Professional article/Strokovni prispevek

ORBITAL AMYLOIDOSIS

AMILOIDOZA ORBITE

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Key words: *orbital amyloidosis; echography; palpebro-epibulbar amyloid*

Abstract – Background. *Authors want to present echographic characteristics of two stages of development of bilateral orbital involvement in primary systemic amyloidosis in 10-year follow-up of a case.*

Methods. *A 65-year old white female with 10-year-long history of orbital involvement in primary systemic amyloidosis presented to us with large nasal left upper palpebro-bulbar mass that produced lateral displacement of the globe, marked reduction of ocular motility in all directions and ptosis covering the pupil. Direct and transbulbar echography, pathohistological analysis, and immunohistochemistry were used to confirm the diagnosis of amyloid. The mass was partially removed and the lid reconstructed.*

Results. *The echographic examination of the orbits performed in 1990 showed an epibulbar and parabulbar low-reflectivity orbital mass in the upper temporal part of the right orbit. A widened right lateral rectus muscle of low reflectivity was also documented. Ten years later direct echography of the medial part of the left upper lid discloses palpebral extension of the orbital mass. It has irregular, inhomogeneous, medium to high reflectivity with rough granular structure and calcifications. Transbulbar echography revealed changes in both orbits. There is widening of the orbital fat echo with the higher reflectivity. All extraocular muscles are enlarged, including insertions. The widest is the right lateral rectus muscle. The muscle sheaths are thickened, widened with easily detected higher inner reflectivity than in the muscle itself. There is irregular, inhomogeneous, medium to high reflectivity of the muscles with scarce calcification.*

Conclusions. *The initial stage of orbital amyloidosis is characterized with low reflectivity. Ten years later, the mass reflectivity inhomogeneously increased and calcifications developed.*

Ključne besede: *amiloidoza orbite; ehografija;*

Izvleček – Izhodišča. *Avtorji predstavljajo ehografske značilnosti dveh faz razvoja obojestranske prizadetosti očesne votline pri primarni sistemski amiloidozi po 10-letnem spremljanju bolnice.*

Metode. *Prikazan je primer 65-letne bolnice z 10-letno anamnezo prizadetosti očesne votline zaradi primarne sistemske amiloidoze z velikim nabreklim tvorom pri nosu na levi strani zgornje očesne veke, ki je povzročil stranski zamik zrkla, opazno zmanjšanje očesne gibljivosti v vseh smereh s povešenjem očesne veke, ki je zakrivala zenico. Za potrditev diagnoze amiloida smo uporabili neposredno ehografijo in ehografijo skozi nabreklino, patohistološko analizo in imunohistokemijo. Tvor je bil delno odstranjen in veka je bila rekonstruirana.*

Rezultati. *Ehografski pregled očesnih votlin, narejen leta 1990, je kazal na epibulbaren in parabulbaren tvor očesne votline z nizko reflektivnostjo v zgornjem senčnem delu desne očesne votline. Ugotovljena je bila tudi razširjena desna stranska mišica rectus z nizko reflektivnostjo. Deset let pozneje je ehografija medialnega dela leve zgornje veke pokazala palpebralno ekstenzijo tvora očesne votline. Vidno je bilo nepravilno, nehomogeno tkivi s srednje do visoko reflektivnostjo z grobo zrnato strukturo in kalcifikacijami. Ehografija skozi nabreklino je odkrila spremembe v obeh očesnih votlinah. Šlo je za širjenje maščobe v očesni votlini, ki je imela višjo odbojnost. Vse zunajočesne mišice vključno z vezmi so bile povečane. Najširša je bila desna stranska mišica rectus. Mišične ovojnice so bile zadebeljene, razširjene s preprosto zaznavno notranjo odbojnostjo, ki je bila višja kot v sami mišici. Šlo je za nepravilno, nehomogeno, srednjo do visoko odbojnost mišic s posamičnimi kalcifikacijami.*

Zaključki. *Značilnost začetne faze amiloidoze očesne votline je v nizki odbojnosti. Deset let kasneje je odbojnost tvora nehomogeno narasla in razvila se je kalcifikacija.*

Introduction

Amyloidosis is a group of disorders of protein metabolism characterised by the extracellular deposition of abnormal insoluble protein, mostly in interstitium and around blood vessels (1). Many organ systems may be affected. The clinical classification recognises primary, secondary and familial subtypes of the disease (2, 3). Currently, a new classification based on the biochemical composition of amyloid subunit protein identifies five subtypes. All forms of amyloid share common light microscopic properties and a fibrillar ultrastructure. Amyloidosis may involve the eye and its adnexa as a localized disorder or as a part of systemic illness. The eyelid is the preferred site for amyloid deposition in patients with primary systemic amyloidosis (4). However, the disease can involve all ocular structures including the anterior eye segment, vitre-

