Visual Disturbances in (Pre)eclampsia

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This review aims to summarize existing information concerning visual disturbances in (pre)eclampsia that have been described in the literature. Preeclampsia is one of the leading causes of maternal and fetal morbidity and mortality worldwide. Visual disturbances in (pre)eclampsia seem to be frequent phenomena. Therefore, the obstetrician/gynecologist may encounter women with serious, and sometimes debilitating, pathology of the visual pathways. Established ophthalmic entities associated with (pre)eclampsia are cortical blindness, serous retinal detachment, Purtscher-like retinopathy, central retinal vein occlusions, and retinal or vitreous hemorrhages. Ensuing visual symptoms include blurry vision, diplopia, amaurosis fugax, photopsia, and scotomata, including homonymous hemianopsia. In general, aside from lowering the blood pressure and preventing (further) seizures with magnesium sulfate, no specific therapy seems indicated for (pre)eclamptics who experience visual changes. Although in most cases visual acuity returns to normal within weeks to months after the onset of symptoms, rarely permanent visual impairment can occur. Health care providers such as emergency room physicians, obstetricians, family physicians, neurologists, and ophthalmologists should be aware that acute onset of visual symptoms in pregnant women can be the first sign of (pre)eclampsia. Given that visual changes are a diagnostic criterion for severe preeclampsia, obstetricians should appreciate the significance of these changes and discuss appropriate diagnostic options with the ophthalmologist. Affected women can be reassured that most cases are transient.

Target Audience: Obstetricians and gynecologists, ophthalmologists, neurologists, family physicians, emergency room physicians

Learning Objectives: After completing this CME activity, obstetricians and gynecologists should be better able to classify visual disturbances at an early stage during pregnancy, interpret acute onset of visual disturbances as the first sign of preeclampsia, and evaluate possible residual visual symptoms during follow-up.

VIGNETTE

A 24-year-old primigravid woman at 37 weeks’ gestation was brought to the emergency department by her family. The family stated that the woman had woken up that morning unable to see. The woman herself denied any visual disturbance but did complain of nausea and frontal headache. Her pregnancy had been uneventful before this time. On examination, she appeared confused and disoriented as to time. Her blood pressure was 165/110 mm Hg, heart rate 128 beats per minute, and she had slight edema in her hands and feet. Neurologic and ophthalmic...
examination revealed no abnormalities, except hyperreflexia and severe impairment of vision, although the woman continued to disagree that she had visual impairment. Pupillary reflexes were intact and the motility undisturbed. Fundoscopic examination showed no abnormalities of the optic disc or macula. Laboratory testing revealed 3+ proteinuria and elevated uric acid. A T2-weighted magnetic resonance imaging (MRI) scan demonstrated bilateral hyperintense signals in the parieto-occipital lobes. Based on the signs and symptoms described earlier, the diagnosis made was preeclampsia complicated by cortical blindness.

**INTRODUCTION**

Pregnancy can affect multiple organs, including the eyes. For example, the pregnant state is associated with increased corneal thickness and curvature, and decreased corneal sensitivity. Furthermore, a decrease in intraocular pressure occurs during the third trimester of pregnancy. Preexisting ocular diseases (e.g., diabetic retinopathy and uveitis) can be exacerbated during pregnancy. In addition to these pregnancy-induced ocular changes, preeclampsia and its complications can be associated with a variety of visual changes. Because the obstetrician/gynecologist may occasionally be confronted with a preeclamptic woman who suffers visual disturbances, this review aims to summarize existing information described in the literature. The search strategy included a MEDLINE search through December 2011, limiting to articles published in English language and reports including humans. The following Medical Subject Headings terms were used: “pregnancy-induced hypertension,” “(pre)eclampsia,” and “visual disorders.” Abstracts were reviewed for suitability. The references of the available articles were screened as well and were included when they represented a unique case report. This literature consisted mainly of isolated case reports or small case series. Not all single case reports were encountered were included in this review because often case reports described nearly identical features, and we decided to include reports that gave the most information on a particular case/condition. For each condition, we described its epidemiology, pathogenesis, and clinical manifestations.

