

Cerebral gas embolism and multifocal ischemic stroke during oxygen-ozone therapy: a case report

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ABSTRACT

Introduction Ischaemic stroke, primarily caused by thromboembolic events, typically arises as a consequence of underlying vascular or cardiac pathology. Non-thrombotic embolic strokes, although rare, are increasingly seen in interventional and intravascular procedures. Oxygen-ozone therapy (OOT) is one of the popular treatments for lumbar disc herniation, providing pain relief. However, it has been linked to gas embolisms, posing severe risks. This article details a case of cerebral gas embolism and multifocal acute ischaemic stroke that occurred during OOT for lumbar disc herniation pain relief.

Case presentation We present a case of a 58-year-old woman with acute onset limb weakness and speech disturbance that happened during a lumbar intradiscal oxygen-ozone injection session. Brain CT and MRI scans showed multiple cerebral gas embolisms and diffusion-restricted areas in both cerebral hemispheres. Echocardiography revealed a patent foramen ovale, hinting at a conduit for paradoxical embolism. Follow-up of the patient after 1 year showed significant improvement.

Conclusion OOT, as a popular treatment for chronic pain, has been associated with severe adverse events. When facing cases of acute postoperative or postinterventional encephalopathy or stroke, arterial cerebral gas embolism should be considered a possibility. The presence of intracardiac defects or intrapulmonary shunts paves the way for paradoxical emboli to happen, resulting in a higher chance of neurological complications.

symptoms associated with non-thrombotic embolic stroke make it a complex condition to diagnose and treat, leading to inconsistent management strategies. The incidence of non-thrombotic causes of embolic stroke, though rare, may see a surge with the expanding utilisation of interventional and intravascular procedures.² Paradoxical emboli from the venous system to the systemic circulation can contribute to stroke in these procedures. Paradoxical emboli occur when thrombi develop in the venous system and migrate through a patent foramen ovale (PFO) or other right to left conduits, entering the systemic circulation and causing strokes or peripheral emboli. While most individuals with a PFO do not display any symptoms, a PFO is identified in approximately 40–50% of cases with paradoxical emboli. Evaluation of PFO is required in cases where paradoxical embolism is a possibility.³

Oxygen-ozone therapy (OOT) has become widely embraced as a therapeutic modality for chronic pain management and is frequently employed in non-clinical settings. Specialised clinics in Iran provide OOT; however, there is a lack of information regarding how often it is utilised and how accessible it is to patients. OOT has been recommended as an effective and safe treatment for improving the quality of life in patients with lumbar disc herniation. This treatment has been proposed to postpone the need for surgery in patients who do not see improvement with conservative measures.⁴ During the procedure, a combination of oxygen-ozone is injected into the nucleus pulposus of the lumbar disc and the paravertebral muscle surrounding the disc. Ozone oxidises the proteoglycans in the nucleus pulposus, resulting in a slight disc volume reduction and subsequent pain relief. In addition, ozone has been shown to have anti-inflammatory, analgesic and disinfectant effects.⁵



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INTRODUCTION

Ischaemic stroke is characterised by the development of infarction in the central nervous system, constituting roughly 71% of strokes seen globally. The majority of ischaemic strokes arise from thromboembolic and thrombotic events, often originating from conditions such as large artery atherosclerosis and cardiac diseases, notably atrial fibrillation. Understanding the aetiology behind each ischaemic stroke is crucial as it can influence treatment approaches aimed at preventing another stroke.¹

Embolic strokes can also originate from different tissue and non-tissue origins despite having comparable symptoms. The uncommon nature and wide array of

According to systematic reviews and meta-analyses, ozone therapy treatments have demonstrated safety and effectiveness, with low adverse effects. However, there have been reports of serious complications, such as gas embolisms.^{6–10} Gas embolism, characterised by the accidental introduction of gas into vascular structures, is a primarily iatrogenic clinical complication that has the potential to cause severe morbidity and mortality. Tiny bubbles moving within blood vessels can lead to the development of thrombi, ultimately obstructing blood circulation and causing an ischaemic stroke. All healthcare professionals must recognise the potential for gas embolism in their practice.^{9 11}

Within this article, we present a case of cerebral gas embolism and multifocal acute ischaemic stroke that occurred during OOT for lumbar disc herniation.

