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ABSTRACT

Introduction
Oculomotor nerve palsy can arise as a result of a number of different conditions, and the differential diagnosis should take into account patient's age, past medical history and clinical presentation. Diplopia, ptosis, restricted ocular movements, exotropia, with or without pupil involvement are common symptoms at presentation.

Case report
We present the clinical case of a 72 years old caucasian male with ophthalmological history of right eye amblyopia caused by an untreated esotropia, who went to the emergency room presenting holocranial headache, ptosis and temporary diplopia. The pupils were symmetric with a present but slowed down right direct reflex, and a doubtful Marcus Gunn pupil. The patient was orthotropic. Ocular motility examination showed a limitation in adduction, elevation and depression of the right eye. The patient had a Computed tomography of the brain and orbits, a analytical study, a CT-angiography, a brain magnetic resonance, a lumbar puncture, a CT scan of the neck, chest, abdomen and pelvis, a flexible cystoscopy, and a Transurethral resection. Once made, the histology of the biopsies of TUR revealed fragments of a infiltrative urothelial carcinoma of high grade.

Conclusion
The oculomotor nerve palsy may be the first manifestation of a serious systemic disease and appear in an atypical form in a patient with a previous esotropia. Careful assessment and investigation should be taken.

Keywords: Oculomotor nerve; third nerve palsy; urothelial carcinoma.
TITLE: Unusual third cranial nerve palsy presentation with unexpected distant departure point

INTRODUCTION
Oculomotor nerve palsy can arise as a result of a number of different conditions, and the differential diagnosis should take into account patient’s age, past medical history and clinical presentation. Oculomotor nerve injuries may be located at different points of its path and the anatomical relationship of the various portions of this nerve are responsible for many of the clinical features of third nerve palsy. Diplopia, ptosis, restricted ocular movements, exotropia, with or without pupil involvement are common symptoms at presentation [1].

CASE REPORT
We present the clinical case of a 72 years old caucasian male with ophthalmological history of right eye (OD) amblyopia caused by an untreated esotropia. No relevant medical history was known, with irregular surveillance by his general doctor and no regular medication.

The patient presented with holocranial headache, OD ptosis and temporary diplopia 7 days prior to emergency room observation. He denied ocular pain, fever, previous trauma or other systemic or neurologic symptoms.

Ophthalmic exam disclosed OD best corrected visual acuity (VA) of the right eye of 20/200 and of the left eye of 20/25. A right ptosis (Figure 1) with attainment of the visual axis, without any inflammatory signs. The pupils were symmetric with a present but sluggish right direct reflex, and a doubtful Marcus Gunn pupil. The patient was orthotropic (Figure 1). The ocular motility examination showed a limitation in adduction, elevation and depression of the right eye (Figure 2). No diplopia was present during observation neither other neurological defects. The slit lamp examination revealed a cataract and funduscopic exam was unremarkable.

Computed tomography (CT) of the brain and orbits did not reveal acute changes and a analytical study revealed raised inflammatory parameters with Neutrophilic Leukocytosis (2000, 92.9) and protein chain reaction PCR slightly elevated (4.69). CT-angiography that did not reveal aneurysmatic dilations. Brain magnetic
resonance imaging (MRI) showed countless small foci of enhancement leptomeningeals with cerebellar predominance and additional cerebral foci and in the the internal acoustic canal on T1 acquisition. These findings suggest a possible Meningeal carcinomatosis.

Lumbar puncture revealed atypical cells (69 mm³), cerebrospinal fluid (CSF) cytology showes neoplasic cells suggesting infiltration by carcinoma (CK 18+). CSF serology was negative for Cryptococcus, Lyme disease and syphilis. CSF bacteriology was negative.

The patient underwent investigation for primary tumor site with CT scan of the neck, chest, abdomen and pelvis. The exam showed multiple lymph nodes on level III and IV referred mainly because of their number and size, the larger one with approximately 21 x 8.5 mm, and a mass with starting point on the left lateral wall of the bladder, with calcifications, measuring approximately 4 x 2 cm.

The patient was submitted to a flexible cystoscopy that showed a sessil lesion with 3 cm and with probable invasion of the meatus; for a best description a Transurethral resection (TUR) of the bladder was proposed. Once made, the histology of the biopsies of TUR revealed fragments of a infiltrative urothelial carcinoma of high grade. The patient started treatment with Corticosteroids and Methotrexate.

DISCUSSION

The oculomotor nerve supplies somatic: superior rectus, inferior rectus, inferior oblique, medial rectus and levator palpebrae superioris as well as autonomic (papillary sphincter and ciliary) muscles of the eye. Oculomotor nerve palsy may be congenital or acquired, complete or partial, pupil sparing or pupil involving, isolated or accompanied by neurological signs. Precise knowledge of its origin and course from nuclear level to terminal muscles is essential to localize the site of involvement [2].