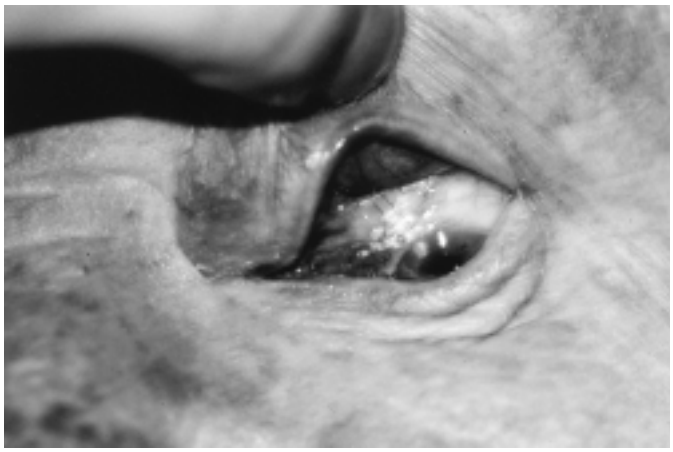

Fig. 1. *A 65-year-old female patient presented with a large nasal left upper palpebro-bulbar mass that produced lateral displacement of the globe, marked reduction of ocular motility in all directions and ptosis covering the pupil.*

Sl. 1. *65-letna pacientka z velikim nabreklim tvorom pri nosu na levi strani zgornje očesne veke, ki je povzročil stranski zamik zrkla, opazno zmanjšanje očesne gibljivosti v vseh smereh s povešenjem očesne veke, da je zakrivala zenico.*

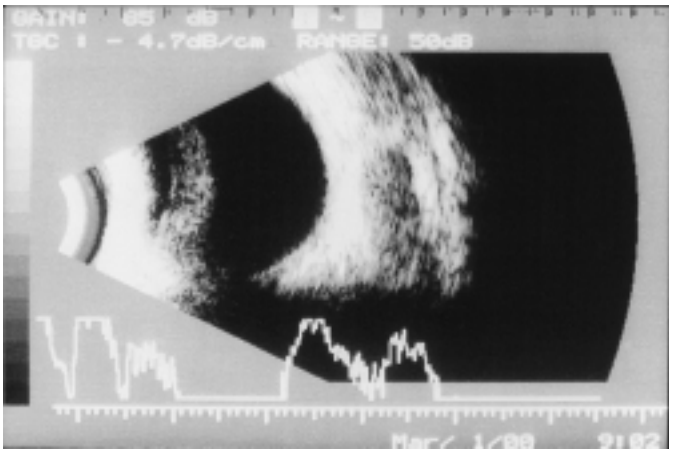

Fig. 2. *Parabulbar echography of the right orbit. The lateral rectus muscle is enlarged, including insertion. The muscle sheath is thickened, widened with easily detected higher inner reflectivity than in the muscle itself. There is irregular, inhomogeneous, medium to high reflectivity of the muscle with large calcification in the upper part of the picture.*

Sl. 2. *Parabulbarna ehografija desne očesne votline. Stranska mišica rectus vključno z vezmi je povečana. Mišična ovojnica je zadebeljena, razširjena s preprosto zaznavno notranjo reflektivnostjo, ki je višja kot v sami mišici. Gre za nepravilno, nehomogeno, srednjo do visoko reflektivnost mišice z visoko kalcifikacijo v zgornjem delu slike.*

ous, retina and its vasculature, choroid, optic nerve and higher visual pathways, extraocular muscles and orbit (4, 6–10).

Case report

A 45-year-old white female presented to us for the first time in 1985 with the mass and the swelling in the lateral corner of the right eye. Apart from recurrent upper respiratory tract infections she had no serious illness. The biopsy of the mass showed only signs of a non-specific inflammatory reaction. No therapy was instituted. During the next five years the mass enlarged and, in addition, masses in the upper medial and lateral corner of the left eye occurred. They were hard, painless subconjunctival tumours, yellow-pink in colour, adhering to the globe on a wide basis. The echographic examination of the orbits showed an epibulbar and parabulbar low-reflectivity orbital mass that measured 12×7 mm in the upper temporal part of the right orbit. A widened right lateral rectus muscle of low reflectivity was also documented (17). Biopsy revealed amyloid deposition. A further thorough diagnostic procedure showed systemic amyloidosis. The right epibulbar mass was excised at the time. The patients received no further local or systemic treatment. Since then she was hospitalised our Department twice when left epibulbar masses were excised.

