# Transient cortical blindness after intradiscal oxygen–ozone therapy

*Agostino Salvatore Vaiano, Cristiana Valente, Giacomo De Benedetti[1], Guido Caramello*

A 54-year-old caucasian male developed bilateral blindness during an oxygen–ozone injection for disc herniation. The visual loss (VL) was immediately followed by severe frontal headache, vomiting, and nausea. The patient underestimated the VL showing Anton's syndrome, with a complete visual recovery after 2-month follow-up. Magnetic resonance data were consistent with recent ischemic lesions in bilateral vascular territories of posterior cerebral arteries.

**Key words:** Anosognosia, Anton's syndrome, cortical blindness, cryptogenic stroke, intradiscal oxygen–ozone therapy, patent foramen ovale

Cortical blindness (CB)–a subset of cerebral blindness–is a neurological syndrome characterized by bilateral visual loss (VL) in the context of normal pupillary function, extraocular eye movements, and fundoscopy results. This syndrome is often associated with ischemia of the visual cortex, head trauma, migraines, hypertensive encephalopathy, and many other lesions of the visual cortex. It is often caused by dysfunction or destruction of both occipital lobes.[1] If no structural abnormality is identified, the prognosis is usually favorable. If the lesion extends beyond the striate cortex into the visual association area,[2] patients with CB may exhibit anosognosia (also known as Anton's syndrome, in which the patient may deny blindness). Anosognosia is often associated with concomitant dysfunction of the parietal lobe, more often on the right side than on the left.

## Case Report

A 54-year-old Caucasian male presented to us with severe bilateral VL. His clinical history was notable for lumbar sciatica and migraine. The acute blindness developed about 1 min after an uncomplicated L5-S1 injection (4 ml intradiscal and 11 ml periganglionic) of an oxygen–ozone mixture (ozone concentration of 27 μg/mL). After 5 min, it was followed by severe frontal headache, vomiting, and nausea. In the emergency room, 1 h after the onset of VL, analgesic therapy was administrated without any significant improvement, and a neurological examination showed no other neurological signs. Blood pressure (BP), heart rate, and oxygenation saturation were monitored during the oxygen–ozone therapy (OOT), and there was no evidence of significant hemodynamic changes. Mean BP measured at the emergency room and every day during the hospitalization was 120 mmHg (range: 100–140) and 70 mmHg (range: 60–80) for systolic and diastolic values, respectively. Ophthalmological evaluation was performed with difficulty in the emergency room because the patient was extremely agitated, but he was spatially and temporally oriented. The bedside ophthalmic examination revealed bilateral blindness with no light perception but with a positive pupillary light reflex. The patient probably underestimated the VL; in fact, he often tried to guess the identity of visual objects, giving the incorrect answer.

A computed tomography scan performed by 2 h after the onset of VL and headache symptoms showed no signs of an acute ischemic lesion or hemorrhagic stroke. Two days after the onset of VL, brain magnetic resonance imaging (MRI) revealed multiple areas of hyperintensity on T2 sequences and diffusion-weighted images. Areas of hypointensity were detected on apparent diffusion coefficient (ADC) mapping involving the right parasagittal occipito-parietal cortex, and with a lesser size, the left homologous area and the right medial thalamus [Fig. 1]. Traditional and MRI angiography were normal.

His headache improved on the 3rd day and disappeared the next day. Visual acuity (VA) began to gradually improve on the 4th day, with a full recovery on the 9th day (20/20 in both eyes). At this time, visual field (VF) was normal.

Transcranial Doppler emboli detection with contrast saline showed the presence of ten microembolic signals (high-intensity transient signals) during baseline conditions and during Valsalva release. Transthoracic echocardiography was completely normal, whereas transesophageal contrast echocardiography revealed the presence of a large patent foramen ovale (PFO) and atrial septal aneurysm associated with the detection of early microbubbles in the left atrium during Valsalva release. There was no evidence of a clot associated either with the atrial septal aneurysm or anywhere in the heart. After 20 days, the patient underwent percutaneous closure of the PFO.

During the follow-up, after 2 months, we observed VA of 20/20 in both eyes. VF, visual-evoked potentials, and optical coherence tomography of the optic nerve head were all normal. Brain MRI performed after 4 months showed size reduction of the hyperintensities compared to the same sequences of the affected areas [Fig. 2].

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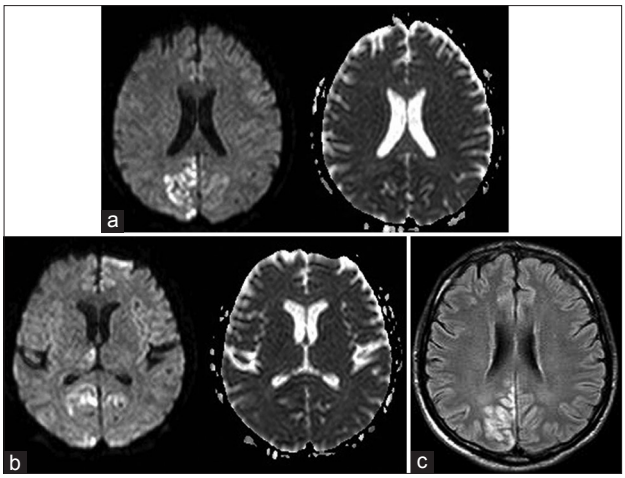