**(PRE)ECLAMPSIA**

Some form of hypertension complicates 5% to 7% of all pregnancies and is one of the leading causes of maternal and fetal morbidity and mortality worldwide. Preeclampsia is a pregnancy-specific disorder, characterized by hypertension and proteinuria after midgestation. The exact pathophysiology of preeclampsia remains to be elucidated but is considered to entail reduced organ perfusion and endothelial dysfunction. Several maternal organs can be affected, including the brain in the form of eclampsia, which is marked by tonic-clonic convulsions. Accompanying symptoms include visual abnormalities, severe headache, nausea, vomiting, and altered mental state. Eclampsia occurs in approximately 0.5% of women with mild preeclampsia and in approximately 2% to 3% of those with severe preeclampsia. The HELLP syndrome is characterized by Hemolysis, Elevated Liver enzymes, and Low Platelet count, and this syndrome significantly increases the risk of preterm birth and perinatal mortality rate compared with isolated preeclampsia. Delivery remains the only cure for preeclampsia/HELLP syndrome with careful scrutiny regarding blood pressure control and seizure prophylaxis, as well as monitoring of fetal well-being.

Neurologic or ophthalmic entities that have been associated with (pre)eclampsia include cortical blindness, serous retinal detachment, Purtzcher-like retinopathy, central retinal vein occlusions, and retinal or vitreous hemorrhages. Ensuing visual symptoms have been described to occur in approximately 25% of preeclamptic and 19% to 45% of eclamptic women, and include blurry vision, diplopia, amaurosis fugax, photopsia, and scotomata, including homonymous hemianopsia. The neurological and ophthalmic entities associated with (pre)eclampsia can arise from different parts of the visual pathway and are described in more detail in the following sections.

**THE VISUAL PATHWAY**

The visual pathways emerge from the eye as the optic nerve, pass the optic chiasm adjacent to the pituitary gland, continue as the optic tract, move through the lateral geniculate nucleus of the thalamus, optic radiations, and end in the primary visual cortex (also known as V1 or striate cortex) (Fig. 1). The primary visual cortex is situated in the most posterior part of the occipital lobes and is the first cortical area to receive visual information. The primary visual cortex subsequently projects visual information via the secondary visual cortex (V2) to higher-order visual areas in the occipital, parietal, and temporal lobes (Fig. 2). These higher-order visual areas are each involved in the processing of specific aspects of visual information. Postchiasmal
lesions of the visual pathway can cause homonymous visual field defects.\textsuperscript{17,18} CORTICAL BLINDNESS

Epidemiology

Cortical blindness is one of the reported complications of (pre)eclampsia. Cunningham et al reported that 15\% of eclamptic women were affected.\textsuperscript{19} The incidence of cortical blindness in preeclampsia without seizures is likely substantially lower. This type of blindness is caused by dysfunction of the optic radiations, primary and secondary visual cortices, and high-order visual areas of the parieto-occipital lobes, hence its name.\textsuperscript{20,21} Cortical blindness is per definition associated with an intact pathway from the eye to the lateral geniculate bodies, and therefore, the pupillary light responses and ocular motility remain intact.\textsuperscript{21,22} Normal ophthalmoscopic findings exclude an ophthalmic cause of blindness.\textsuperscript{19,23,24}

Fig. 1. Visual pathways from the eyes to the primary visual cortex.

Fig. 2. Visual information streams from the primary visual cortex to the higher-order visual areas. The primary visual cortex (V1) projects visual information via the secondary visual cortex (V2) and the association visual cortex (V3) to higher-order visual areas in the occipital, parietal, and temporal lobes using a dorsal and a ventral stream. The ventral stream passes V4 (in the ventral occipitotemporal region) and ends in high-order visual areas in the inferior temporal lobe (ITL). The dorsal stream passes V5 (in middle temporal area) and ends in higher-order visual areas in the posterior parietal cortex (PPC).

