Ocular presentation of Wegener granulomatosis

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SUMMARY

A 55-year-old woman presented with swelling of the right upper and lower eyelid, diplopia and proptosis. The clinical findings combined with imaging, pathology and full internal work-up allowed to make a diagnosis of limited Wegener granulomatosis.
Treatment with systemic corticosteroids and cyclophosphamide markedly decreased the orbital swelling and diplopia.

RÉSUMÉ

Nous rapportons le cas d'une femme de 55 ans avec une tumeur de la paupière supérieure et inférieure droite, diplopie et proptose.
Après examen clinique, tests sérologiques et biopsie de la lésion, le diagnostic de granulomatose de Wegener a été posé.
Un traitement avec des corticostéroïdes oraux et de la cyclophosphamide a fortement diminué la taille de la tumeur orbitaire et les plaintes de diplopie.

KEY WORDS

Wegener granulomatosis, orbital involvement

MOTS-CLÉS

granulomatose de Wegener, manifestation orbitaire

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INTRODUCTION

Wegener granulomatosis is a systemic vasculitis of the medium and small arteries, as well as of the venules, arterioles and occasionally large arteries. ''Classic'' Wegener granulomatosis is a form of systemic vasculitis that primarily involves the upper and lower respiratory tracts and the kidneys.

However, a limited form without renal involvement, with swelling of the right upper eyelid and diplopia, has been described (4).

Here, we report a new case of limited Wegener granulomatosis with orbital involvement.

CASE REPORT

A 55-year-old woman, suffering from a right chronic maxillary sinusitis, proved on CT scan, was treated by an ENT surgeon with a combination of surgical draining of the maxillary sinus, azithromycin 500 mg and methylprednisolone 16 mg.

Six months later, there was no improvement of the symptoms, and a second draining of the right maxillary sinus (Caldwell Luc procedure) with biopsy was performed. The biopsy revealed Aspergillus fumigatus and methicillin resistant Staphylococcus aureus (MRSA). Subsequently azithromycin was stopped but methylprednisolone 16 mg was continued. Two weeks later, the patient developed on the right side proptosis and a marked swelling of upper and lower eyelid, associated with diplopia. The patient was then referred to our department with suspicion of extensive aspergillosis of the right maxillary sinus with secondary orbital involvement.

Ophthalmological examination showed a mass lesion stuck to the inferior orbital floor with a marked restricted abduction and depression. Best corrected visual acuity was 10/10 in both eyes. Slit lamp examination revealed chemosis of the conjunctiva of the right eye and a normal left anterior segment. Intraocular pressure and fundoscopy were normal. As this patient had been treated for at least 3 months with corticosteroids, Aspergillus fumigatus could have invaded bony structures (6). Imaging of the orbits and sinuses was performed. Computerized Tomography (CT) demonstrated a mass within the right maxillary sinus with breakthrough of the orbital floor and diffuse orbital involvement (fig.1). Magnetic Resonance Imaging (MRI) showed a retrobulbar mass, with additional enhancement of the medial rectus, inferior rectus and inferior oblique muscle (fig.2) and a vasculo-ischemic insult at the level of the brain stem (fig 3). The orbital mass encircled the proximal optic nerve and reached the orbital apex without involvement of the cavernous sinus. A surgical biopsy of the orbit was performed (fig 4) and Amphotericin B (1mg/kg/day) and Vancomycine (2.5 gr/24h) were started intravenously as Aspergillus and methicillin resistant Staphylococcus aureus had been identified in the biopsy of the maxillary sinus by the ENT surgeon in this patient with pharmacological immunosuppression (methylprednisone).