**Figure 1:** (a and b) Magnetic resonance imaging: diffusion-weighted imaging (on the left) and corresponding apparent diffusion coefficients map (on the right). Hyperintensity in diffusion-weighted imaging and hypointensity in apparent diffusion coefficient map can be seen in the occipito-parietal cortex bilaterally, with a significant larger extension on the right side (a) and also in the right medial thalamus (b). (c) Fluid-attenuated inversion recovery magnetic resonance imaging confirms asymmetrical, mainly on the right side, ischemic lesion showing bilaterally high signal intensity areas in the occipito-parietal cortex

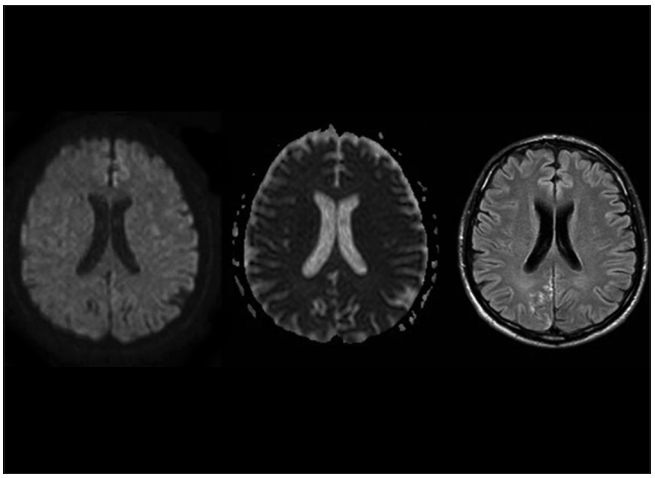

**Figure 2:** After 4 months: Diffusion-weighted imaging (on the left) and corresponding apparent diffusion coefficient map (in the middle) magnetic resonance imaging show size reduction of the hyperintensities compared to the same sequences of the affected areas. Fluid-attenuated inversion recovery (on the right) suggests both resorption of the vasogenic edema and signs of poststroke gliosis

## Discussion

We herein describe a case of CB as a result of bilateral occipito-parietal lobe ischemia following OOT medical application. The patient was reportedly blind, showing confabulations only in the first 2 days after the onset of VL. We can explain the confabulations by referring to Anton's syndrome. According to our MRI data, the CB was caused by recent ischemic lesions in the bilateral posterior cerebral artery's (PCA) vascular territories.

Bilateral occipital cortex vascular diseases are relatively frequent because the two PCAs are terminal branches of a single basilar artery (BA). This simultaneous bilateral ischemia is generally due to a mechanism of embolism or hypotensive episode.

Moreover, we excluded posterior reversible encephalopathy syndrome because the systemic arterial pressure was always normal and the MRI features were not typical.

Further, the possible etiologies could be an incidental stroke unrelated to the procedure or a direct toxic effect of the ozone, but the latter is unlikely because of the low ozone concentration.

Although the underlying pathophysiology remains elusive, we support air embolism as the most likely cause of CB. We found a PFO and it is well accepted that it is highly prevalent in patients with cryptogenic stroke.[3,4]

Most nonaccidental causes of arterial cerebral air embolism are iatrogenic (microbubble studies, central venous catheter,[5] or surgery[6]), as a result of direct introduction of air into the arterial system, incomplete filtration by pulmonary capillaries, or paradoxical right-to-left embolization.[6] The frequency reported is 0.1% of all cerebral ischemic events.[6] Interaction between bubbles and blood components (activated platelets) may lead to their stabilization.[7] It would be desirable for the diagnosis of air embolism to demonstrate bubbles with angiographic study, but the early resolution of small bubbles is described. Therefore, diagnosis of air embolism is based on clinical examination together with the anamnestic temporal relationship with air entry into the systemic circulation.[6]

In our patient, emboli are probably produced by oxygen–ozone injection that released dissolved gases in the blood. Normal neuroimagings are consistent with small gaseous emboli. Emboli reach the cerebral circulation, through the PFO with right-to-left shunt, switching BA. They are fragmented in the two PCAs with the temporary occlusion of both the right P1 segment, including perforating arteries for the posteromedial thalamus (area for consciousness and spatial orientation) and a more distal occlusion of the left P1 segment downstream of thalamus perforating arteries.

To our knowledge, only four cases of vertebrobasilar stroke during OOT exists in literature[8-11] but only one refers to intradiscal therapy and none of them had cardiac abnormalities.

Ozone therapy is a widely used treatment for lumbar disc herniation that has failed to respond to conservative management. A recent review has summarized the complications of this procedure that are rarely documented in literature.[12] Besides disc herniation, we found some studies on other possible indications of medical OOT such as lower limb atherosclerosis, chronic limb ischemia, diabetic foot, osteoarthritis, hepatitis and heart infarction, and stroke.[13] Therefore, further studies must demonstrate the reliability and safety of this medical treatment.

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### Conflicts of interest

There are no conflicts of interest.

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