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Amyloidoma of the gasserian ganglion as a cause of symptomatic neuralgia of the trigeminal nerve: report of three cases

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Abstract Three cases of symptomatic neuralgia of the trigeminal nerve due to an amyloidoma in the gasserian ganglion are described. The correct diagnosis was not made prior to histological examination of the surgical biopsy specimens. Medical history and clinical observation led to the diagnosis of a malignant process of the nasal cavities in the first patient; of an inflammatory dental focus in the second patient; and of multiple sclerosis in the third patient. CT findings were normal in cases 1 and 2; in case 3, a schwannoma was suspected from the CT appearances. In case 1, MRI had not been performed; in cases 2 and 3, MRI revealed a tumour mass which was also considered to be a schwannoma. Histologically, the tumours consisted of masses of amyloid deposits which had largely replaced the pre-existing ganglionic cells and satellite cells. Electron microscopy confirmed the fibrillar structure of the deposits. Immunohistochemistry and immunocytochemistry revealed the amyloid to belong to the AL-lambda subtype.

Key words Amyloid · Tumour
Trigeminal ganglion · Surgery
Immunocytochemistry

Introduction

Amyloid is a fibrous protein. In healthy individuals it is never deposited in any one organ. Under certain pathological conditions it is stored in the extracellular space in one or more organs as an amyloidosis [2]. In old age, many individuals also store amyloid in the brain as senile plaques. If amyloid deposit becomes a space-occupying lesion, an amyloidoma results [8]. Amyloidomas of the gasserian ganglion are a rare cause of trigeminal neuralgia. The aetiology of the disease is unknown. So far, only three cases have been reported [1, 3, 4]. We now report three more cases. In addition to the earlier reports we were able to investigate the biopsy specimens with antibodies against different subtypes of amyloid by immunohistochemistry and immunocytochemistry and to show that they belong to the AL-lambda subtype, i.e. they are biochemically ho-

mologous to the lambda class of the plasma immunoglobulin light chains [7] which are produced by plasma cells.

Case reports

Case 1

A 32-year-old female patient complained of continuous pain in the left frontal and maxillary regions. Clinical examination revealed numbness and hypalgesia in left trigeminal nerve branches II and III as well as atrophy of the ipsilateral masticatory muscles. Trigger points were not found. A malignant process of the nasal cavities was transiently considered as a possible cause but was soon disregarded because after careful examination of the case history it proved that the patient's husband had recognized slight atrophy of the masticatory muscles as early as the time when they first met, i.e. 10 years earlier. EMG of the masticatory muscles revealed signs of severe neurogenic atrophy. A tumour in the left gasserian ganglion was suspected although CT did not reveal any abnormalities. The tumour was expected to be too small as to be discernible by CT, and surgical exploration was decided upon. At surgery, a greasy yellowish mass the size of a red bean was removed from Meckel's cave. The neuralgic symptoms subsided immediately after surgery, whereas sensory and motor deficits were still present 9 years after surgery. Circulating B lymphocytes did not reveal a monoclonal population and no abnormal immunoelectrophoretic bands could be detected in her serum.

Case 2

This 49-year-old female patient had experienced a herpes zoster infection of the left trigeminal nerve 10 years earlier. Since then, she had suffered from continuous pain in the left cheek and mandible region. Clinical examination revealed hypaesthesia and hyperalgesia of all three trigeminal branches of the left hand side. No trigger points could be found. Motor deficits were absent. Corneal reflexes were normal. The patient complained of dry gingiva and cornea which were occasionally infected. A CT scan appeared normal. As an inflammatory focus of the teeth was suspected to be the cause of her illness, several teeth were removed, which did not improve her condition. MRI showed a dense mass with enhancement after gadolinium injection. The tumour filled Meckel's cave and extended to the proximal parts of the maxillary and the mandibular branches. A schwannoma was suspected. At surgery, a reddish firm mass was removed from Meckels' cave. Pain subsided immediately after surgery, whereas hypaesthesia and hypalgia and paresis and atrophy of the masticatory muscles of the left hand side were still present one year later. No abnormal immunoelectrophoretic findings in her serum could be found. A monoclonal population of circulating B lymphocytes was not present.

