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Case Report

Enhancement of the Third Cranial Nerve due to Microvascular Ischemia: Case Report

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Abstract
Third nerve palsy (3NP) commonly results from a microvascular ischemic insult. Typically, computed tomography or magnetic resonance angiography is performed to rule out a posterior communicating artery aneurysm. If this is normal and the pupil is spared, patients are often observed with the expectation of spontaneous improvement within 3 months. Oculomotor nerve enhancement on MRI with contrast in the context of microvascular 3NP is not well recognized. Here, we report third nerve enhancement in a case of a 67-year-old woman with diabetes and other vascular risk factors who presented with left eye ptosis and a limitation of extraocular eye movements consistent with 3NP. She underwent an extensive inflammatory workup that was negative and the diagnosis of a microvascular 3NP was made. A spontaneous recovery was achieved within 3 months, and she did not receive any treatment. She remained clinically well, although increased T2 signal in the oculomotor nerve persisted after 10 months. While the exact mechanism remains unknown, it is likely that microvascular ischemic insults lead to intrinsic changes of the third nerve that may result in enhancement and persistent T2 signal. Additional workup for inflammatory causes of 3NP may not be required when enhancement of the oculomotor nerve is seen in the right clinical context. Further study is required to understand why enhancement is a rarely reported finding in patients with microvascular ischemic 3NP.

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Introduction

The most common cause of third nerve palsy (3NP) is microvascular ischemia, accounting for a reported 42% of cases [1]. It is recommended that the patient undergoes computed tomography or magnetic resonance angiography to exclude a posterior communicating artery aneurysm. If this is normal and the pupil is spared, patients are typically observed as spontaneous improvement is expected within 3 months. When magnetic resonance imaging of the brain and orbits with contrast is obtained in patients with 3NP to exclude other causes, one would expect the third cranial nerve to appear normal in cases of microvascular ischemia. Enhancement of the oculomotor nerve is not well recognized in microvascular ischemic 3NP with limited case reports and series outside of North America. In this case, we demonstrate that enhancement of the third cranial nerve may be seen in microvascular ischemia 3NP and provide imaging follow-up.

Case Report

A 67-year-old woman of Chinese origin was referred to neuro-ophthalmology for a 3NP. She had a past medical history of type 2 diabetes for 15 years with a recent HbA1c of 11.1%, hypertension, dyslipidemia, liver fibrosis, and hemorrhoids. Her medications included irbesartan, simvastatin, empagliflozin, semaglutide. One week prior to presentation, she reported new-onset left-eye ptosis and double vision, in addition to mild pain around her left eye. She presented to the emergency room and had a CTA of the head that was normal. She was referred to neurology who ordered an MRI of the brain and orbits with contrast. This was reported to show abnormal enhancement with slight thickening of the cisternal segment of the left third cranial nerve (Fig. 1a–d). There was also increased T2 signal in the cisternal and cavernous portions of the third nerve. She was referred to neuro-ophthalmology. At that time, her visual acuity was 20/25 OD and 20/50 OS due to cataract. She had left complete ptosis and a complete limitation of elevation, depression, and adduction. The right ocular ductions were full, and cranial nerve function was otherwise normal. The pupils were equal sizes and both reactive to light. She was diagnosed with a complete, pupil-sparing 3NP. However, given the abnormal enhancement of the optic nerve, she underwent an extensive workup. This included inflammatory bloodwork that was normal (ANA, ANCA, ACE, IgG4 serum levels, NMO-IgG, MOG-IgG, ESR, CRP, VDRL, HIV) and a lumbar puncture that showed normal cell count, glucose, and protein levels. Her clinical course was monitored, and a repeat MRI was performed 1 month after onset, and there was persistent thickening and enhancement of the third nerve. The 3NP spontaneously resolved after 2 months. No new diabetes or hypertension medications were started within this time. She had a repeat MRI 10 months later that showed significant improvement with only faint, minimal enhancement at that time (Fig. 2a–d). Increased T2 signal in the cisternal, cavernous, superior, and inferior portions of the third nerve persisted. The patient had no recurrence and remained clinically well 1 year after the onset. She was started on insulin 6 months after the onset of the 3NP.

