual disturbances. The episodes began abruptly without prodrome or aura. A flickering phenomenon in the far temporal periphery that was described as "spinning ceiling fan" heralded the episode. Darkness and vision loss then progressed from the temporal periphery of one eye to the

center of vision eventually covering the entire temporal crescent. Several "black spots" appeared in the middle of her visual fields, with this phenomenon disappearing and reappearing over a 10 to 20-minute period. These episodes occurred in both the left and right eye on separate occasions. Ten minutes after one episode, a constant, non-throbbing, right temporal and retro-orbital headache developed and lasted fifteen minutes. While in the ED a slightly different visual phenomenon occurred. An array of "black spots" developed in the periphery of the left eye; these "black spots" slowly enlarged and moved across the visual field towards midline with slow resolution over a ten-minute period. Approximately twenty minutes later a neurological examination demonstrated: mild inattention while reciting the months of the year backwards and performing serial three's, striking sustained end gaze nystagmus on rightward gaze, and sustained left eye nystagmus on leftward gaze along with the development of retrobulbar pain. Fundoscopic examination was unremarkable.

The patient originally presented four years earlier with left lower extremity pain and swelling. A lower extremity ultrasound was negative at that time. On her way to return for a repeat ultrasound, the patient developed shortness of breath and chest pain. A pulmonary embolism was confirmed by imaging and the patient was started on Coumadin for anti-coagulation. At the time of presentation, the patient was using oral contraceptive pills and was smoking cigarettes. She discontinued these activities after her initial hospitalization. A hypercoagulation workup (**Table 1**) revealed the Factor V Leiden and Prothrombin 20210 mutations. After miscarrying two fetuses, the patient was changed to Lovenox 60mg SQ BID.

Family history revealed that the patient's mother had two DVT's in her 50's and a paternal uncle had one DVT. The patient's maternal and paternal grandmothers both had strokes, but neither stroke occurred early in life, and one of the patient's two siblings tested negative for the Factor V Leiden mutation while the other sibling had not been tested.

The patient was admitted to the neurology service for observation and to rule out stroke. An MRI with diffusion and MRA of the intercerebral and neck vessels were both normal. An echocardiogram with bubble study demonstrated no cardiac abnormalities or right-to-left shunt. The patient was restarted on Lovenox with resolution of her symptoms.

## DISCUSSION

In these two cases we discuss patients with transient visual loss with headaches. In the first case, the young girl developed vision loss with and without headache. When the vision loss was accompanied by headache, the visual loss developed after the headache had developed; thereby suggesting that this was not part of the headache aura, but part of the etiology that caused the headache. In addition, the third episode occurred in the setting of probable dehydration, thereby putting this patient at risk for hypercoagulability. All episodes in this patient could be explained by a posterior circulation defect.

The second patient developed transient Amaurosis type visual loss while subtherapeutic on anti-coagulation medication. This was most likely due to ophthalmic artery circulation dysfunction.

Sudden visual loss can result from occlusion of the ophthalmic arteries or the posterior cerebral circulation resulting in retinal or cortical ischemia. Amaurosis with and without permanent sequelae has been reported in several patients with hypercoagulability disorders and states. For example, retinal artery and/or vein occlusion has been reported in the setting of thrombotic thrombocytopenic purpura<sup>1</sup> and the prothrombin 20210 A mutation.<sup>2</sup> During pregnancy unilateral visual loss has occurred in the setting of internal carotid artery moyamoya<sup>3</sup> and the Factor V Leiden mutation.<sup>4</sup>

Although, transient cortical blindness has been reported in severe pre-eclampsia patients,<sup>5</sup> permanent unilateral cortical visual loss is more commonly in hypercoagulable states. Occipital strokes have been reported in adults with Lupus<sup>6</sup> and with L-asparaginase administration in the setting of acute lymphoblastic leukemia and Protein S deficiency,<sup>7</sup> and in children with the heterozygous Factor V Leiden mutation in the setting of marijuana smoking<sup>8</sup> and hemophilia A.<sup>9</sup>

Although the factor V Leiden mutation has been implicated in patients with large vessel strokes<sup>10</sup> and cerebral venous thrombosis,<sup>11</sup> others have implicated this factor in patients who develop ischemic events in the setting of migraine with aura.<sup>12</sup> Although, Corral et al.<sup>13</sup> found a non-significant increase in factor V Leiden mutation prevalence in migraine with aura sufferers as compared to normal participants, D'Amico et al.<sup>14</sup> found a significant increase in the prevalence of the factor V Leiden and protein S deficiency in both migraine with aura sufferers and patients with ischemic stroke as compared to non-migraine normal participants. In addition, the prothrombin factor 1.2 has been shown to be elevated in migraine with aura sufferers but not in normal participants or migraine without aura sufferers.<sup>15</sup>

In this article we present two cases of visual disturbance in patients with the Factor V Leiden mutation. Case 1, at first glance, may be interpreted as an atypical migraine; however this case had several features, suggestive of transient ischemia. The visual disturbance in Case 2 was most likely caused by an ischemic event. If migraines are associated with an abnormal coagulable state, patients with both migraines and a hypercoagulability disorder may be more sensitive to dysregulation of the coagulation cascade, leading to transient ischemic attacks and strokes. Alternatively, it may be that patients with hypercoagulability states have transient ischemic events which are misclassified as migraine with aura, and represent an entirely separate population. This population may be part of what has been described as acephalgic migraine.<sup>16</sup> Of course the workup should be comprehensive including a full ophthalmological evaluation ocular causes such as increased intraocular pressure and include other important disorders in the differential diagnosis such as idiopathic intracranial hypertension.

**CONFLICT OF INTEREST**

The author has no conflicts of interest to declare.

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