Objectives: To characterize the pathogenesis and clinical features of optic disc edema associated with obstructive sleep apnea syndrome (SAS).

Methods: A series of 4 patients with SAS and papilledema (PE) underwent complete neuro-ophthalmologic evaluation and lumbar puncture. In 1 patient, continuous 24-hour intracranial pressure (ICP) monitoring was also performed.

Results: All 4 patients had bilateral PE that was asymmetric in 2. Three patients had optic nerve dysfunction, asymmetric in 1, unilateral in 2. Daytime cerebrospinal fluid pressure measurements were within normal range. Nocturnal monitoring performed in one patient, however, demonstrated repeated episodes of marked ICP elevation associated with apnea and arterial oxygen desaturation.

Conclusions: We propose that PE in SAS is due to episodic nocturnal hypoxemia and hypercarbia resulting in increased ICP secondary to cerebral vasodilation. In these individuals, intermittent ICP elevation is sufficient to cause persistent disc edema. These patients may be at increased risk for developing visual loss secondary to PE compared with patients with obesity-related pseudotumor cerebri because of associated hypoxemia. The diagnosis of SAS PE may not be appreciated because daytime cerebrospinal fluid pressure measurements are normal and because patients tend to present with visual loss rather than with symptoms of increased ICP.


Obstructive sleep apnea syndrome (SAS) is characterized by recurrent interruption of normal breathing during sleep owing to upper airway obstruction. Patients are typically obese, middle-aged men who have a history of loud snoring and excessive daytime somnolence. In addition to the hypoxia and hypercarbia caused by inadequate respiration, repetitive sympathetic activation during arousal from sleep may cause arterial hypertension, cardiac arrhythmias, and epinephrine-induced platelet activation. These metabolic changes may have several cardiovascular and neurologic consequences. Sleep apnea syndrome has been implicated as a cause of myocardial infarction, stroke, chronic headache, and cognitive dysfunction. Neuro-ophthalmic manifestations include visual field defects, ischemic optic neuropathy, glaucoma, and optic disc edema. The mechanism for the optic disc swelling associated with SAS has not been fully elucidated. We describe 4 patients with disc edema and SAS to better characterize the pathogenesis and the clinical features of this syndrome.

CASE REPORTS

CASE 1

A 20-year-old man was found to have marked loss of vision in the left eye. He denied headache, tinnitus, transient obscurations of vision (TOVs), and diplopia. Findings from his medical history included mild mental retardation, asthma, and morbid obesity (height, 5 feet 7 inches; weight, 373 pounds). Obstructive sleep apnea was diagnosed 2 years earlier and treated with continuous positive airway pressure (CPAP).

Findings from examination showed visual acuity of 20/20 in the right eye and counting fingers at 4 feet in the left. He identified all 15 Ishihara color plates in the right eye and none in the left. The right pupil was briskly reactive, the left sluggish with a 2+ relative afferent defect. Results of Humphrey automated perimetry in the right eye showed a dense inferonasal defect and moderate generalized depression. In the left eye, there was a dense central scotoma and severe generalized depression. Findings from
fundus examination showed bilateral disc edema, mild on the right and marked on the left, with peripapillary hemorrhages in both eyes. There was mild retinal venous engorgement in the right eye, moderate in the left.

Computed tomography and magnetic resonance imaging (MRI) scans of head and orbits were normal. Cerebrospinal fluid (CSF) pressure was 16 cm H₂O with normal findings from measurements of protein, glucose, and cell count. Results of pulse oximetry measurements were normal in room air. Findings from complete blood cell count was normal. The patient was admitted for 24-hour intracranial pressure (ICP) measuring. A Camino fiberoptic ICP monitor (Integra, Redwood, Calif) was placed after obtaining informed consent from the patient. During sleep, findings from pulse oximetry demonstrated repeated apneic spells associated with a drop of oxygen saturation to 20% to 52% with an accompanying rise of ICP to 48 cm H₂O. Acetazolamide treatment was administered, and a tracheostomy was performed. Within 5 days he exhibited dramatic improvement of optic nerve function. Visual acuity improved to 20/100 OS, and there was improvement of the visual field in both eyes. Bilateral disc edema was also much improved.