CASE PRESENTATION

A 58-year-old woman without any known previous medical history was brought to the emergency department with an abrupt onset of speech disturbance with weakness in her left upper and right lower limbs. Her symptoms started earlier that evening during a lumbar intradiscal oxygen-ozone injection at a local pain clinic. On admission, she was awake, dysarthric and had no complaints of headache, nausea or vertigo; the neurological examination showed a flattened nasolabial fold on the left side, weakness of the left upper limb, Medical Research Council (MRC) grade 4 and right lower limb MRC grade 4. Both plantar responses were flexor and cerebellar, and sensory examinations were unremarkable. Following the initial brain CT scan, it was noted that multiple gas bubbles were present, suggesting the presence of cerebral gas embolism (as seen in figure 1A–F). Subsequent examination using diffusion-weighted MRI revealed multiple restriction areas in both cerebral hemispheres, which correlated with areas of acute infarction (figure 1G–L).

She was admitted for further investigations and received antiplatelet therapy. Her symptoms improved during her hospital stay, her speech disturbance resolved, and her muscle power improved in a few days. Her ECG was unremarkable for any cardiac dysrhythmia. She had normal carotid arteries with normal waveforms and antegrade flow on ultrasound. A transthoracic echocardiogram with contrast demonstrated bubbles passing through the intra-atrial septum, suggestive of a small-sized PFO.

Several days later, while in the hospital, she tested positive for COVID-19 and was treated with remdesivir for 5 days. On finishing her treatment, she was discharged from the hospital and prescribed antiplatelet therapy with aspirin 80 mg/day and clopidogrel 75 mg/day. During a subsequent examination conducted 12 months later, she exhibited no symptoms with a Modified Rankin Scale of 0.