Case 3

A 45-year-old female patient had complained for 10 years of continuous pain in her left cheek and mandibular regions. The symptoms were perceived as being slowly progressive. Clinical examination revealed an extinct corneal reflex and hypaesthesia of trigeminal nerve branches II and III of the left side. Multiple sclerosis was at first suspected, but cerebrospinal fluid, visual and acoustic evoked potentials as well as EEG were all unremarkable. Both CT and MRI revealed a space-occupying lesion in the left Meckel's cave (Fig.1). The ganglion appeared to be more voluminous than the contralateral one, with ill-defined margins and slight marginal enhancement. The dural covering was slightly bulged towards the external surface. A schwannoma was suspected. At surgery, the tumour was easily removed from the adjacent structures. The neuralgia subsided immediately after surgery, whereas hypalgesia persisted. There was no further follow-up.

In the general clinical examination of the patients, no pathological findings which retrospectively might be indicative of a systemic amyloidosis were detected. Follow-up was limited to serum immunoelectrophoresis and to a search for monoclonal B-cell populations, as mentioned in the first two cases. The family history turned out to be unremarkable in terms of systemic amyloidosis.

Materials and methods

Light microscopy

Formalin-fixed specimens from the trigeminal ganglia obtained at surgery were fixed in 4% buffered formaldehyde and embedded in paraffin. Stainings included Congo red with and without potassium permanganate treatment [12]. For the immunohistochemical staining, non-specific binding was blocked with normal horse or normal goat serum except for anti-AF which was not blocked. Antibodies were diluted in phosphate buffered saline containing 1% bovine serum albumin, except for anti-AF which was diluted only in phosphate buffered saline. The following primary antibodies were used (clonality, dilution and source in parentheses): AA (monoclonal; 1:200; Dako), AB (polyclonal; 1:600; Dako), AF (polyclonal; 1:600; Dako), AL kappa (polyclonal; 1:1200; donated by Dr. R. Linke), AL lambda (polyclonal; 1:3000; donated by Dr. R. Linke). As secondary antibodies, biotinylated horse anti-mouse (1:200; Vector) was used for the anti-AA antibody and biotinylated goat anti-rabbit (1:200; Vector) for the polyclonal antibodies. In each case, horseradish-peroxidase-conjugated avidin-biotin-complex (Vectastain Elitekit) was added. The reaction product was made visible with 0.05% diaminobenzidine (Sigma) and 0.03% H_2O_2. For the negative control, the primary antibody was omitted. Positive control sections for the AA and the AL-lambda subtypes were run in parallel.

Electron microscopy (cases 2 and 3 only)

Specimens were fixed in 3% buffered glutaraldehyde, postfixed in osmium tetroxide, dehydrated in alcohol and embedded in epoxy resin.

Immunoelectron microscopy (cases 2 and 3 only)

Mounted paraffin sections were deparaffinized and blocked with normal goat serum and incubated with the same antibody against the AL-kappa and AL-lamba subtypes as described above except that higher concentrations (1:600 and 1:1500, respectively) were used. The reaction product was made visible with a polyclonal goat anti-rabbit antibody conjugated with 5 nm gold particles (1:20; Amersham). The sections were postfixed in 2% glutaraldehyde for 10 min and then, while still on the slides, osmicated, dehydrated in alcohol and embedded in epoxy resin as in the ordinary electron microscopic embedding procedure. After the embedding process, slides were removed from the specimen by liquid nitrogen. Ultrathin sections were cut from the block and stained with lead citrate and uranyl acetate.