Clinical Manifestation

Cortical blindness has been described to occur not only several hours before or after eclamptic seizures but also, although rarely, for several days up to weeks postpartum.\textsuperscript{24–26} The bilateral vision loss often begins with blurry vision and progresses within a couple of hours to bare light perception. Prodromal symptoms are similar to imminent eclamptic seizures and include nausea, vomiting, and severe (often frontal) headache. Blindness can also be the presenting symptom in preeclampsia.\textsuperscript{27} Cortical blindness is an anxiety-provoking condition that fortunately resolves completely in most cases. Sometimes, and as presented in the case report, the patient is unaware of her blindness and feels that she can see (visual anosognosia or Anton syndrome), indicating involvement of the visual association cortex (Fig. 2).\textsuperscript{26,28}

A computerized tomographic (CT) scan may show low-density areas (corresponding with cerebral edema) in both occipital lobes, which can extend to the frontoparietal and parietal lobes. On T2-weighted MRI, these areas appear hyperintense and are mainly located in the parieto-occipital lobes, but they can also occur in the frontal and temporal lobes and basal ganglia.\textsuperscript{24,29–31} Cases have been described in which the CT scan appeared normal, whereas major abnormalities were found on T2-weighted MRI,\textsuperscript{23,29,32} emphasizing the superiority of MRI for the evaluation of sudden bilateral vision loss in (pre)eclampsia. Delefosse et al reported an interesting case of a woman who had preeclampsia, and whose hypertension recurred 3 weeks postpartum.\textsuperscript{24} This case illustrated an uncommon evolution of severe preeclampsia with secondary onset of neurologic symptoms, including cortical blindness, which the authors determined to be associated with intrauterine retention of placental products. After curettage and removal of the placental fragments, the woman was able to distinguish bright light within 12 hours. Visual acuity returned to normal after 4 days.
Pathophysiology

Cortical blindness in (pre) eclampsia is usually related to the occurrence of the Posterior Reversible Encephalopathy Syndrome (PRES). PRES is a clinical-neuroradiological entity characterized by headache, vomiting, seizures, altered mental status, and visual abnormalities (including blurry vision, homonymous hemianopsia, visual neglect, cortical blindness, and visual anosognosia), together with cranial imaging findings consistent with vasogenic edema. PRES is thought to be due to loss of cerebral autoregulation in the context of endothelial dysfunction. Increased blood pressure overcomes the cerebrovascular autoregulation, resulting in hyperperfusion and vasogenic edema. This edema is presumably the cause of the neurologic symptoms of PRES, including cortical blindness, when the edema affects the primary visual cortex in the occipital lobes.

The occipital lobes seem more susceptible to autoregulation breakthrough and subsequent hyperperfusion than other regions. This may be explained by differences in innervation: the internal carotid system is better supplied with sympathetic nerves than the vertebrobasilar system. With acute hypertension, protective sympathetic nerves enhance vascular autoregulation. Severe autoregulation breakthrough can cause fibrinoid necrosis of the vessel wall and subsequent extravasation leading to accumulation of extracellular fluid, hypoperfusion of affected areas by increased hydrostatic pressure, and petechial hemorrhages.

Prognosis

Lowering blood pressure and preventing seizures with magnesium sulfate are the primary objectives in (pre) eclamptic patients with cortical blindness. Women typically regain normal vision within a couple of hours or days after the onset of treatment. Complete resolution of the high-intensity signals (cerebral edema) on MRI can usually be expected as well. However, residual symptomatic visual field defects and visuospatial deficits have been described in patients with concomitant presence of multiple bilateral parieto-occipital hemorrhages. Although most women can expect full recovery, the combination of (pre)eclampsia-related cortical blindness and involvement of the eye (often a retinal detachment and/or Purtscher-like retinopathy) has been described to result in permanent visual impairment, and even blindness, in a few case reports. In such cases, the bilateral retinal detachments and Purtscher-like retinopathies were accompanied by brain infarcts.

Murphy and Ayazifar reported diffuse optic disc and intraretinal and cerebral hemorrhages in a woman with eclampsia and HELLP syndrome who subsequently suffered permanent visual deficits.

