

## Brief Communication

### Diabetes mellitus-associated ocular motor nerve palsies

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Etiologic diagnosis of ocular motor palsy enables prognosis and assists in treatment. In adults, the most common causes of ocular motor palsy are aneurysm, microvascular disease (such as diabetes mellitus [DM]), and trauma. In patients with DM, ocular motor nerve palsy is a common cause of acquired diplopia and/or ptosis.<sup>1,2</sup> In diabetics, the calculated incidence of cranial nerves palsies is 5-10 times higher than in non-diabetics. Approximately 1-14% of diabetics have ocular motor nerves palsies during the course of the disease.<sup>3</sup> The purpose of this study was to describe the demographic and the clinical characteristics of ocular motor nerves palsies in diabetics, to access associated risks factors, as well as, to determine the value of neuroimaging in these patients.

Medical files of patients with ocular motor nerve palsies admitted to the Department of Neurology and Ophthalmology of the University Hospital of Monastir, Monastir, Tunisia, between January 1997 and December 2007 were analyzed. Patients were included in this study if DM was identified to be the etiology of ophthalmoplegia. The following data were collected from patients' files: age, gender, date of onset, and type of cranial nerve palsy, type and duration of DM, presence or absence of diabetes retinopathy, and other vascular risk factors (arterial hypertension, hyperlipemia, and coronary artery disease). The results of cerebral neuroimaging (brain CT scan and/or MRI) were also recorded.

The data were analyzed using the Epi-Info 6 database program. Results were expressed as mean  $\pm$  SD values.

Sixteen patients with DM associated ocular motor nerve palsies were recorded. There was a female predominance (12 female, and 4 male patients) with a mean age of  $67 \pm 13.9$  years (range from 30-89 years). In 13 patients, DM was type 2, and type one in the other 3 cases. All patients complained of acute diplopia with headaches. A partial or complete extrinsic palsy of the third cranial nerve was seen in 13 patients. This third cranial nerve palsy was isolated in 11 patients, and associated to other ocular motor cranial nerve palsies' in 2 cases. Isolated sixth cranial nerve palsy was seen in 3 patients (patients 4, 5, and 6). In the remaining 2 cases, there was a palsy of at least 2 nerves (patient 10 has a third and sixth nerves palsy; palsy of the third, fourth, and sixth nerves was found in patient one). Data of patient's are summarized in Table 1. A long history of DM was

observed in all patients, with a mean duration of  $16 \pm 5.8$  years (range from 5-27 years). Other vascular risk factors or chronic diseases were also recorded: arterial hypertension (AHT) in 9 patients, and hyperlipemia in 4 cases. Diabetic retinopathy was observed in 10 patients from 16. The brain CT scan performed in 9 patients was normal in 8 and showed an old ischemic infarct in the left cerebellum in patient 14. Brain MRI performed in 5 patients (during the first 2 weeks after clinical symptoms onset), showed lacunar infarcts in the brain stem, which can explain cranial nerve paralysis in patients 6, 10, and 11. This exam was normal or showed old lacunar infarcts in patients 5 and 16.

In the present study, we report 16 patients with DM-associated ocular motor nerve paralysis. The mean age at onset was of  $67 \pm 13.9$  years. These palsies occurred mainly in female patients. Acute diplopia and headaches were the main complaints. The third cranial nerve was the most frequently involved nerve, followed by the sixth, and only patient one had a fourth nerve palsy associated to the third and the sixth nerves involvement. The diabetic ophthalmoplegia occurred more frequently in DM type 2 than in type one. It also occurred more frequently in patients with a long history of DM with a mean duration of  $16 \pm 5.8$  years, and associated to other vascular risk factors. Neuroimaging (brain CT scan or MRI), performed in the acute period was usually normal, or showed in 3 patients brain stem infarcts, which can explain clinical symptoms. All these clinical characteristics of DM ophthalmoplegia, including mean age at onset of palsy and duration of DM were similar to previous reports.<sup>3,4</sup> Diabetic ocular motor palsies, which typically occur as a unilateral mononeuropathy, may be the presenting sign of DM. Patients often experience pain, and recurrent paresis either ipsi or contralateral may occur. Occasionally, patients may have multiple unilateral or bilateral palsies simultaneously,<sup>3</sup> as seen in 2 of our patients.