Microscopic examination of the specimen (fig.5) showed extensive fibrotic change of the orbital fatty tissue and an inflammatory infiltrate mixed

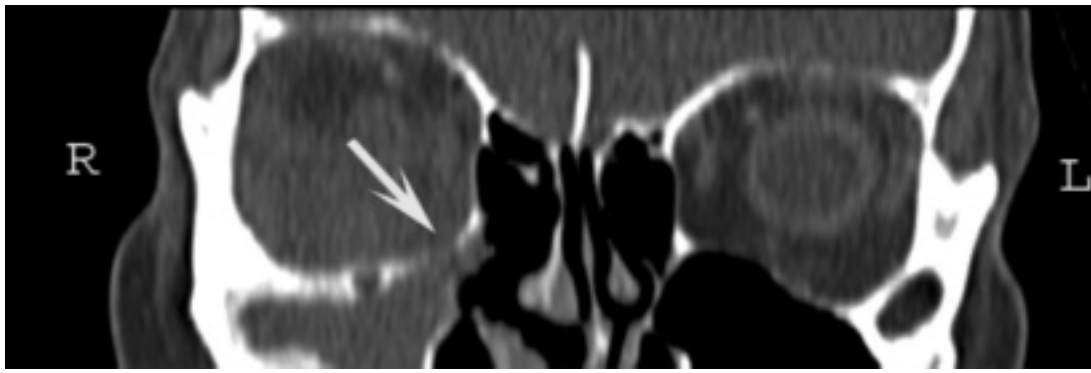

Fig. 1: coronal CT scan showing orbital involvement (arrow).

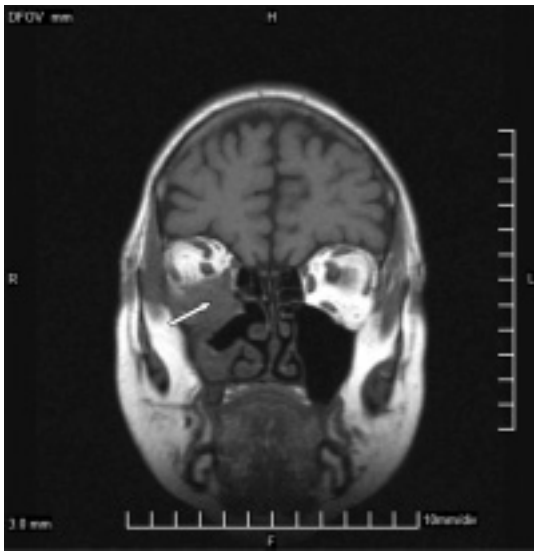

Fig. 2: Coronal T1-weighted MRI image showing massive orbital involvement (arrow).

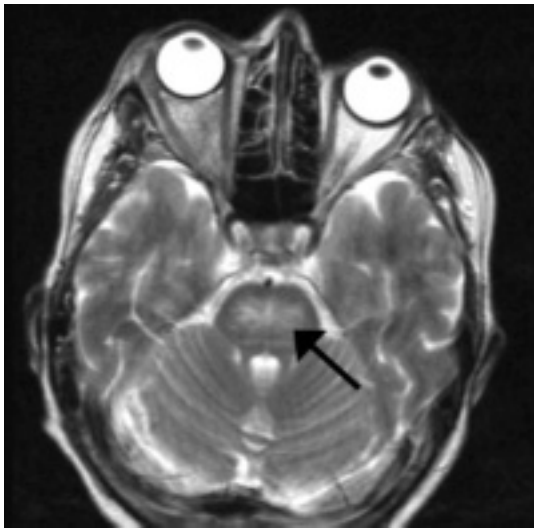

Fig 3: Axial T2 weighted image showing an ischemic lesion in the brain stem (arrow).

with foci of granulomatous aspect. The infiltrate, consisting mainly of lymphocytes and neutrophils, was located around vascular structures and also in the vessel wall. The vessel wall showed extensive fibrosis with narrowing of the lumen. There was no increased number of eosinophils. These findings are consistent with the diagnosis of vasculitis . PAS and Grocott staining were performed but no aspergillosis was