**CASE 2**

A 60-year-old man experienced onset of visual loss in his right eye on awakening. He denied headache or eye pain, tinnitus, TOVs, and diplopia. Findings from his medical history included obesity, lumbar disc disease, and depression. Obstructive sleep apnea was diagnosed 2 years earlier and treated initially with uvulopharyngeal palatoplasty. Nasal CPAP was added 2 months earlier because of secondary polycythemia.

Three weeks after onset of visual loss, his visual acuity was 20/25−3 OD and 20/20 OS. He missed 2 of 15 color plates in both eyes. Results of Goldmann perimetry showed an inferior altitudinal visual field defect in his right eye and a full field in his left. There was a 0.9 log unit relative afferent pupillary defect in his right eye. Both optic discs were swollen with an area of segmental pallor superotemporally in his right eye (Figure 1). There was mild engorgement of retinal veins bilaterally.

Hemoglobin levels were 183 g/L. Findings from an MRI scan of the head were normal, including no sign of venous sinus thrombosis. The CSF opening pressure was 21 cm H₂O with normal findings from measurements of protein, glucose, and cell count. He was treated with acetazolamide, 500 mg twice daily, phlebotomy, more aggressive CPAP with decongestants, and a weight reduction regimen. During the next few months, disc edema resolved bilaterally, and optic nerve function showed mild improvement in the right eye (Figure 2).
CASE 3

A 40-year-old man noted a dark spot in the temporal field of his left eye unassociated with eye pain or photopias. In addition, he described brief episodes of “snowy vision” inferiorly in his left eye on arising and intermittent pulsatile tinnitus. There was a history of chronic daily headache for several years without recent change. Findings from his medical history included obesity and recently diagnosed hypertension.

On examination, visual acuity, color vision, and pupillary responses were normal. Results of Goldmann perimetry showed enlargement of the physiologic blind-spot in his left eye. The right optic disc was mildly full; the left, swollen with nerve fiber layer opacification and mild venous engorgement.

Findings from computed tomography of the head and routine blood tests were normal. Lumbar puncture opening pressure was 19.5 cm H2O with normal CSF constituents. He was treated with weight reduction diet and exercise and was able to lose 80 pounds over the next 3 years. Disc edema showed improvement though not complete resolution. The patient was then lost to follow-up for the next 4 years. In this interval he regained some of his weight. Sleep apnea was diagnosed 1 year earlier and treated with CPAP. Headaches and tinnitus improved; vision was stable. Findings from neuro-ophthalmic examination showed persistent disc edema in his left eye with normal optic nerve function.

CASE 4

A 58-year-old nonobese man developed a gray spot in the superior field of the right eye. This defect was subjectively stable for a few weeks and then became more dense. He denied headache or eye pain, tinnitus, TOVs, and diplopia. On examination, his visual acuity was 20/30 OD and 20/20 OS. He missed 3 of 17 Ishihara color plates in his right eye and none in his left. Results of Goldmann perimetry demonstrated an inferonasal visual field defect in the right eye and a full field in the left. His pupils were of equal size and briskly reactive with a 0.6 log unit relative afferent defect in his right eye. Both discs were swollen; the right also showed an area of pallor superiorly (Figure 3). There was mild engorgement of retinal veins in both eyes.

Findings from an MRI scan of the head were normal. His CSF pressure was 23 cm H2O with normal constituents. He was treated with acetazolamide, 500 mg twice daily. Further evaluation led to the diagnoses of hypertension and sleep apnea. The latter was secondary to an anatomic variation of the pharynx and was treated with uvulectomy. Findings from follow-up examination 1 month later showed improved disc edema bilaterally and modest improvement of the right optic neuropathy.