Now 65-year-old, our female patient presented again to us in January 2000, with a large nasal left upper palpebro-bulbar mass that produced lateral displacement of the globe, marked reduction of ocular motility in all directions and ptosis covering the pupil. The mass involved the skin in the nasal part of the left upper lid that was yellow, waxy, with irregular, thickened surface revealing a palpable lobular structure of the underlying lesion (Fig. 1). No pathological vascularisation was seen on the involved skin. The mass permeated all the layers of the lid, conjunctiva and Tenon's fascia of the upper nasal bulbar quadrant, fixating the globe and crawled along the bulbus into the upper nasal orbit. The right eye ocular motility was also restricted. Direct echography of the medial part of the left upper lid discloses palpebral extension of the orbital mass. It is 17 × 13 mm massive lesion of the irregular, inhomogeneous, medium to high reflectivity and rough granular structure. Two small highly reflective areas, 5 and 3 mm in diameter, correspond calcifications. Parabulbar echography revealed changes in both orbits. There is widening of the orbital fat echo with increased reflectivity. The retrobulbar fat close to sclera has the reflectivity almost comparable to sclera. All extraocular muscles are enlarged, including insertions. The widest is the right lateral muscle. There is irregular, inhomogeneous, medium to high reflectivity of the muscles with scarce calcification (Fig. 2). These muscles are more easily seen in the relatively high reflective orbital. The muscle sheaths are also thickened, widened with easily detected higher inner reflectivity than in the muscle itself.

An operation was performed in local anaesthesia by one of us (BK). The mass was partially removed. The local rotation conjunctival flap was used to cover the conjunctival defect of the globe. The tarsal conjunctiva defect was covered with buccal mucous membrane graft. Levator palpebrae muscle aponeurosis could be identified only in the central and lateral part of the lid. It was reattached to the upper tarsus. The skin-muscle contralateral upper lid graft was used to cover the defect. The excised material stained by Congo red that imparts an orange pink tint to the amyloid deposit. When viewed by polarization microscopy it showed an apple-green birefringence that is the sine qua non of the diagnosis of amyloidosis (Fig. 3). The immunohistochemistry (ABC) method was performed as a final marker for amyloid. A lymphocytic infiltration and abundance of plasma cells were also seen. The left upper lid is still low 3 months postoperatively, but uncovers the pupil (Fig. 4). The motility is satisfactory.

Discussion

Orbital amyloidosis is rare. It is predominantly of the localised nonmyelomatous type (1, 3). In 31 reported cases of localised orbital amyloidosis (3, 11) six were bilateral. Only two protein subunits are pertinent to the subject of orbital amyloidosis (3). The protein amyloid A (AA) is associated to secondary

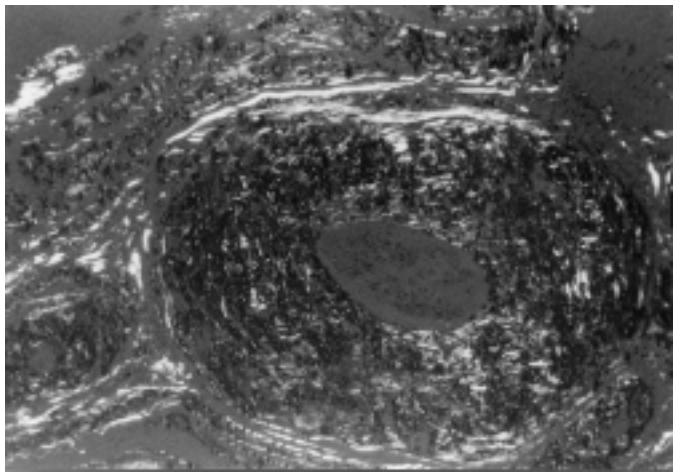

Fig. 3. *Acellular aggregates of amyloid found in walls of blood vessels seen as whitish areas on this black and white photograph of Congo red staining. A characteristic apple green birefringence is produced under the polarised light.*

Sl. 3. *Necelična kopičenja amiloida, ki ga najdemo v stenah krvnih žil in so vidna kot belkasti madeži na črno-beli fotografiji pri Kongo rdečem barvanju. Značilna jabolčno zelena birefringenca nastane pod polarizirano svetlobo.*

