Diabetic Inferior Division Palsy of the Oculomotor Nerve

Hwi-Ju Kao[1], Yung-Yee Chang[2], Min-Yu Lan[2], Yi-Fen Kao[2], Hsiu-Shan Wu[2], and Jia-Shou Liu[2]

Abstract- In this case report we present a diabetic patient with isolated, pupil-sparing, incomplete inferior division third cranial nerve palsy. Laboratory tests for the evaluation of thyroid function, infection, myasthenia gravis and autoimmune diseases were normal. Cranial computed tomography, magnetic resonance imaging and magnetic resonance angiography also showed normal findings. Accordingly, diabetes related vasculopathic third nerve palsy was suggested. The ocular signs of oculomotor palsy completely disappeared 2 months later. Although this clinical entity is rarely reported, differential diagnosis with pupil-sparing third nerve palsy of other etiologies such as compression by an aneurysm or tumor still need to be investigated.

Key Words: Oculomotor nerve, Pupil, Diabetic cranial neuropathy, Magnetic resonance imaging (MRI)

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INTRODUCTION

The oculomotor nerve bifurcates into the superior and inferior divisions when it reaches the superior orbital fissure. The former supplies the rectus superioris and the levator palpebrae superioris muscles. The latter innervates the medial and inferior rectus muscles, the inferior oblique muscle, the sphincter of the pupil and ciliary body[1]. Isolated paralysis of the inferior division of the oculomotor nerve is rarely reported[2-13]. Etiologies of this clinical manifestation have been reported to be head trauma[2,4,11], mesencephalic vascular malformation[5], ependymal cyst[6], ischemia following the clipping of a basilar artery aneurysm[7], arteriovenous fistula[9], intraorbital dural arteriovenous malformation or varix[11,12], ophthalmoplegic migraine[11], presumed vasculitis or demyelinating disease[8,11], inflammatory[3,10] and even undetermined disorder[3,11]. Now we report a case of diabetic inferior division palsy of the oculomotor nerve, which resolved gradually 2 months after the event.

CASE REPORT

A 26-year-old woman was admitted for an acute onset of the right periocular pain with horizontal binocular diplopia. There was no history of vertigo, nausea, vomiting, facial numbness, tinnitus, dysarthria, dysphagia, choking or hiccups. She had been diagnosed as having type 1 diabetes mellitus (DM) and hypertension at age 24. At the time of admission, a complete examination disclosed a multi-focal polyneuropathy, mild proteinuria, and a proliferative diabetic retinopathy (PDR). She received laser therapy treatment for the PDR of the right eye 6 months later. After the procedure, the visual

From the Departments of Neurology, [1]Cheng-Ching Hospital, Taichung, Taiwan; [2]Chang Gung Memorial Hospital, Kaohsiung, Taiwan.
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Reprint requests and correspondence to: Jia-Shou Liu, MD, PhD. Department of Neurology, Chang Gung Memorial Hospital, No.123, Ta-Pei Road, Niaosung, Kaohsiung, Taiwan.
E-mail: josefliu@ms15.hinet.net

acuity of the right and left eye was 20/100 and 20/20 with eyeglasses, respectively. Following that, she reported not regularly taking her medications for the control of her diabetes and hypertension during the follow-up period. Then, because of an acute onset of dizziness, right periocular pain and binocular double vision she visited our emergency room for help. At that point, she reported having had no history of migraine, cranio-facial trauma, systemic vasculopathy or any recent infection.

On admission, her blood pressure was 180/100 mmHg. A check-up of her visual acuity demonstrated a best-corrected acuity of 20/200 OD and 20/25 OS. Ophthalmoscopic examination showed findings compatible with PDR. The pupils were isocoric and reacted properly to both direct and indirect light stimuli. Mild extropia and hypertropia of the right eye were noted in natural position. The right eye movement showed poor adduction with a mild limitation of depression (Figure) while the left eye showed full motility in all directions. There was no blepharoptosis (Figure). Examination of the other cranial nerves was normal. Tendon reflexes of the four limbs showed generalized hyporeflexia. No evidence of abnormal pyramidal, extrapyramidal or cerebellar signs was found. Our clinical impression was isolated inferior division paresis of the right oculomotor nerve.