Balint’s Syndrome

Another complicated form of cortical blindness is Balint’s syndrome, a rare condition usually associated with cerebral infarction or neurodegenerative diseases. This triad is characterized by simultanagnosia (inability to integrate complex visual scenes), ocular apraxia (inability to voluntarily control gaze), and optic ataxia (inability to benefit from visual guidance in reaching an object). Balint’s syndrome is believed to be the result of a bilateral dysfunction of the dorsal stream in the parieto-occipital cortices. To date, only 2 reports have described the development of this syndrome in an eclamptic woman. The second case report was written in Italian, but it has an English abstract. Because of the rarity of Balint’s syndrome in eclampsia, this case report is included in this review. In both reports, bilateral parieto-occipital infarcts were seen on CT scanning, which might reflect infarction of the cerebral posterior border zone region. Both women experienced improvement in object recognition and other higher-order visual functions after several months. One of the few existing studies evaluating neurologic functioning in eclampsia examined 30 women for the presence of simultanagnosia. This evaluation took place in the first hours after eclamptic convulsion(s), after magnesium sulfate administration but before MRI scanning. All but one appeared to experience simultanagnosia. However, none of these women had ocular apraxia or optic ataxia to complete Balint’s syndrome. Unfortunately, whether these women were symptomatic was not indicated in this article. In 87% of the women, diffusion weighted imaging showed reversible bilateral focal hyperintensity lesions, which correlated well with the simultanagnosia. On repeat examination (after 3–5 days), simultanagnosia had resolved in all cases.

SEROUS RETINAL DETACHMENT

Epidemiology

Serous retinal detachment is a well-documented ocular manifestation occasionally seen with (pre)eclampsia. The occurrence in women with preeclampsia varies from 1% to 3%. In eclamptic patients, this rate is 5 to 10 times higher. Routine ophthalmic examination in 71 women admitted with severe preeclampsia/eclampsia...
revealed a prevalence of 32%. Of the 3 cases presented in more detail by the authors, only one woman reported visual symptoms. Unfortunately, whether the 71 studied women experienced visual symptoms was not mentioned in the article.

Clinical Manifestation

Preeclampsia-related serous retinal detachment has been described to occur before, during, or after delivery. In an interesting case report, bilateral serous retinal detachment was reported to reveal an occult pregnancy. The onset of preeclampsia-related serous retinal detachment is sudden, the main symptoms are a visual field defect and loss of visual acuity. Photopsia and floaters, which are usually present in rhegmatogenous retinal detachment, are absent. Retinal detachments in preeclampsia are often bilateral, but unilateral detachment can also occur. Occasionally, retinal detachments coexist with cortical edema. Fundoscopy reveals, in addition to the detached retina, retinal and/or macular edema, exudates, hemorrhages, and cotton wool spots (retinal nerve fiber swelling due to ischemia).

Pathophysiology

The retinal pigmented epithelium (RPE) facilitates the exchange of water, salts, nutrients, and metabolites between the retina and the choroid, and prevents the accumulation of fluid in the subretinal space, which is a potential space in healthy eyes. Tight junctions between the RPE cells form the blood-retinal barrier, which can be disturbed by conditions such as severe acute hypertension, inflammation, infection, neoplasm, hypoproteinemic states, and subretinal neovascularization. One or more of these processes is likely at play in preeclampsia. Some reports suggest hormonal involvement (by releasing endogenous vasoconstrictors). Vasospasm, generalized or localized, is seen in the choroidal arterioles and the central retinal and posterior ciliary arteries. Intense spasm of the choroidal arterioles results in choroidal ischemia, and this increases vascular permeability. Subsequently, serous fluid accumulates in the subretinal space, separating the retina from the RPE. Photoreceptors located in the retina become devoid of nutrients and stop functioning.

Fluorescein angiography in (pre)eclamptic women with serous retinal detachment demonstrates areas of choroidal hypo- and nonperfusion (Elschnig spots). Abnormalities in preeclamptic women may also be found by multifocal electroretinography and optical coherence tomography. Changes in ocular blood flow, indicating vasospasm, can be found with color flow Doppler ultrasonography. As an alternative to the vasospasm theory, it is suggested that hyperperfusion and breakthrough in autoregulation of orbital vessels, especially choroidal arterioles, increase permeability of retinal and choroidal arterioles, causing retinal edema and serous detachment. Systemic magnesium sulfate therapy has been described to significantly increase retinal perfusion. Simultaneously, headache and visual symptoms resolve. This effect of magnesium sulfate could explain why systemic treatment of (pre)eclampsia is more effective in reducing visual symptoms than specific ocular treatment.