SUMMARY OF CASES

Our patient group consists of 4 men ranging in age from 20 to 60 years with obstructive SAS (Table 1). In 3 pa-

<table>
<thead>
<tr>
<th>Case No./Age, y</th>
<th>Weight, kg</th>
<th>Headache</th>
<th>TOV</th>
<th>Tinnitus</th>
<th>Diplopia</th>
<th>Visual Acuity</th>
<th>Visual Field Defects</th>
<th>Findings From Fundus Examination</th>
</tr>
</thead>
<tbody>
<tr>
<td>1/20 20</td>
<td>168</td>
<td>N</td>
<td>N</td>
<td>N</td>
<td>N</td>
<td>20/20 OD</td>
<td>Inferonasal defect, right eye</td>
<td>Asymmetric papilledema OS&gt;OD</td>
</tr>
<tr>
<td>2/60 60</td>
<td>117</td>
<td>N</td>
<td>N</td>
<td>N</td>
<td>N</td>
<td>20/25-3 OD</td>
<td>Central scotoma, left eye</td>
<td>Bilateral disc edema right eye</td>
</tr>
<tr>
<td>3/40 40</td>
<td>126</td>
<td>Y</td>
<td>Y</td>
<td>N</td>
<td>Y</td>
<td>20/20 OD</td>
<td>Inferior altitudinal defect, right eye</td>
<td>Segmental pallor right eye</td>
</tr>
<tr>
<td>4/58 NA</td>
<td>NA</td>
<td>N</td>
<td>N</td>
<td>N</td>
<td>N</td>
<td>20/30 OD</td>
<td>Normal, right eye</td>
<td>Bilateral disc edema right eye</td>
</tr>
</tbody>
</table>

*TOV indicates transient obscuration of vision; N, no; Y, yes; and NA, not available.

Figure 3. Case 4. At initial examination, fundus photographs show bilateral disc edema. A, The right disc is quite hyperemic except for a wedge of pallor superotemporally. B, The left disc is less swollen and there is a small nerve fiber hemorrhage superotemporal to the disc.


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patients, SAS was related to obesity; in 1 (case 4), the anatomic configuration of the nasopharynx caused obstruction without associated obesity. All 4 patients had unilateral visual loss at initial examination. Only 1 patient (case 3) had typical symptoms of increased ICP (headache, tinnitus, and TOVs). Each was found to have bilateral disc edema with asymmetric (case 1) or unilateral (cases 2 and 3) optic nerve dysfunction. Vision was markedly reduced in 1 eye (case 1). The visual field was abnormal in 5 of 8 eyes (Figure 4). Results of neuroimaging in all 4 patients showed no evidence of mass lesion, hydrocephalus, or venous sinus thrombosis. Daytime CSF pressure measurements were within normal range or only slightly elevated in each case (range, 16-23 cm H2O), and findings from CSF studies were normal in all. One patient (case 1) underwent continuous ICP monitoring, which revealed marked ICP elevations associated with periods of apnea and arterial oxygen desaturation. One patient (case 2), had a history of polycythemia with borderline elevation of hematocrit on presentation. Results of complete blood cell counts in other patients were normal.

Treatment consisted of CPAP in 3 patients, acetazolamide in 2, pharyngeal surgery in 2, and tracheostomy in 1 (Table 2). Three patients (cases 1, 2, and 4) showed improved papilledema (PE) and optic nerve function (quite dramatic in one). In 1 patient (case 3), mild disc edema persisted, but symptoms of increased ICP resolved.

It is well known that sustained elevation of ICP causes PE due to obstruction of retrograde axonal transport at the level of the optic disc. The effect of transient elevations of ICP is less clear. In patients with SAS, daytime measurements of CSF pressure are within normal range, yet these patients can have numerous episodes of marked pressure elevation during sleep ranging from 50 to 750 mm H2O, as demonstrated by continuous ICP monitoring.11 These pressure waves are preceded by and accompanied by apnea with significant reductions of arterial oxygen saturation. Physiologic studies in animals and humans suggest that hypercarbia-induced cerebral vasodilation is the main underlying mechanism for the nocturnal elevation of ICP in this setting.12 Elevated central venous pressure due to forced expiration against a closed glottis and arterial hypertension may also play a role. In some individuals, this episodic ICP elevation seems to be sufficient to cause persistent PE. For example, Bloomfield et al13 described a patient with SAS who had severe