Third cranial nerve palsy may be the first manifestation of a serious systemic disease and accounts for about one third of presenting cranial nerve palsies. The pupil involvement is commonly related to compressive lesions, in particular aneurysms, on the other hand, pupil sparing third nerve palsy suggest microvascular etiologies [3].
This case reveals an atypical presentation in a patient with previous esotropia and amblyopia and therefore diplopia was not an important symptom for the patient as well as exotropia was not present. For this reason, the patient was orthotropic. The pupil involvement was not obvious so we could consider it as an incomplete palsy (anisocoria was not present), but since there was a sluggish right direct reflex, and a doubtful Marcus Gunn pupil, neuroimaging was mandatory to exclude life threatening compressive causes. The management of acute partial pupil-sparing is controversial, some suggest that the incidence of aneurysms in this group is low enough that imaging is not necessary, others advocate angiography for all and others suggest a period of observation, since a pupil-sparing partial third nerve palsy from an aneurysm usually develops papillary involvement within a few days [4]. Once excluded aneurysmatic causes further investigation was needed. In this case the oculomotor nerve palsy appears as a direct compression or infiltration of the oculomotor nerve in his pathway. There are some reports in literature of isolated oculomotor nerve palsy as a paraneoplastic manifestation: gastric diffuse large B-cell lymphoma with neoplastic infiltration, although isolated neuropathy is rare, non-small cell lung cancer and Burkitt lymphoma. The majority of the patients with paraneoplastic manifestations and oculomotor nerve palsy exhibited cavernous sinus involvement rather than oculomotor nerve infiltration [5-7]. Literature has described a case of a multiple cranial palsies associated with gallbladder cancer [8]. Brain MRI combined with cerebrospinal fluid cytology examination is considered optimal for evaluating the cause of oculomotor nerve palsy, but may not be diagnostic in every case.

CONCLUSION
In conclusion, this case demonstrates that isolated oculomotor nerve palsy demands a careful assessment and complete investigation. This case of isolated nuclear oculomotor nerve palsy with atypical features may mimic oculomotor ischemic nerve palsy usually associated with diabetes mellitus and hypertension. The outcome of oculomotor nerve palsy is related to its cause.
CONFLICT OF INTEREST
Authors have not received grant support or research founding and do not have any proprietary interests in the materials described in the article.

AUTHOR’S CONTRIBUTIONS
NOT GIVEN

REFERENCES
1. Keane JR. Third nerve palsy: analysis of 1400 personally-examined inpatients. Can J Neurol Sci, 2010 Sep. 37:662–670
2. JP Chugh, Prachi Jain, RS Chouhan, Ashok Rathi. Third nerve palsy: an overview. Review article. Indian Journal of Clinical Practice, 2012 May, 22(12), 17-20
3. Shechtman DL, Woods AD, Tyler JA. Pupil sparing incomplete third nerve palsy secondary to a cavernous sinus meningioma: challenges in management. Clinical an Experimental Optometry, 2007 Mar; 90(2), 132-138.
4. Jason Barton. Neuropathies and nuclear palsies. Canadian neuro ophthalmology textbook. Jun 2008
5. Shang-Yih Yan, Yi-Jen Peng, Chun Shu Lin, Giia-Sheun Peng, Ping Ying Chang. Isolated oculomotor nerve palsy as a paraneoplastic manifestation of gastric diffuse large B-cell lymphoma: a case report. Oncol Lett. 2014 Nov; 8(5): 1983-1985.
6. Yun Liang, Luyin Ding, Xian Li, Weiqin Wang, Xiaohong Zhang. Oculomotor nerve palsy as a preceding symptom of adult sporadic Burkitt lymphoma: a case report and review of the literature. Oncol Lett. 2017 Mar. 13(3):1315-1318.
7. Young Mi Lee, Woo Ho Sim, Sun Och Yoon, Song Yee Kim, et al. A case of cranial nerve palsy as a paraneoplastic syndrome in non-small cell lung cancer. Tuberculosis&Resp Disease. 2011 Feb; 70(2):160-164.
8. Misako Kaido, Yoshihito Yuasa, Tameyoshi Yamamoto, Satoru Munakata et al. A case of possible paraneoplastic neurological syndrome presenting as multiple cranial. PubMed Journals. 2016 Aug; 56(9):617-21.

**FIGURE LEGEND**

Figure 1: Ptosis and ortotropia in primary position

Figure 2: Restriction on supraduction, infraduction and adduction of the right eye

**FIGURES**

![Figure 1: Ptosis and ortotropia in primary position](image-url)
Figure 2: Restriction on supraduction, infraduction and adduction of the right eye