A Mayo Clinic study,<sup>4</sup> of over 4000 patients with ocular motor cranial nerves palsy of any etiology showed that the sixth cranial nerve was the most frequently involved (44%), followed by the third (28%), and the fourth nerve (15%). Like our report, several previous reports,<sup>2,3</sup> showed that the third and the sixth cranial nerves were consistently more frequently affected than the fourth. This phenomenon may not be unique to diabetic ophthalmoplegia.<sup>1,2</sup> Some studies<sup>3,4</sup> showed that the diabetic ophthalmoplegia occurred more frequently in DM type 2 than in type one, which is similar to our findings. In our report, type 2 DM patients with oculomotor cranial neuropathies have a significantly higher prevalence of diabetic retinopathy, such as earlier reported.<sup>3,4</sup> However, recently, Acaroglu et al,<sup>5</sup> reported that the presence, and level of diabetic retinopathy are

**Table 1** - Data of patients.

Patient	Age (years)	Gender	Past medical history	Type of diabetes	Duration of diabetes (years)	Diabetic retinopathy	Type of OMP	Brain CT or MRI
1	89	M	DM AHT	2	17	-	Left III, IV and VI	Normal brain CT
2	71	M	DM	2	18	+	Left III	Normal brain CT
3	72	F	DM	2	13	+	Right III	Normal brain CT
4	30	F	DM Hypothyroidism	1	20	+	Right VI	Normal brain MRI
5	52	F	DM	2	5	-	Left VI	Normal brain CT
6	63	M	DM AHT Cardiac failure Glomerular nephropathy	2	17	+	Left VI	MRI, brain stem infract
7	63	F	DM	2	17	+	Right III	NP
8	79	F	DM	2	14	+	Left III	Normal brain CT
9	71	F	DM AHT Hyperlipemia	2	15	-	Right III	Normal brain CT
10	69	F	DM AHT Hyperlipemia Hypothyroidism	2	25	+	Right III and VI	MRI, right bulbar and pontine infarct
11	55	F	DM	1	17	-	Left III	MRI, left mesencephalic and pontine infarct
12	69	F	DM AHT	2	6	-	Right III	Normal brain CT
13	57	F	DM AHT	1	17	+	Left III	Normal brain CT
14	79	F	DM AHT	2	20	+	Right III	Old right cerebellar infarct on brain CT scan
15	72	M	Cerebellar ischemic stroke AHT	2	10	-	Left III	NP
16	81	F	Hyperlipemia AHT Hyperlipemia	2	27	+	Right III	Normal brain CT MRI: cerebral lacunar infarcts

M - male, F - female, NP - not performed, OMP - oculomotor palsy, DM - diabetes mellitus, AHT - arterial hypertension, +: present, -: absent.

significantly lower in diabetics with cranial nerve palsy than in the age-, gender- and disease-duration-matched controls. Both cranial nerves palsy and retinopathy seem to be the result of microvascular function abnormalities, which can be associated to systemic vascular diseases like DM and co-morbid factors, such as atherosclerotic and hypertension, which can also contribute to the development of these ocular motor palsies. This comorbidity (high prevalence of associated vascular risk factors in patients with DM-associated ocular motor palsies) was frequently seen in our report and in some other studies.<sup>3</sup>

In our study, brain CT scan was usually normal, and MRI showed brain stem infarcts in 3 patients, mainly those with associated vascular risk factors.

Some previous reports,<sup>1,2</sup> showed that the brain stem infarct seems to be an uncommon cause of cranial nerve palsy in diabetic patients, especially the third one, and microvascular infarcts of the peripheral segment of nerves is more likely the cause of this palsy. On the other hand, most studies showed that most patients with a cranial nerve palsy caused by peripheral ischemia improved by 100% within 12 weeks after the onset of symptoms.<sup>1,3,4</sup> Based on these findings, it is generally accepted that a pupil-sparing third cranial nerve palsy in patients with a history of DM is most likely attributable to the extranodal segment of the nerve, and patients may be treated with close observation. If symptoms do not improve substantially within 3 months, then another cause must be considered, and brain MRI may be undertaken at this time.<sup>1</sup>

This is a retrospective cohort study, and the small number of patients had limited our study.

In conclusion, in diabetic patients, ocular motor nerves palsies showed a propensity for the third and the sixth nerves, with relative sparing of the fourth. Type 2 DM patients with diabetic retinopathy were most frequently affected. Prospective studies with a larger number of patients are required to confirm or dispute our findings.

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