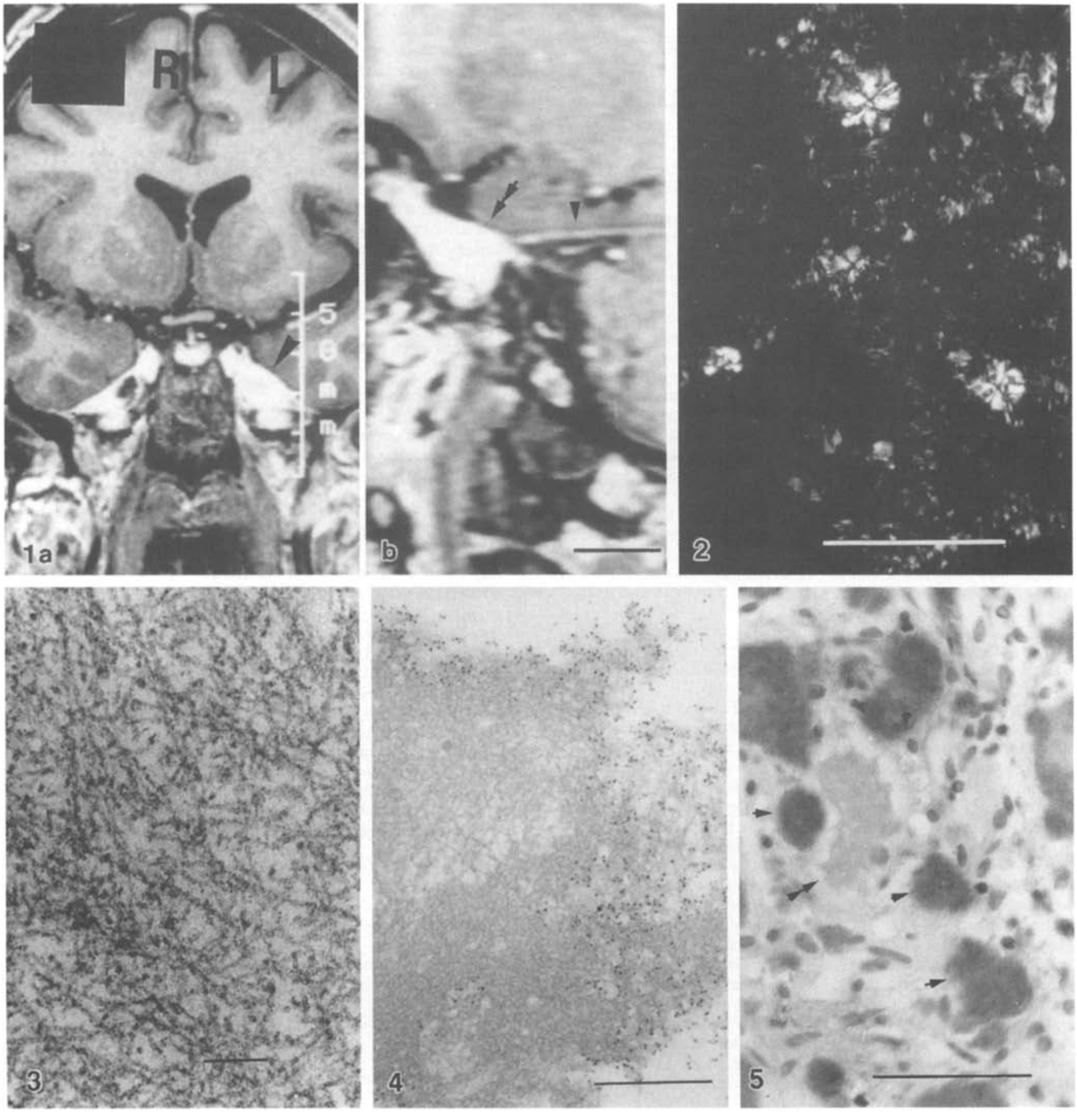

Fig. 1 Case 3. T1-weighted volume sequence after intravenous injection of gadolinium (0.2 mmol/kg body weight). **a** Coronal plane. Note tumour mass (*arrowhead*) in left Meckel's cave. **b** Parasagittal plane. Secondary reconstruction showing the trigeminal nerve's (*arrowhead*) course through the cistern to the tumour (*double arrowhead*). *Bar*: 10 mm