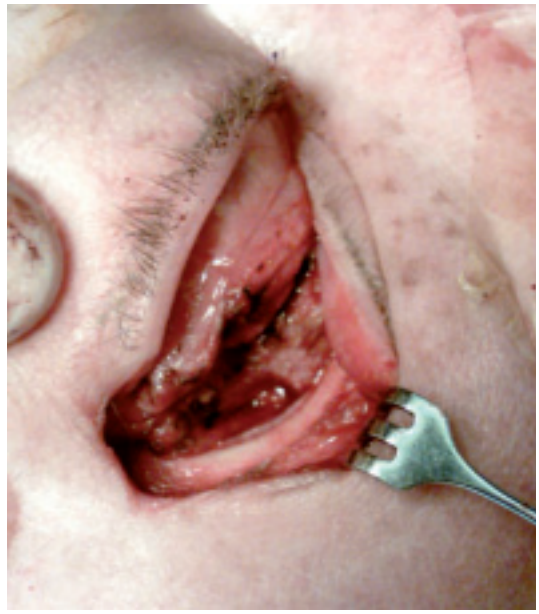

Fig. 4: orbital biopsy (swinging eyelid procedure) (7).

found in the orbital biopsy. As pathology showed vasculitis, our differential diagnosis of orbital vasculitis included Wegener granulomatosis, allergic granulomatosis (Churg-Strauss syndrome), hypersensitivity angiitis, giant cell arteritis and polyarteritis nodosa (PAN).

The patient was referred for multidisciplinary evaluation and revealed normal vital signs and no pathology of heart, abdomen and skin. Urinanalysis was normal.

Echography of the kidneys was normal as well as the bone scan. On electromyelography, there was a sensorimotor demyelinating polyneuropathy of the lower limbs.

CT thorax revealed a subpleural nodular lesion in the superior segment of the upper lobe of the right lung. Indirect immunofluorescence on polymorphonuclear leucocytes was strongly positive for antineutrophil cytoplasmic antibodies (C-ANCA) and an ELISA for proteinase 3 (PR 3) revealed a concentration of C-ANCA of 110 U/ml (normal value < 2 U/ml).

The combination of a granulomatous vasculitis in the right orbit, the EMG findings, the vasculo-ischemic infarction in the brain stem, together with the elevated C-ANCA led to the diagnosis of Wegener granulomatosis. Amphotericin B and Vancomycin were stopped after one week and a systemic treatment for Wege-

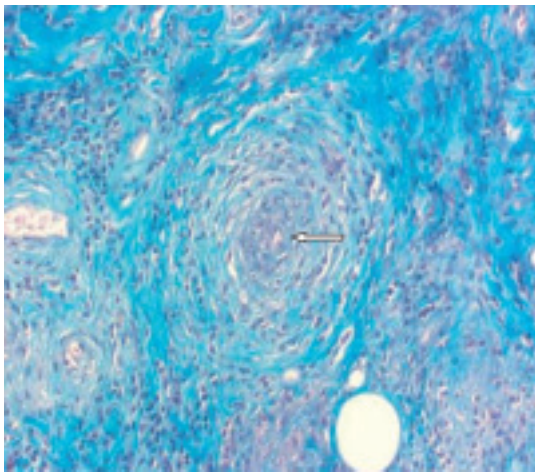

Fig. 5 : inflammatory infiltrate mixed with foci having a granulomatous aspect. Extensive fibrosis of the vessel wall and narrowing of the lumen (arrow).

ner granulomatosis with cyclophosphamide (2 mg/kg/day) and methylprednisolone 64 mg was started immediately. The oral steroids were gradually tapered with 10 % per month. Itraconazol was started prophylactically at a dose of 400 mg/day to prevent systemic aspergillosis in a patient with Aspergillus in the maxillary sinus under pharmacological immunosuppression. Within one month, the swollen eyelids, the diplopia and the proptosis regressed markedly. Only in extreme positions of gaze, small motility restrictions were still present. Unfortunately this patient died two months later as a passenger in a car accident.