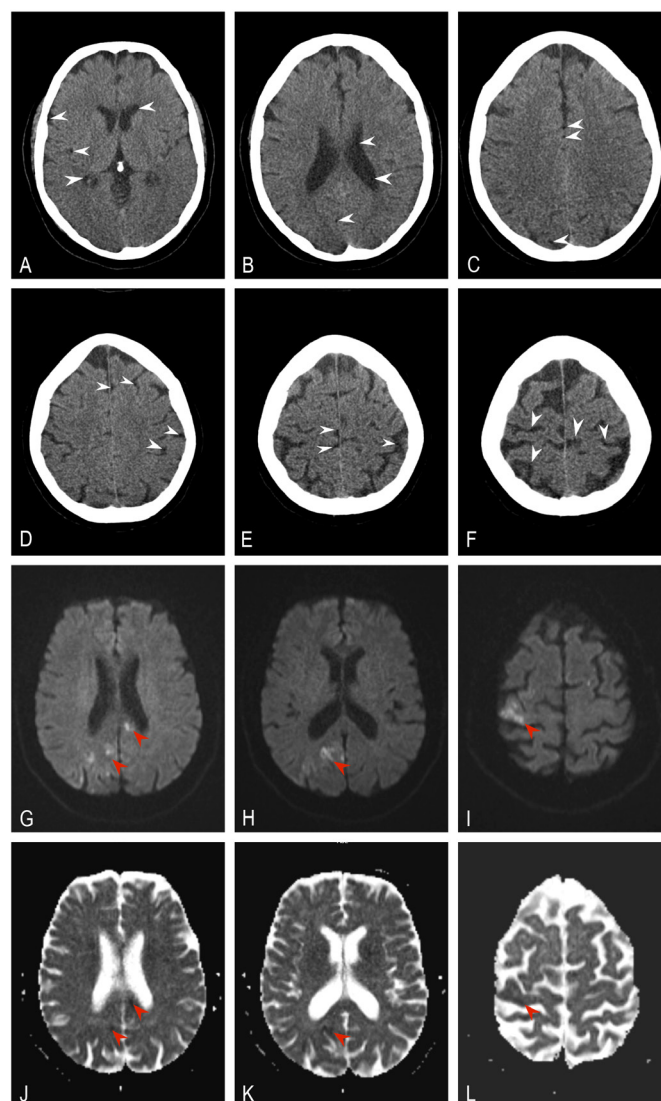


Figure 1 Brain CT scan showing the presence of multiple gas bubbles (white arrowheads), indicative of cerebral gas embolism (A–F). Diffusion-weighted imaging (G–I) and apparent diffusion coefficient (J–L) showing multiple areas of diffusion restriction in both cerebral hemispheres, suggestive of acute ischaemic stroke of embolic source (scarlet arrowheads).

DISCUSSION AND CONCLUSIONS

OOT is popular for treating chronic pain outside of medical settings, even though there is limited evidence and insufficient clinical trials. Evidence from reported cases suggests that the potential for severe adverse events in OOT may have been underestimated. It has been associated with cases of vertebrobasilar occlusion, cortical blindness, encephalopathy and seizures, with cases leading to severe and life-threatening complications, including status epilepticus, as reported in previous studies.^{6 7 9 10 12 13}

Numerous pathways are available for the introduction of gas into the circulatory system. Air may access the arterial system through direct entry, commonly resulting from chest or abdominal injuries, or it can be unintentionally introduced

during medical interventions. In previous cases, the presence of gas bubbles in and around the cervical arteries has indicated a potential direct entry of ozone into the arterial circulation. However, the exact underlying mechanisms are not fully grasped. Another possibility is that venous emboli may pass into the arterial circulation through intracardiac defects or intrapulmonary shunts.

When assessing cases of acute postoperative or postinterventional encephalopathy or stroke, it is crucial to consider arterial cerebral gas embolism as a potential cause, given its ability to present with varied combinations of altered alertness, focal deficits and seizures. A high degree of clinical suspicion is crucial in identifying these patients due to the non-specific examination findings and the suboptimal ability of brain CT scans to identify gas.¹⁴

Observations from in vivo studies have indicated that mobile bubbles present in small vessels can induce thrombus formation, leading to circulatory occlusion. Furthermore, they can exacerbate the ischaemic condition by directly harming the endothelium, triggering the release of inflammatory mediators, commencing the complement system and forming thrombi locally.^{9,15}

This case demonstrates the occurrence of gas embolism and stroke as complications of intradiscal and intramuscular injections during OOT. In our case, the likelihood of paradoxical emboli is increased due to the presence of a PFO.

The scenario involving our patient suggests that oxygen-ozone bubbles may have entered the carotid arteries and moved towards the most distal and narrow vessels in the arterial circulation, ultimately causing bilateral cortical lesions.

Atrial septal defects and PFOs, as examples of right-to-left shunts, are being increasingly recognised for their role in transmitting thrombi and other substances from veins to arteries, consequently elevating the risk of paradoxical stroke.² A paradoxical embolism occurs when air or gas enters the venous system and crosses over into the systemic arterial circulation, leading to symptoms of blockage in the end arteries.¹¹ A patent foramen ovale, present in approximately 25 per cent of individuals, enables the movement of gas bubbles in a right-to-left direction. Several factors have been suggested to identify a greater likelihood of stroke in people with PFO, such as the degree of shunting and an aneurysmal interatrial septum.¹ PFO closure could offer advantages to certain individuals dealing with recurrent strokes and no identifiable cause, but current guidelines do not suggest it as a routine procedure.²

Our findings align with previous cases, highlighting the essential consideration of arterial cerebral gas embolism as a potential cause in instances of postinterventional stroke and advocating for more extensive research on possible complications and their management in these interventions.

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