Fig. 2 Case 1. Typical pattern of birefringence is seen in the biopsy specimen of the tumour mass stained with Congo red and viewed with polarized light. *Bar*: 100 μm

Fig. 3 Case 2. Electron microscopy of the amyloidoma reveals unbranched fibrils distributed at random. *Bar*: 0.1 μm

Fig. 4 Case 2. Electron micrograph of an amyloid plaque within the tumour mass, stained with the anti-AL amyloid subtype and labelled with 5 nm gold particles. There is reactivity at the periphery of the plaque. *Bar*: 0.5 μm

Fig. 5 Case 3. Anti-AL subtype amyloid-stained peroxidase-labelled section of tumour mass. Amyloid plaques (*arrowheads*) are localized in-between satellite cells and a nerve cell (*double arrowhead*). Differential interference contrast optics. *Bar*: 25 μm

Results

Case 1

Histological examination of the biopsy specimen with Congo red staining revealed masses of amyloid plaques interspersed among ganglionic cells and myelinated nerve fibres. Small blood vessels were sometimes surrounded by amyloid, and occasionally amyloid was found to be present within vessel walls. Amyloid was stained with Congo red with and without prior potassium permanganate treatment, which is a most sensitive method for the detection of amyloid [12]. In polarized light, Congo red showed typical apple-green birefringence (Fig.2). The plaques revealed expression of the AL-lambda amyloid subtype, while antibodies against the other subtypes resulted in negative staining. No inflammatory infiltrates or aggregates of plasma cells were seen in the biopsy specimen.

Case 2

The bulk of the biopsy specimen revealed masses of plaques among ganglionic cells and nerve fibres. As in patient 1, Congo red staining with and without potassium permanganate pretreatment, and birefringence in polarized light showed that the plaques consisted of amyloid. Immunoperoxidase also revealed the amyloid subtype AL lambda. Electron microscopy showed unbranched fibrils 10 nm in diameter which were distributed at random (Fig. 3). Immunocytochemistry revealed expression of AL-lambda within the amyloid plaques (Fig.4). No inflammatory infiltrates or aggregates of plasma cells were seen.

Case 3

As in the first two patients, amyloid plaques of the AL-lambda subtype were detected extracellularly among ganglionic cells and satellite cells (Fig.5), around blood vessels and, occasionally, within vessel walls. Electron microscopy revealed typical haphazardly arranged fibrils. No inflammatory cells could be found.

Discussion

It is obviously difficult, if not impossible, to make the diagnosis of an amyloidoma of the gasserian ganglion prior to histology. In reporting three more cases here we wanted to draw attention to this unusual cause of symptomatic neuralgia of the trigeminal nerve in order to include it in the differential diagnosis. In our three cases, the clinical data were not different from more frequent causes of trigeminal neuralgia such as inflammation or schwannoma. No plasma dyscrasia was found. CT was either negative or misleading, and MRI led to the diagnosis of a schwannoma.

What makes the diagnosis so difficult is the fact that amyloidomas behave more like a tumour than like an amyloidosis. First, they usually occur in isolation and are not generalized. This is also true of amyloidomas which occur in intracranial sites other than the trigeminal ganglion such as the skull base [5] or the cerebellopontine angle or the jugular foramen [11]. Secondly, they do not produce monoclonal proteins in the patients' serum ([4, 11], our cases) as opposed to two thirds of patients with AL amyloidosis [9]. Accordingly, the amyloidoma's content of lymphocytes or plasma cells is scattered at most [1, 5, 11]. In our biopsy specimens, no plasma cells were found at all. The term "burnt-out plasmocytoma" has been coined for this type of tumour [6]. In our cases, the patients' age and sex exclude them from being typical candidates at risk for AL amyloidosis, which is a disease of "older male patients" [9].

The aetiology of amyloidomas is not known. It is also not known why the gasserian ganglion is preferred as the site of occurrence over other cranial ganglia. Our second patient had experienced herpes zoster infection of the ipsilateral trigeminal ganglion 10 years earlier. It is tempting to speculate that this infection led to the development of an amyloidoma. However, there is no morphological evidence to support this.

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