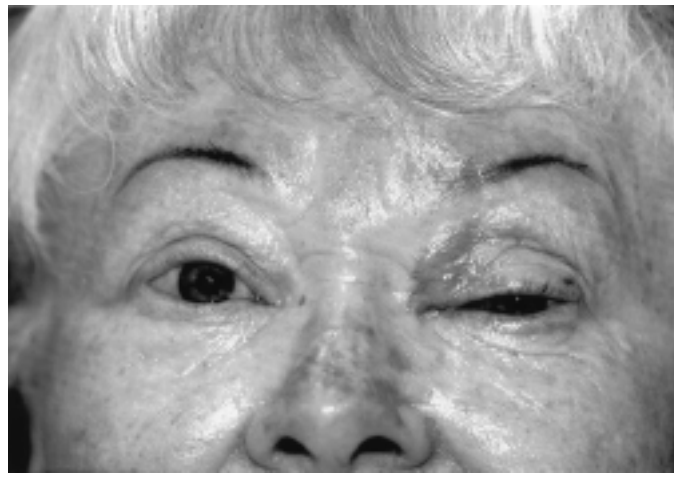

Fig. 4. *The left upper lid is still low 3 months postoperatively, but uncovers the pupil.*

Sl. 4. *Leva zgornja veka je 3 mesece po operaciji še nizka, vendar ne pokriva več zenice.*

amyloidosis while amyloid AL, consisting of either kappa or lambda immunoglobulin light chain, is common to primary amyloidosis. The presented signs of orbital amyloidosis vary according to the amyloid deposition site. Some have proptosis and displacement of the eye due to the lacrimal gland involvement as in 5 out of 6 cases in Murdoch et al. report (1). Others might have ocular motility disturbances with deposition in extraocular muscle/s and/or blepharoptosis (7, 8, 12). Purpura of the upper lid strongly suggests systemic disease (3). The universal constituent of amyloid is the amyloid P component (AP). It is derived from normal circulating plasma protein, serum amyloid P component (SAP). The isolated pure humane SAP radiolabelled with ^{123}I is a highly specific tracer for all types of amyloidosis (1). It has been used to prove confinement of the amyloid to the orbit (1).

The most used method of orbital imaging is CT (3). Its ability to detect calcification that is helpful in differentiation of amyloid from other lesions makes it dominant over MRI (1). Ultrasound is of great value in the differential diagnosis of the lesion. The first and to our knowledge the only description of echographic characteristics of orbital amyloidosis was done by us in 1992 (13). It was the early stage of the disease and its ultrasound picture differs a lot from the one found now. The then echographic examination of the orbits showed an epibulbar and parabulbar low-reflectivity orbital pseudotumour in the upper temporal part of the right orbit and a widened right lateral rectus muscle of low reflectivity (13). In 10-year period reflectivity of all orbital structures rose. Echo became inhomogeneous, it got a rough granular structure with scarce calcifications.

Amyloid is an acellular aggregate that may be found in adipose tissue, walls of small blood vessels, extraocular muscles and lacrimal gland (3). »Some amyloid deposits incite very little reactive response in the host tissue«, while others may show granulomatous foreign body response (3). These are the reasons why amyloid can be missed if not explicitly looked for. The granulomatous foreign body response of the host tissue might be the reason for the changed echographic picture of the long-standing orbital amyloidosis in our case. It speaks in favour of increased echogenicity, irregularity of the orbital mass and appearance of calcifications. A 10-year period of follow-up of our patient was very instructive to us for, among other things, the orbital amyloidosis echographic picture development documentation. We succeeded to record what we consider, the initial stage of orbital amyloidosis 10 years ago. Low reflectivity of the lesion back then was due to acellular aggregates in adipose tissue, walls of small blood vessels and extraocular muscles. The granulomatous foreign body response of the host tissue inhomogeneously increased the mass reflectivity and secondary changes resulted in calcifications.

In the differential diagnosis of orbital amyloidosis we have to consider other causes of muscle enlargement (14, 15) such as dysthyroid orbitopathy, orbital myositis, orbital venous congestion, metastatic disease, lymphoma and lithium therapy, as well as orbital mass lesions: cavernous haemangioma, pseudotumour, lymphoma, metastatic tumours and mucocele.

Echography is a usefull method in the differential diagnosis of the orbital mass. The purpose of this paper is to present 10-year echographic follow-up of orbital amyloidosis in the patient with systemic amyloidosis. We documented echographic picture of two stages of orbital amyloidosis. Echography is an affective, safer alternative to computed tomography for orbital amyloidosis.

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