Prognosis

In general, the visual acuity gradually improves and the visual field defects disappear within 3 months postpartum, and the patients regain normal vision. Within 1 week from the initial ophthalmoscopic examination, three-quarters of the serous retinal detachments will have resolved. Although visual acuity recovers and the retinal detachment spontaneously resolves in most patients, a small percentage will show retinal abnormalities during follow-up weeks to 1-year postpartum with subtle changes in visual acuity. None of the reviewed articles mentioned accompanying visual symptoms in the following months; therefore, it is likely that the subtle visual changes have no consequences in daily life.

Purtscher-like Retinopathy

Purtscher’s retinopathy, first reported by Otmar Purtscher in 1910, is a specific appearance of the fundus characterized by multiple areas of retinal whitening and intraretinal hemorrhages, usually caused by trauma. Systemic conditions, including acute pancreatitis, renal failure, fat embolism syndrome, connective tissue disorders, and (pre)eclampsia, have been associated with the same specific appearance of the fundus, and which is therefore named Purtscher-like retinopathy. Only a few case reports of Purtscher-like retinopathy in (pre)eclamptic patients could be retrieved from the literature, suggesting that it is an extremely rare complication of (pre)eclampsia.

Clinical Manifestation

In the 6 (pre)eclamptic patients with Purtscher-like retinopathy described in the literature, visual abnormalities developed in the first 24 hours after urgent
Complaints included blurry vision, floaters, and complete bilateral vision loss. On ophthalmic examination, the visual acuity ranged from light perception to 20/400 and was bilateral in all cases. In all patients, fundoscopic examination revealed multiple, discrete areas of retinal whitening, so-called Purtscher flecken, mostly within the macula and around the optic disc. In addition, small, characteristic, flame-shaped hemorrhages were found in 4 of the patients. Fluorescein angiography revealed capillary nonperfusion in areas of retinal whitening, and narrowing or occlusion of retinal arterioles.

Pathophysiology

Agrawal and McKibbin postulate that, considering the specific appearance of the fundus, Purtscher flecken may be caused by embolic occlusion of the precapillary arterioles of the retina by fat, air, platelets, or leukocyte aggregates. The latest hypothesis is the formation of leuko emboli by complement activation. Previous reports suggest a role of amniotic fluid in activating complement and inducing leuko-embolization, which may contribute to complications of late pregnancy, such as Purtscher-like retinopathy.

Prognosis

Improvement of visual acuity can be seen within a couple of weeks after the initial insult. Some recovery of visual acuity is accompanied by partial resolution of the retinal whitening and delayed filling of the retinal vasculature. Apart from treating the underlying systemic condition, no specific treatment is available, although it has been suggested that high-dose steroids might be effective. Unfortunately, none of the reported 6 (pre)eclampsia-related cases experienced complete recovery of visual acuity. In fact, one preeclamptic woman had unchanged visual acuity of 4/200 in both eyes 2 months postpartum. Another preeclamptic woman, who also suffered pancreatitis, experienced slight improvement from bare light perception in the acute phase to counting fingers at 1 meter (i.e., a visual acuity of 1/60) in both eyes after 6 months.

Central Retinal Vein Occlusion

Two case reports describe sudden vision loss in preeclamptic women caused by central retinal vein occlusion (CRVO). Both women developed bilateral loss of vision 10 to 21 days postpartum. At the onset of vision loss, blood pressure was normal in both cases. In both women, ophthalmologic examination revealed the classical picture of CRVO, that is, multiple retinal hemorrhages in all 4 quadrants, venous dilatation, and macular edema. In the next months, the hemorrhages resolved and macular edema reduced. Visual acuity improved significantly, but did not return to normal. The pathophysiology of CRVO in (pre)eclampsia is not fully understood. Although the name CRVO suggests otherwise, CRVO is primarily an arterial problem. Central retinal artery thickening is thought to cause compression of the central retinal vein thereby leading to venous occlusion. Interestingly, the risk factors for CRVO, hypertension, and coagulation disorders are also associated with preeclampsia.