Discussion

Our patient was found to have abnormal enhancement of the left third cranial nerve on MRI of the orbits and brain with contrast, following a presumed microvascular ischemic 3NP. The diagnosis of microvascular ischemic 3NP was made since the patient had significant uncontrolled vascular risk factors, her pupil was spared in a complete 3NP, and she had

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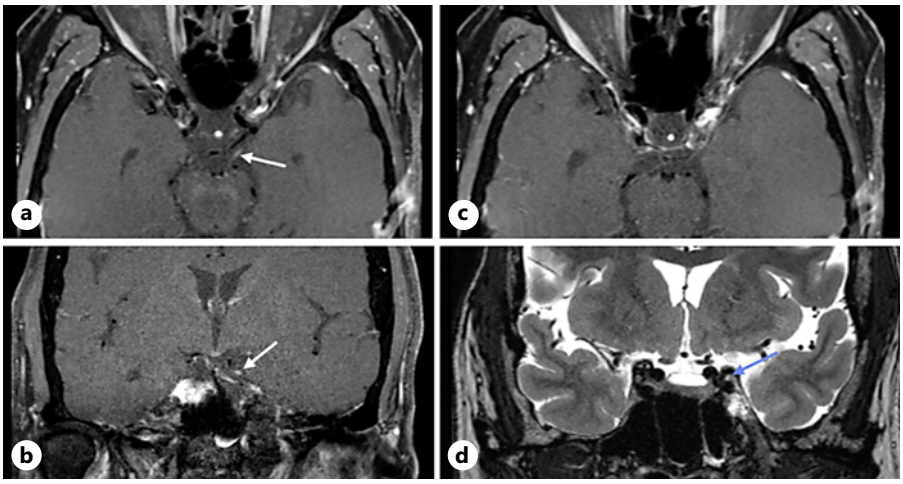

Fig. 1. Axial (top) and coronal (bottom) magnetic resonance imaging with contrast of the third cranial nerve at presentation. This shows enhancement (white arrows) in the T1 postcontrast images and increased T2 signal (blue arrow) in the third cranial nerve.

spontaneous recovery within 3 months. Moreover, an extensive inflammatory workup and lumbar puncture were unremarkable.

Enhancement of the third cranial nerve is not a well-recognized finding in microvascular ischemic third nerve palsies. This may be because it is not always present, the MRIs that are performed do not have high enough resolution, or it may only be present in a small proportion of cases. Few reports have identified enhancement of the third cranial nerve in microvascular ischemic 3NP [2–5]. To our knowledge, the only case in North America of third nerve enhancement in the context of possible microvascular ischemic 3NP was identified by Tamhankar et al. [5]. In this prospective study, MRI of the orbits revealed enhancement of the oculomotor nerve in one patient with 3NP and vascular risk factors. The authors deemed this idiopathic after further workup and spontaneous improvement without treatment. Roques et al. [2] reported oculomotor nerve enhancement using contrast-enhanced CISS imaging in a 55-year-old male with poorly controlled diabetes diagnosed with microvascular 3NP. The authors suggest that adding contrast-enhanced 3D-CISS imaging to radiologic protocols may reveal enhancement and thickening of the intracavernous segment of the oculomotor nerve in the case of ischemic 3NP, as seen in the case reported here. Unlike our case, these reports did not have follow-up imaging to ensure that the enhancement resolved and did not assess intrinsic T2 signal on follow-up.

There are larger studies that have examined this question. Zhao et al. [3] examined the imaging features of isolated 3NP in patients with diabetes. In this retrospective review, enhancement of the ipsilateral third cranial nerve was detected in 64% of patients. The most common findings included thickening and enhancement of the cavernous segment and inferior division of the intraorbital segment of the posterior ON. Blood sugar control was not positively correlated with the occurrence of nerve enhancement. Instead, elevated inflammatory biomarkers were hypothesized to accompany nerve enhancement in a hyperglycemia-independent manner via the breakdown of the blood-nerve barrier that allows leakage and accumulation of contrast material [3]. The authors postulated that differences in the variety and concentrations of metabolic and inflammatory elements may represent the underlying mechanism for observed nerve enhancement in diabetic 3NP palsy [3]. However, a complete workup such as inflammatory bloodwork and lumbar puncture was not performed in all patients. The authors also treated many patients with

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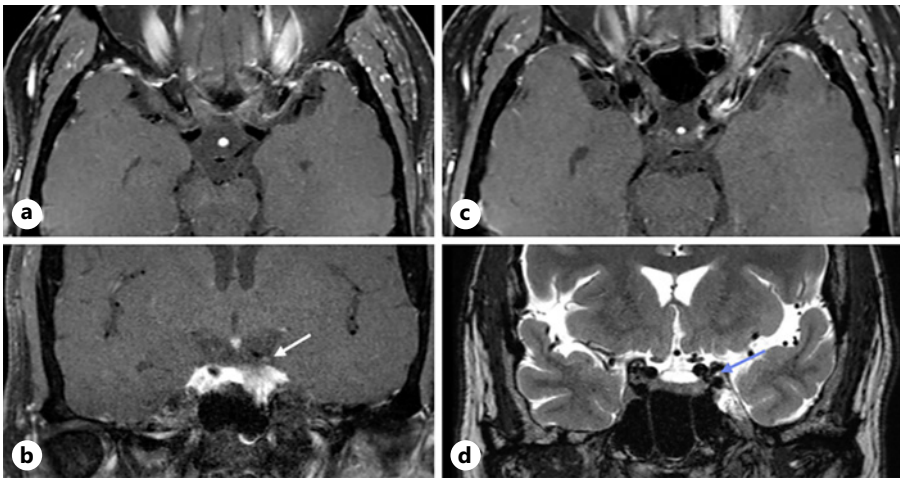