A complete blood cell count, liver and renal function, electrolytes, uric acid assay and thyroid function were all within normal limits. The erythrocyte sedimentation rate (ESR) was 14 mm/hour. Tests of her fasting blood glucose ranged from 256 to 277 mg/dl and her index of glycosylated hemoglobin was 9.6%. The lipid profile showed dyslipidemia (total cholesterol was 242 mg/dl and triglyceride was 339 mg/dl). Tests for VDRL, anti-acetylcholine receptor antibody and antinuclear

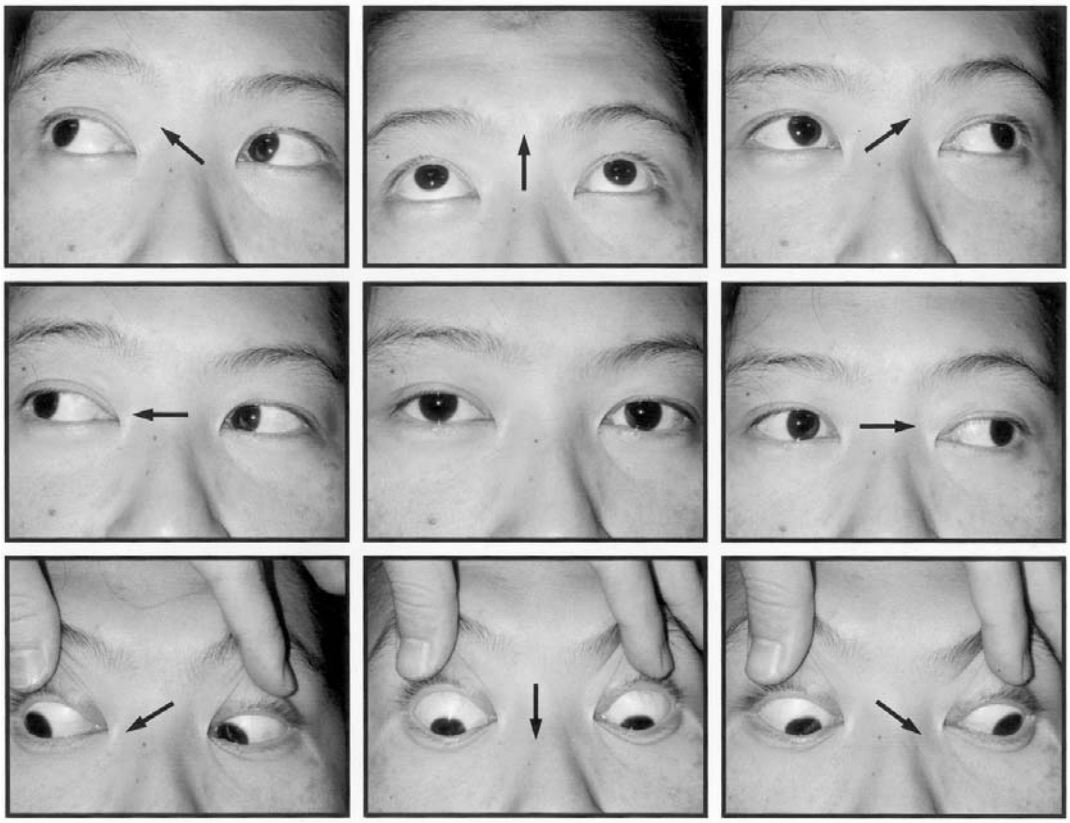

Figure. Ocular motility of the patient with right inferior divisional oculomotor nerve paresis. Exotropia and hypertropia of the right eye are seen in the primary position. Note that the superior rectus and the levator palpebrae muscles are not involved. Arrows indicate the direction of gaze.

antibody were all negative. An enhanced computed tomography (CT) of the head showed no vascular abnormality, mass lesion, or meningeal enhancement. Magnetic resonance imaging (MRI) with gadolinium diethylenetriamine penta-acetic acid (Gd-DTPA) enhancement and magnetic resonance angiography (MRA) did not reveal any lesion in the intrinsic brainstem, cavernous sinus, or posterior orbit (findings not shown). Insulin and anti-hypertensive agents were administered and some amelioration of both the periocular pain and the limitation of eye movement were observed during the admission. In addition, during her stay we added an antiplatelet medication to her drug regimen as we attributed her medical problems to diabetes-related vasculopathic cranial mononeuropathy. Two months after the event, a complete recovery of the right ocular movement was observed.

DISCUSSION

Our patient's clinical manifestation was characterized by weakness of the right medial rectus, inferior rectus and inferior oblique muscles with normal function of the superior rectus and levator palpebrae muscles. The clinical constellation indicated that the palsy was limited to the inferior division of the oculomotor nerve with sparing of pupil. Selective involvement of the inferior division of the oculomotor nerve is rarely reported and only twenty-two cases have been documented[2-13].