Table 2. Clinical Course

<table>
<thead>
<tr>
<th>Case No.</th>
<th>Imaging†</th>
<th>ICP (cm H2O)</th>
<th>Treatment</th>
<th>Response</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>MRI</td>
<td>16.0</td>
<td>CPAP</td>
<td>Much-improved optic neuropathy</td>
</tr>
<tr>
<td></td>
<td>CT</td>
<td></td>
<td>Acetazolamide</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Furosemide Tracheostomy</td>
<td></td>
</tr>
<tr>
<td>2</td>
<td>MRI</td>
<td>21.0</td>
<td>Palatoplasty</td>
<td>Papilledema resolved</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>CPAP Acetazolamide</td>
<td></td>
</tr>
<tr>
<td>3</td>
<td>CT</td>
<td>19.5</td>
<td>CPAP</td>
<td>Symptoms better</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Improved papilledema and optic neuropathy</td>
</tr>
</tbody>
</table>
bilateral disc edema and normal daytime CSF pressures. His PE resolved following tracheostomy. A similar patient was reported by Bucci and Krohel. In each case, nocturnal elevation of ICP was the presumed mechanism, though continuous monitoring was not performed.

Pseudotumor cerebri (PTC) is a syndrome of elevated ICP with a variety of causes, including chronic obstructive pulmonary disease. The mechanism in chronic obstructive pulmonary disease is believed to be increased cerebral blood volume due to chronic hypercarbia-induced vasodilation. In such patients the CSF pressure is persistently elevated. In contrast, patients with SAS have intermittent elevation of CSF pressure, rising only nocturnally during apneic spells. Thus, patients with SAS-related PE can be considered to have a form of PTC syndrome, even though they do not strictly meet the usual criteria for the diagnosis because their daytime CSF pressure measurements are normal. The diagnosis in these patients may easily be missed for several reasons. First, the normal ICP measurement leads the clinician away from pressure as the cause of disc swelling. Second, these patients do not fit the typical clinical profile that we associate with PTC in that they are most often middle-aged men, not young women. Third, as suggested by our series, they may be more likely to present with visual loss rather than with the usual symptoms of increased ICP (headache and tinnitus). Based on data from previous studies and from case 1 in our series, ICP is elevated in patients with SAS-related PE during sleep and is normal when these patients are awake. This mechanism of nocturnal intracranial hypertension would explain the absence of headache, TOVs, and tinnitus in some patients (cases 1, 2, and 4).

The incidence of visual loss in patients with idiopathic PTC is only 23%, whereas 3 of 4 patients had optic neuropathy. Although the patient group is small, based on our data, patients with SAS-related PE seem to be at a particularly high risk for visual loss compared with patients with typical PTC. Reasons for this may include their older age, nocturnal hypoxia, epinephrine-induced platelet activation, and fluctuations in systemic blood pressure. Vigorous efforts to improve nocturnal oxygenation can be vision saving, as illustrated by case 1 in whom vision improved from counting fingers to 20/100 following tracheostomy.

Clinicians should have a high index of suspicion for this entity. The diagnosis of SAS-related PE should especially be considered for patients with unexplained unilateral or bilateral disc edema with normal or borderline CSF pressures who are obese and/or have a body habitus that might predispose them to sleep apnea. Pertinent questioning should include inquiries regarding excessive daytime somnolence and restless, noisy sleep.

Nocturnal apnea may also play a role in the pathogenesis of visual loss in some patients with obesity-related PTC. Risk factors for visual prognosis in PTC remain incompletely defined. It is possible that nocturnal oxygen desaturation represents an independent risk factor for the development of visual loss secondary to PE in this group of patients. The patient reported by Doyle and Tami may be an example of this mechanism. These authors described a morbidly obese man with SAS and PE in whom daytime CSF pressure was markedly elevated. He presented with severe bilateral visual loss that was permanent despite treatment with tracheostomy and lumboperitoneal shunt. Such patients may have a combination of obesity-related PTC and obesity-related SAS. Adequate treatment in these individuals must address nocturnal oxygenation as well as standard management of PTC.

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REFERENCES