Fig. 2. Axial (top) and coronal (bottom) magnetic resonance imaging with contrast of the third cranial nerve 10 months after initial presentation. This shows less and only faint enhancement (white arrow) in the T1 postcontrast images and persistently increased T2 signal (blue arrow) in the third cranial nerve.

corticosteroids, raising the question as to whether these patients truly had microvascular ischemic 3NP. Yang et al. [4] published a retrospective review of 45 patients with presumed microvascular ischemic 3NP and found that 32 (71.1%) had enhancement of the third cranial nerve in the cavernous sinus. Like the previous case series, not all patients had a complete workup that included inflammatory bloodwork and lumbar puncture. They found that while not significant, patients who received 80 mg of methylprednisolone along with routine therapy showed numerically greater improvement scores. The authors suggest that these findings may indicate an inflammatory process as a key mechanism [4]. This raises the possibility that some patients may not have truly had microvascular ischemic 3NP.

Oculomotor nerve enhancement in the context of 3NP has additionally been identified in cases of vascular compression and idiopathic cases [6, 7]. Shimizu et al. [6] presented two cases of third nerve enhancement occurring in patients with atherosclerotic risk factors, who were diagnosed with direct posterior communicating artery compression of the third nerve, in the absence of a cerebral aneurysm. Spontaneous resolution occurred in both cases raising the possibility that these were related to microvascular ischemia. Additionally, Park et al. [7] reported 6 patients with 3NP following "idiopathic oculomotor nerve neuritis". In this retrospective study, neuritis was defined as cranial nerve palsy with definite enhancement of the corresponding nerve on MRI. Patients responded well to steroid treatment and tended to have favorable prognoses. In contrast to the case reported here, patients with vascular risk factors were excluded from the review conducted by Park et al. [7].

It remains unknown why some patients with microvascular ischemic 3NP develop enhancement of the third nerve. It is possible that this was a more severe ischemic injury, and decreased blood flow in the small arteries supplying the third nerve resulted in decreased flow and an increased signal from the intravascular contrast material. However, this would not explain why the enhancement persisted beyond the duration of symptoms. Likely, the ischemic injury resulted in intrinsic changes to the third cranial nerve, which is why there was persistent increased T2 signal in the nerve at follow-up. In addition, this case indicates that T2 enhancement persists after spontaneous resolution of the ischemic event. As such, the enhancement may be present prior to the onset of an ischemic 3NP, and the causal relationship remains unknown.

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This persistently increased T2 signal is similar to what one would see as sequelae of an ischemic optic neuropathy. This case demonstrates that increased T2 signal in the third cranial nerve may be a consequence of a previous ischemic 3NP. Increased T2 signal of the third nerve may be attributed to an inflammatory process and ultimately treated with steroids. Recognizing that this finding is nonspecific and can also be present following an ischemic 3NP may prevent clinicians from pursuing unnecessary or inappropriate evaluation and treatment. Further studies are needed to know the incidence of oculomotor nerve enhancement in ischemic 3NP. The CARE Checklist has been completed by the authors for this case report, attached as online supplementary material (for all online suppl. material, see www.karger.com/doi/10.1159/000529669).

Conclusion

In summary, here, we present a patient with a history of poorly controlled diabetes who was found to have enhancement and thickening of the cisternal segment of the third cranial nerve on MRI imaging in the context of a complete pupil-sparing 3NP. Steroid therapy was not initiated, and she remained clinically well at 10-month follow-up with minimal enduring enhancement and persistently increased T2 signal. The spontaneous improvement indicates this was related to microvascular ischemia. This case is the first to provide follow-up imaging and demonstrate persistent T2 signal in the oculomotor nerve may occur.

Acknowledgment

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Statement of Ethics

Ethical approval is not required for this study in accordance with local or national guidelines. Written informed consent was obtained from the patient for publication of the details of their medical case and any accompanying images.

Conflict of Interest Statement

The authors have no conflicts of interest to declare.

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Author Contributions

Jonathan A. Micieli developed the concept of the case report, and both Jonathan A. Micieli and Justin Kritzinger were involved in interpreting the data and drafting and critically revising the manuscript.

Data Availability Statement

All data generated or analyzed during this study are included in this article and its online supplementary material. Further inquiries can be directed to the corresponding author.

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