DISCUSSION

Patients with the chronic indolent form of invasive fungal sinusitis usually present with symptoms of chronic sinusitis and few, if any, systemic complaints. They often endure the symptoms of chronic sinusitis for months which in immunosuppresed patients may lead to bone erosion and orbital and even brain involvement (9). If the orbit becomes involved, additional symptoms may include blurred vision, proptosis and chemosis, two of which were present in this patient (2). Whenever orbital cellulitis is suspected, radiographic imaging (preferably a CT scan) should be taken. In our patient, Aspergillus fumigatus was found on culture of the biopsy taken by the ENT surgeon. Unfortunately, no systemic antifungal therapy was started but rather methylprednisolone was continued. This could have worsened the aspergillosis. Consequently, aspergillosis breakthrough with orbital involvement was one of the possible differential diagnoses in our patient. The biopsy of the orbit, subsequently performed in our department, revealed no aspergillosis but rather vasculitis and necrotizing granulomas, which in combination with elevated C-ANCA, was highly suggestive of Wegener granulomatosis (11). According to the ''Chapel Hill Consensus Conference'' classification, ANCA-associated vasculitis is characterized by prevalent involvement of small-size vessels, which was the case in this patient, whereas medium and large-size arteries involvement is more indicative of polyarteritis nodosa. The Chapel Hill Consensus Conference has clarified some existing controversies in nomenclature of the systemic vasculitides, although robust diagnostic criteria for the various forms of vasculitis have remained elusive. We used the following diagnostic criteria for Wegener granulomatosis, as proposed by Sorensen et al in accordance with the Chapel Hill nomenclature (10) : a) biopsy or surrogate parameter for granulomatous inflammation in the respiratory system and b) biopsy verified necrotizing vasculitis in small to medium sized vessels or biopsy/ surrogate parameter for glomerulonephritis or positive PR-3-ANCA test and c) lack of eosinophila in blood and biopsy samples. In this patient a chronic sinusitis was a surrogate parameter for granulomatous inflammation of the respiratory system, whilst necrotizing granulomatous vasculitis was seen on biopsy of the orbit with a lack of eosinophilia in both blood and biopsy samples.

The ''classic'' form of Wegener granulomatosis involves the upper and lower respiratory tracts and kidneys. Ocular manifestations may occur secondary to contiguous granulomatous sinusitis or as a result of focal vasculitis (3). The common ocular features include proptosis, scleritis and episcleritis, peripheral corneal ulceration, nasolacrimal duct obstruction, optic nerve vasculitis, retinal artery occlusion, conjunctivitis and uveitis (1). The detection of antineutrophil cytoplasmic antibodies directed against proteinase 3 (PR3-ANCA) is highly specific for Wegener granulomatosis. ANCA positivity is

found only in 50 % of the patients with localized disease, whereas PR 3-ANCA positivity is seen in 95 % of the patients with generalized Wegener granulomatosis (5).

Diagnostic surgical procedures followed by aggressive medical treatment can markedly decrease the symptoms of Wegener granulomatosis. This medical treatment usually consists of immunosuppressive agents (such as steroids and cyclophosphamide). In resistant cases cyclosporine, azathioprine, anti-thymocyte globuline or plasmapheresis may be useful (8).

CONCLUSION

In summary, we report a patient with apparent chronic fungal sinusitis who developed signs of orbital involvement. Further ophthalmological and multidisciplinary work-up, however, revealed limited Wegener granulomatosis in the right orbit. Considerable decrease of the orbital swelling and diplopia was obtained following a treatment with systemic steroids and cyclophosphamide.

This case report shows the necessity to combine the clinical and pathological findings to achieve a diagnosis of limited Wegener granulomatosis. Orbital inflammation may be the first sign of Wegener granulomatosis, proving that the ophthalmologist may contribute considerably to its diagnosis

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