Anatomically, the oculomotor nerve divides into a superior and inferior division as it reaches the superior orbital fissure[1]. Hence isolated divisional oculomotor paresis usually indicates a lesion at the anterior cavernous sinus or the posterior orbit. Nevertheless, more proximal lesions in the subarachnoid space[14] or intrinsic brainstem[5,6] have been reported. Based on this, functional segregation of the nerve fiber should appear before division of the oculomotor nerve in the anterior cavernous sinus. On the other hand, topographic distribution of the fascicles of the oculomotor nerve in the ventral midbrain tegmentum from lateral to medial has been proposed as follows: inferior oblique, superior rectus, levator palpebrae, medial rectus, inferior rectus and pupillary fibers[1,5]. Selective involvement of the inferior oblique, medial rectus and inferior rectus muscles in our patient made intrinsic brainstem lesion unlikely.

With regard to the etiological diagnosis of the oculomotor nerve palsy, screening for hyperthyroidism, myasthenia, infection and autoimmune disease should be done. In addition, absence of severe headache and sparing of the pupil with gradual recovery of eye movement were major against the existence of intracranial aneurysm. Cranial CT scan and MRI revealed no evident lesion in the brainstem, cavernous sinus, or posterior orbit. In a patient with similar clinical manifestation, Ohtsuka and his colleagues, by using a fat suppression MR technique, revealed a Gd-DTPA enhanced lesion at the inferior division of the oculomotor nerve. They proposed that the imaging findings might indicate the inflammatory change of the oculomotor nerve caused by a preceding viral episode[10]. The fact that there was no enhanced lesion in our study results suggested a vasculopathy in the pathogenesis of the isolated inferior divisional oculomotor paresis in this patient.

Combination of mononeuropathy multiplex and focal cranial neuropathy in this patient is highly suggestive of a dispersed process such as diabetic vasculitic disorder. Isolated "nontraumatic", "noncompressive" oculomotor nerve palsy has been attributed to in situ microinfarction of the nerve, a possible complication of diabetes, hypertension or generalized atherosclerosis[15]. In particular, the pathogenesis of vasculitic oculomotor nerve palsy has been well studied in the context of diabetes. Asbury and his colleagues identified hyalinization of the arterioles with endothelial proliferative degeneration and resultant stenosis[16]. Although the nature of the lesion has been considered ischemic biologically, direct evidence of vessel occlusion was rarely found[16]. Classical oculomotor lesion in patients with diabetes has reportedly involved the nerve in the subarachnoid[17] or cavernous portion[16]. The lesion is normally located at the boderzone areas between the blood supplies from the perforating branches of the posterior cerebral artery, the posterior communicating and basilar arteries, the tentorial and meningeal branches from the meningohypophyseal trunk of internal carotid artery, the ramus of the

artery of the inferior cavernous sinus and collateral arteries from the ophthalmic artery[16].

A recent study showed that the pupil is affected in only one-third of patients with ischemic injury[18]. Of patients with relative pupil-involvement, the degree of anisocoria is generally less than 2 mm with prompt reaction to light[18]. The anatomical basis for the pupil-sparing third nerve palsy is thought to involve vasa vasorum with secondary destruction of central axons and the surrounding myelin sheath[16,17]. In contrast, the peripherally located pupillary-motor fibers, receiving blood supply from the arachnoid vessels, are spared as the core of the oculomotor nerve is injured by an ischemic condition[16,17]. In daily clinical practice, a normal pupil implies intrinsic nerve lesion while a dilated pupil suggests extrinsic lesion such as nearby tumor or aneurysm. However, incomplete ophthalmoplegia with pupil sparing has been reported as a sign of aneurysmal compression[19-22], none of this class of patients sustained the inferior divisional palsy, as in our patient. To further evaluate a possible extrinsic lesion, MRA was performed and no cerebral aneurysm was ever discovered in our patient. Her ophthalmoparesis remained isolated with some improvement during her hospital stay, and recovered gradually without signs of aberrant regeneration within 2 months. Her outcome is compatible with other reported observations that complete recovery is usually found within 3 months in more than 90% of patients with isolated diabetic oculomotor nerve palsy[23].

