Cranial nerve palsy in Wegener’s granulomatosi – Lessons from clinical cases

Introduction

Peripheral and central neuropathies, including cranial neuropathies, are regular sequelae of systemic vasculitides (SV), documented in case series and retrospective analyses [1, 2]. Their diagnosis is challenging, especially when they occur independent of other SV manifestations. We report two patients with Wegener’s granulomatosis (WG), who developed cranial neuropathies in the course of their disease and were successfully treated with standard induction protocols for SV despite the absence of an organ-specific proof of vasculitis.

Case 1

A 69-year-old male noticed horizontal diplopia when looking to the right. Idiopathic abducens nerve palsy was diagnosed in a clinical neurology department. CT (technical data: 2 × 35/43, transversal scan, bone-window) and MRI scans (technical data: sagittal T1, axial T1, axial T2, axial T2-Flair, DWI, 3D-TOF (6 × 35/43), 1.5 Tesla) of the brain, as well as blood and cerebrospinal fluid analyses were normal (spinal tab: slightly elevated protein (530 mg/l (normal range 150–450)), slightly increased glucose (92 mg/dl (normal range 45–75)), cell count: 8/μl (normal range: < 4): monocytes and scattered chromatin-dense lymphocytes, no atypical cells). The patient was discharged from the hospital without having received medical treatment. His diplopia had not improved, and he had been advised to wear an eye-cap.
Two years earlier, WG with positive anti-neutrophil-cytoplasm autoantibodies (ANCA) directed against proteinase3 (PR3-ANCA), ENT manifestations, arthritis, and renal failure due to necrotizing glomerulonephritis had been diagnosed. A combination of oral cyclophosphamide (CYC) and corticosteroids (CS) had induced disease remission, and maintenance treatment with mycophenolate mofetil (MMF) had stabilized the disease for another year. At the onset of the neuropathy, the patient was free of other clinical disease activity and negative for ANCA.

After his discharge from the department of clinical neurology, the patient consulted his nephrologists and another neurologist. The persisting 6th nerve palsy was then interpreted as vasculitic relapse manifestation of WG, although there were no other disease exacerbations. Another course of CYC and CS resulted in prompt improvement of the palsy and a full recovery within 6 weeks. The medication was continued for 4 months and later switched to MMF again. With this maintenance treatment the patient has now remained free of symptoms for more than a year after the onset of the 6th nerve palsy.

Case 2

A 31-year-old female admitted for otitis media, tinnitus, nasal stenosis, dyspnea with a diffuse lung infiltrate and headache with nausea and vomiting was diagnosed with WG based on a positive PR3-ANCA. CT and MRI scans were both normal with respect to the CNS, but revealed activity in the left mastoid, the left maxillary sinus, the left side of the nasopharynx and the ethmoid sinuses on the MRI scan. Several biopsies from the nose and sinuses only revealed a dense inflammatory response. The patient was treated with oral CS and CYC within a clinical trial (NORAM study [3]). Seven months later, when prednisolone had been tapered to 10 mg/day and CYC had been replaced by azathioprine (AZA)(100 mg/day), the patient developed swallowing difficulties, hoarseness and breathing difficulties. A left-sided vagal nerve paresis with left recurrent nerve palsy was diagnosed. C-reactive protein (CRP) and ESR were just above the normal limits and the MRI with i.v. gadolinium was normal. The prednisolone dose was raised to 75 mg/day with a prompt effect on the vagal paresis. AZA was stopped 12 months after diagnosis, and prednisolone tapered to 2.5 mg/day by 20 months when she developed headache, nausea and vomiting, dyspnea, right-sided vagal nerve paresis, slight right-sided hypoglossal nerve paresis and left-sided abducens nerve paresis. There were no other symptoms, normal laboratory values, PR3-ANCA just above detection limits, normal chest X-ray and again normal CT scans and MRI scans including MRI-based angiography, as well as a normal spinal tab (normal protein, slightly increased glucose, 984 mill erythrocytes 10/u litre and 1 mill leukocytes 1/u litre). Prednisolone (75 mg/day) and CYC (100 mg/day) were again administered with prompt effect. However, the patient developed CS induced psychosis and required anti-psychotic treatment. The disease course was then uneventful until 26 months after diagnosis when a right-sided abducens nerve palsy occurred. The maintenance treatment with AZA was again switched to CYC (100 mg/day) while the dosage of prednisolone (15 mg/day) was maintained to avoid psychiatric complications. MRI scans with i.v. gadolinium were again normal. The disease became further complicated by a retrobulbar granuloma in the left orbit which caused double vision. Although this typical manifestation of WG was again treated with CYC it did not respond with complete remission. Now, 86 months after diagnosis, the growth of the retrobulbar granuloma had halted but has compromised the vision of the left eye. Further MRI scans with gadolinium have repeatedly shown lack of meningeal enhancement with the left-sided retrobulbar granuloma and now also a smaller retrobulbar granuloma on the right side (Fig.1). The patient is presently treated with anti-TNF-alpha antibodies (Remicade) and there are no active disease manifestations.

Fig. 1 Cranial MRI-angiogram of case 2 showing bilateral retrobulbar granulomata, but no meningeal enhancement (Siemens Vision MR scanner, using Multihance (gadolinium) 0.1 mmol/kg at 1.5 Tesla, T1-weighted spin echo)