

DIPLOPIA AS AN INITIAL MANIFESTATION OF DISSEMINATED NON-HODGKIN'S LYMPHOMA

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SAMENVATTING

Een 37-jarige man werd in urgentie onderzocht wegens een acute diplopie. Na oftalmologisch onderzoek werd een abductiebeperking ter hoogte van het linker oog vastgesteld, progressief evoluerend naar een totale oftalmoplegie. Bijkomende onderzoeken toonden een intra-orbitale massa aan, immunohistologisch getypeerd als een diffuus grootcellig B-cel lymfoom (DLBCL) volgens de WHO classificatie. Gezien het gevorderd stadium van de ziekte (IV_{A-E}), bestond de behandeling uit systemische en intrathecale chemotherapie met pancraniële radiotherapie. Desondanks was er een snelle ziekte-progressie en overleefde de patiënt slechts 10 maanden. Bij jonge patiënten die zich aanbieden met een acute oftalmoparese is orbitale neoplasie een belangrijk element in de differentiaaldiagnose.

ABSTRACT

A 37-year-old male presented a sudden diplopia. Ocular examination showed a partial paresis of the left eye (LE) on the left gaze, progressing in a few days towards a total ophthalmoplegia. Further investigation revealed an intra-orbital mass, immunohistologically diagnosed as a Diffuse Large B-cell Lymphoma (DLBCL), according to the WHO classifica-

tion. Since the patient was in an advanced, disseminated stage of the disease (IV_{A-E}), treatment was based on systemic and intrathecal chemotherapy with a pancranial radiotherapy. The clinical course was poor with only a 10-month survival. We wish to stress that the possibility of orbital malignancy in young adults with acute onset of ophthalmoplegia should be included in the differential diagnosis.

RÉSUMÉ

Un homme de 37 ans a présenté une diplopie survenue brutalement. L'examen ophtalmologique montrait une paralysie partielle de l'œil gauche dans le regard vers la gauche. En quelques jours une ophthalmoplégie totale s'installait. Un examen plus approfondi a révélé une masse intra-orbitaire, diagnostiquée immunohistologiquement comme un Lymphome Large Diffus de type Cellulaire B (DLBCL), suivant la classification de l'OMS.

Vu le stade avancé (IV_{A-E}) de l'affection, le traitement fut basé sur une chimiothérapie systémique et intrathécale ainsi qu'une radiothérapie pancranienne. L'évolution fut médiocre avec seulement 10 mois de survie. Nous tenons à signaler que chez des jeunes adultes manifestant une ophtalmoplégie, une pathologie néoplasique de l'orbite demeure un élément important du diagnostic différentiel.

KEY-WORDS

lymphoma, diplopia, ophthalmoplegia

MOTS-CLÉS

lymphome, diplopie, ophtalmoplégie

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INTRODUCTION

Non-Hodgkin's lymphomas (NHL) are a heterogeneous group of neoplasms characterized by proliferation of malignant lymphocytes. This heterogeneity is due to the multiple histological subtypes, clinical presentations (nodal and/or extranodal) and tumour behaviour (localised versus disseminated).

Isolated, unilateral, progressive ophthalmoplegia and visual loss, as in our case report are seldom reported as initial manifestations. (3)

CASE REPORT

A 37-year-old Caucasian male consulted the Ophthalmology Department because of a sudden painless horizontal diplopia on left gaze. His personal and familial history were unremarkable. There was no history of fever, weight loss or nocturnal sweating. He was not using any medication, smoked twenty cigarettes daily and occasionally drank alcoholic beverages.

Ophthalmologic examination

First ophthalmologic examination revealed a parietic abduction of the LE, with limited downward and upward gaze. Further examination showed no other abnormality and included corrected visual acuity (V.A.) (1.0 on both eyes),

slitlamp examination, pupils equal and reactive to light (direct and consensual) and near stimuli (both direct and consensual), exophthalmometry, intra-ocular pressure, visual fields, fundi and fluo-angiography.

During the following days, he progressively developed a total ophthalmoplegia including ptosis and mydriasis. There was a slight visual acuity loss (0.7) on the L.E. and colour vision testing revealed a red-green deficiency in the same eye. Visual evoked potentials (VEP's) showed a unilateral alteration of the response (P100) with decreased amplitude (\downarrow 50%) and a prolonged latency (\uparrow 20%) in comparison with the normal values of the R.E. During the follow-up period ophthalmic symptoms remained stable.

Further *neurological and physical examination* were completely normal.

Radiological examination of the orbits

Computed tomography (CT) of the orbital region was suspicious for an intra-orbital mass with optic nerve involvement on the LE and infiltration of the right ethmoidal sinus (fig 1). Orbital MRI confirmed the presence of a contrast enhancing lesion originating in the orbital apex, surrounding the optical nerve of the LE (fig 2) and a second enhanced irregular mass in the



Fig 1. (left) CT demonstrating a lesion at the left orbital apex, with thickening of the optic nerve.