Clinically, third cranial nerve palsy is one of the most common diabetes related cranial neuropathies[23]; nevertheless, isolated divisional palsy is still a rarity[24,25]. Of special note, diabetic superior division palsy has been reported in few patients[24,25]. Inferior division palsy has been documented in only one multiple sclerosis (MS) patient with long-standing type 1 DM, however the MS demyelinating process was proposed as the pathogenesis in that case[11]. The presentation of our patient suggests that diabetic ophthalmoplegia may, in an isolated way, affect the superior or the inferior division. In conclusion, although inferior division oculomotor paresis is a rare manifestation, its value in the differential diagnosis of isolated oculomotor palsy should not be overlooked.

REFERENCES

1. Leigh RJ, Zee DS. The Neurology of Eye Movements, 2nd ed. Philadelphia: Davis, 1991:293-377.
2. Cross AG. The ocular sequelae of head injury. Ann R Coll Surg 1948;2:233-40.
3. Susac JO, Hoyt WF. Inferior branch palsy of the oculomotor nerve. Ann Neurol 1977;2:336-9.
4. Saul RF, Danville PA, Selhorst JB. Traumatic inferior division oculomotor palsy. Neurology 1986;36(Suppl 1):250.
5. Ksiazek SM, Repka MX, Maguire A, et al. Divisional oculomotor nerve paresis caused by intrinsic brainstem disease. Ann Neurol 1989;26:714-8.
6. Eggenberger ER, Miller NR, Hoffman PN, et al. Mesencephalic ependymal cyst causing an inferior divisional paresis of the oculomotor nerve: case report. Neurology 1993;43:2419-20.
7. Goto K, Imai H, Nakazato O, et al. Inferior branch palsy of the oculomotor nerve following clipping of basilar apex aneurysm. Rinsho Shinkeigaku 1993;33:203-6.
8. Cunningham ET Jr, Good WV. Inferior branch oculomotor nerve palsy. A case report. J Neuroophthalmol 1994;14:21-3.
9. Nagata E, Tanahashi N, Koto A, et al. A case of spontaneous arteriovenous fistula presenting as the partial oculomotor nerve palsy. Rinsho Shinkeigaku 1995;35:808-10.
10. Ohtsuka K, Hashimoto M, Nakamura Y. Enhanced magnetic resonance imaging in a patient with acute paralysis of the inferior division of the oculomotor nerve. Am J Ophtalmol 1997;124:406-9.
11. Kushner BJ. Surgical treatment of paralysis of the inferior division of the oculomotor nerve. Arch Ophthalmol 1999; 117:485-9.
12. Gray LG, Galetta SL, Hershey B, et al. Inferior division third nerve paresis from an orbital dural arteriovenous malformation. J Neuroophthalmol 1999;19:46-8.
13. Go T. Partial oculomotor nerve palsy associated with elevated anti-galactocerebroside and anti-GM1 antibodies. J Pediatr 2000;137:425-6.
14. Guy J, Savino PJ, Schatz NJ, et al. Superior division paresis of the oculomotor nerve. Ophthalmology 1985;92:777-84.
15. Raff MC, Asbury AK. Ischemic mononeuropathy and mononeuropathy multiplex in diabetes mellitus. N Engl J

Med 1968;279:17-22.
16. Asbury AK, Aldredge H, Hershberg R, et al. Oculomotor palsy in diabetes mellitus: a clinico-pathological study. Brain 1970;93:555-66.
17. Weber RB, Daroff RB, Mackey EA. Pathology of oculomotor nerve palsy in diabetics. Neurology 1970;20:835-8.
18. Jacobson DM. Pupil involvement in patients with diabetes-associated oculomotor nerve palsy. Arch Ophthalmol 1998;116:723-7.
19. Keane JR. Aneurysms and third nerve palsies. Ann Neurol 1983;14:696-7.
20. Kissel JT, Burde RM, Klingele TG, et al. Pupil-sparing oculomotor palsies with internal carotid-posterior communicating artery aneurysms. Ann Neurol 1983;13:149-54.
21. Nadeau SE, Trobe JD. Pupil-sparing in oculomotor palsy: a brief review. Ann Neurol 1983;13:143-8.
22. Trobe JD. Isolated pupil-sparing third nerve palsy. Ophthalmology 1985;92:58-61.
23. Smith BE. Cranial neuropathy in diabetes mellitus. In: Dyck PJ, Thomas PK, eds. Diabetic Neuropathy. Philadelphia: W. B. Saunders, 1999:457-67.
24. Bregman DK, Harbour R. Diabetic superior division oculomotor nerve palsy. Arch Ophthalmol 1988;106:1169-70.
25. Masucci EF, Kurtzke JF. Diabetic superior branch palsy of the oculomotor nerve. Ann Neurol 1980;7:493.