Retinal and Vitreous Hemorrhages

Retinal and vitreous hemorrhages, preceding the presentation of preeclampsia, although rare, have been described each in the literature once. One case report described sudden vision loss in the left eye of a normotensive pregnant woman. Ophthalmologic examination revealed white-centered retinal hemorrhages (Roth spots). Within 48 hours, this previously healthy pregnant woman developed preeclampsia. During the first 6 months after delivery, visual acuity returned to normal, and the retinal hemorrhages resolved. The other case report described sudden vision loss in the left eye of a normotensive pregnant woman, resulting from a vitreous hemorrhage. This vitreous hemorrhage gradually resolved over the next 2 weeks. However, the woman developed preeclampsia with HELLP syndrome, another 2 weeks later, which may or may not have been coincidental.

Conclusions

Visual symptoms during preeclampsia are a frequent phenomenon. Therefore, the obstetrician/gynecologist can encounter women with serious, and sometimes debilitating, pathology of the visual pathways. This review describes the most common presentations, including cortical blindness, serous retinal detachment, Purtscher-like retinopathy, central retinal vein occlusion, and retinal and vitreous hemorrhages. Unfortunately, the existing literature largely consists of single case reports or small case series. Routine follow-up with standardized history taking of visual complaints/symptoms and standardized ophthalmic examination, was not necessarily performed or described. Moreover, the frequency of occurrence of the reported visual man-
ifestations in uncomplicated pregnancy and in the healthy young population is largely unknown. All this hampers drawing firm conclusions regarding the etiology of visual disturbances in preeclampsia and the existence of a causal relationship.

In general, aside from lowering blood pressure and preventing (further) seizures with magnesium sulfate, no specific therapy seems indicated for (pre)eclamptic women who experience visual changes. When not rapidly transient, ophthalmic evaluation is helpful in distinguishing the underlying pathology. MRI may be helpful in delineating features of cerebral edema/PRES in the occipito-parietal lobes. In most cases, visual acuity returns to normal within weeks to months after the onset of symptoms. Rarely, permanent visual impairment in (pre)eclamptic women has been described to occur, generally associated with occipital hemorrhages or brain infarcts, alone or in combination with retinal hemorrhages (e.g., Purtscher-like retinopathy).

The follow-up in the described case reports typically included ophthalmoscopic examination and, in some cases, an MRI scan. However, a few articles report visual symptoms experienced by the formerly (pre)eclamptic women. The fact that most articles do not mention any visual symptoms during follow-up may tentatively lead to the conclusion that most women with visual disturbances during (pre)eclampsia experience no permanent visual symptoms.

Health care providers such as emergency room physicians, obstetricians, family physicians, neurologists, and ophthalmologists should be aware that acute onset of visual symptoms in pregnant women can be the first sign of (pre)eclampsia. An ophthalmologist or neurologist faced with such a woman should consult an obstetrician or refer the woman without delay. Given that visual changes are a diagnostic criterion for severe preeclampsia, obstetricians should appreciate the significance of these changes and discuss appropriate diagnostic options with the ophthalmologist. Affected women can be reassured that most cases are transient. In addition, obstetricians should refer pregnant women with persistent visual symptoms to an ophthalmologist, as some ophthalmic entities may require specific therapy (e.g., central retinal vein occlusion) or follow-up by an ophthalmologist.

CONTINUATION VIGNETTE
The patient was administered magnesium sulfate for seizure prevention, and her blood pressure was lowered with intravenous antihypertensive medication. Labor was induced, and she spontaneously delivered a healthy female infant of 2850 g. In the 3 days after delivery, she gradually regained complete vision. MRI obtained 6 weeks postpartum revealed complete resolution of cerebral edema and no other abnormalities.

REFERENCES
Visual Disturbances in (Pre)eclampsia • CME Review Article