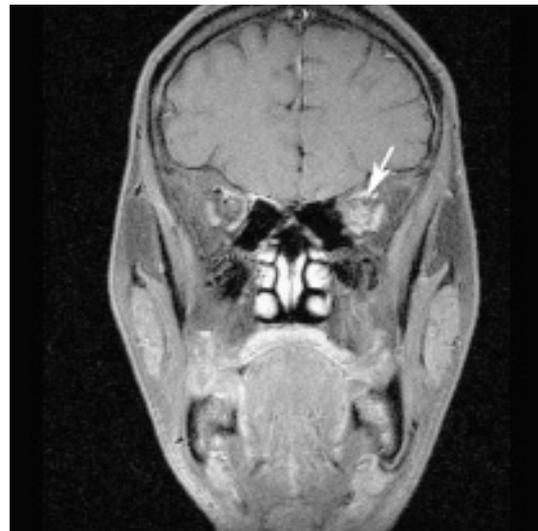


Fig 2. (right) MRI coronal T1 weighted spin-echo with fat suppression confirming the enhanced mass lesion at the apex of the left orbit

dorsal part of the right ethmoidal sinus (image not shown). Because of the delicate anatomic localisation, a biopsy was not performed.

Laboratory findings

Blood examination demonstrated raised lipase (1900 IU/L; ref 50-200) and amylase (250 IU/L; ref <113), the remainder of the laboratory findings being within normal limits.

Cerebrospinal fluid examination was within normal limits and no abnormal cells were found.

Other clinical tests

Chest radiography was consistent with diffuse pulmonary infiltrates; CT of the chest showed alveolar infiltrates and limited mediastinal lymph nodes. A bronchoscopy with biopsy and broncho-alveolar lavage with immunophenotypic typing was performed. The biopsy at first was suggestive for granulomatous disease as seen in sarcoidosis. The washing however yielded 8% monoclonal B-lymphocytes (centrocytic type). Abdominal echography completed with CT showed a hypodense, nodular pancreatic lesion and multiple lesions in both kidneys.

Histological examination of the pancreatic mass revealed a DLBCL. Finally, needle aspiration of bone marrow showed no arguments for invasion by malignant lymphoma.

Diagnostic work-up concluded to a DLBCL with multiple extranodal localisations (left orbital, ethmoidal, pancreatic, pulmonary and renal), stage IV_{A-E}, requiring multi-drug therapy type CHOP (cyclophosphamide, doxorubicine, vincristine, prednisone), intrathecal methotrexate based chemotherapy and pancranial radiotherapy (25 Gray). Two attempts for stemcell mobilisation failed. Despite a temporary improvement of ophthalmic (recovery of ptosis) and general disturbances, the patient showed progressive disease. He died ten months after diagnosis as a result of respiratory failure caused by extensive central nervous system invasion. Autopsy was refused by the relatives.

DISCUSSION

Lymphomas are the commonest neoplasm of patients between the ages of 20 and 40. Moreover, they rank fourth in the total number of person-years of life lost each year from cancer (10).

Despite advances in treatment, long-term outcome of patients with DLBCL is not better today than reported in 1975 (2).

The current incidence reaches 12 to 15 cases per 100000 individuals in Europe and is still increasing, especially for extranodal disease. DLBCL constitute 30-40 % of adult NHL (9). Extranodal sites may be affected, although the orbit is a rare primary site for NHL, accounting for less than 1% of primary presentations and an estimated 5 to 14 % of all extranodal presentations (8). Ophthalmoplegia without other systemic or neurological deficits are seldom-reported as initial manifestations of NHL (1,3,4). Differential diagnosis is broad: ophthalmoplegia in the absence of trauma usually indicates neoplasm (invading the brain stem, basal meninges or cavernous sinus) or an inflammatory process at the superior orbital fissure or cavernous sinus. However, attention should be paid for the possibility of cavernous sinus thrombosis, aneurysms of the communicating posterior or vertebral artery and carotid-cavernous sinus fistula. Also Wernicke's encephalopathy, basilar meningitis, Miller-Fisher variant of Guillain-Barré syndrome, neuro-muscular junction abnormality as seen in myasthenia and presence of neurotoxic agents should be excluded (6).

This report is unique in respect that we present a young man with a sudden, painless diplopia as presenting symptom of an advanced B-cell non-Hodgkin's lymphoma.

Although suspicion of involvement of the superior orbital fissure was imminent, histological confirmation of the diagnosis required a number of invasive procedures, which at first suggested the possibility of sarcoidosis (lung-biopsy). Finally, broncho-alveolar washing and pancreatic biopsy confirmed the presence of the B-cell lymphoma. After appropriate staging, the disease was found to be disseminated, exclusively affecting other extranodal sites.

Orbital lymphoid neoplasms occur primarily in the sixth and seventh decades of life (7), in contrast to our patient who was only 37 years old. Furthermore up to 70% of cases reported as ocular adnexal lymphoma are low-grade lymphoma with favourable prognosis (5), opposed to our patient who suffered from intermediate grade lymphoma.

When ocular adnexal lymphoma is diagnosed, systemic work-up including full physical examination, biology, CT of brain, chest and abdomen and bone marrow aspiration or biopsy is mandatory to screen for nodal or extranodal tumour spread.

Virtually every specialist can be involved in diagnosing first symptoms of NHL. We wish to stress the importance of evaluation of the orbital apex and cavernous sinus by magnetic resonance imaging in any patient with the symptoms mentioned above.

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