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Primary Localized Ocular Amyloydosis: A Rare Case Report

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ABSTRACT

Introduction: Amyloidosis is a complex, heterogeneous set of illnesses characterized by the deposition of hyaline extracellular material into many tissues throughout the body, including the eye and ocular adnexa. Therefore, we would like to present a case report about ocular Amyloidosis.

Case Illustration: 17 years-old-female complained tumor in both eye since 5 years ago. Visual acuity (VA) and Intraocular Pressure (IOP) for both eye within normal limits. Ocular motility (OCM) within normal limits. Anterior segment examination for the right eye (RE), swelling on inferior palpebra, with solid mass throughout the inferior conjunctival palpebra, defined border, uneven surface, immobile, hyperaemia with size 21x5mm, for the left eye (LE), swelling on superior palpebra, with solid mass, defined border, uneven surface, immobile, hyperaemia with size 12x5mm in 2/3 medial and 10x10mm in 1/3 lateral of the superior conjunctival palpebra. Both tumors were easy to bleed. Funduscopic examination were within normal limits for both eyes. We've done our excisional biopsy, and came with Amyloidosis. We consult this patient to Internal department for any systemic manifestation. She got Metatrexate for a month and changed to Myfortic for a month too, but there are no changes on the tumors condition. Internal Department concluded that its more to primary Amylodosis rather than secondary Amyloidosis.

Discussion: The ophthalmic manifestations for Amyloidosis are uncommon, can affect any ocular and periocular structure. Periocular and orbital amyloidosis is a slow-progressing illness. Visible or palpable periocular mass or tissue infiltration, ptosis, are the most common indications and symptoms which matched with our patient condition. Management for ocular amyloidosis may be vary, most studies recommend debulking excision with low recurrence and progression rate.

Conclusion: Although we can suspect Amyloidosis through examination, histopathologic examination is necessary for definite diagnosis. There are no definite management for Amyloidosis, but we can relief patient discomforts depend on the complaint.

Keywords: *Amyloidosis, Isolated Amyloidosis, Ocular Amyloidosis, Bilateral Ocular Amyloidosis, Non-hereditary Amyloidosis.*

INTRODUCTION

Amyloidosis is a word used to describe a group of clinical illnesses caused by the deposition of insoluble amyloid fibrils in extracellular and intracellular spaces, which causes multiple tissue dysfunctions and disrupts tissue architectures in the human body. Protein deposition in diverse tissues is caused by a group of illnesses with comparable pathophysiology and metabolic pathway involvement. It deposits can form in a variety of tissues and organs across the body (systemic amyloidosis) or in a single location (localized amyloidosis). Ocular adnexal and orbital amyloidosis is a rare presentation and can occur with localised or systemic disease. The most reported affected ocular tissues are eyelid, extraocular muscles, lacrimal gland or sac, conjunctiva, levator palpebrae muscle, and orbital fat.

Ravichandran et al. reported in United Kingdom, 11,006 people diagnosed with amyloidosis between 1987 and October 2019. The number of incidents grew by 670% between 1987 and 1999 and 2010 to 2019, with Systemic light-chain (AL) amyloidosis remained the most common type1. Kang et al. also reported in their case series in United Kingdom, 41 patients were indentified with vary clinical presentations from 1980 – 2016. They stated several ocular and adnexal structures were frequently impacted by the disease. Conjunctival or subconjunctival deposits were observed in 20 (49%) of the patients, and eyelid involvement was present in 23 (56%). Sixteen (16/23; 70%) of these cases showed unilateral eyelid involvement (10 upper lid, 5 lower lid, 1 upper and lower lid). Bilateral eyelids were implicated in seven cases (7/23; 30%) (4 bilateral upper lids and 3 bilateral upper and lower lids). Less frequently implicated locations included the lacrimal gland (4 cases [10%]; 3/4 bilateral), the lacrimal sac (2 unilateral cases; 5%), and the superior rectus/levator complex in one patient (2%)2.

Study in Italia by Dammacco et al reported that ocular morbidity was found in 41 of the 178 amyloidosis patients (23%). 18 individuals with systemic illness, 3 with multiple myeloma, and 11 with localized amyloidosis were diagnosed with AL

amyloidosis. Transthyretin amyloidosis was found in four patients, two with rheumatoid arthritis and three with Behçet disease3. According to Seo SR et al's study in Korea, the total age-standardized prevalence of amyloidosis was around 2 people per 100,000 people in 2015. Between 2006 and 2015, the total age-standardized prevalence of amyloidosis increased, particularly in people aged 45-64 and above 654.

Amyloidosis cases worldwide still rare and difficult to diagnosis. Ocular adnexal and orbital amyloid is uncommon, manifests in unexpected ways, sometimes be coupled with systemic involvement, and has previously only been published as case reports or a small case series. Therefore, in this paper, we would like to present a case report about primary localized ocular amyloidosis on conjunctiva and how to comprehend its characteristics as well as the effects of future treatments.

CASE ILLUSTRATION

17 years-old-female came to outpatient of Ophthalmology Oncology Unit at Dokter Soetomo General Academic Hospital with chief complaint of tumor in both eye since 5 years ago. The tumor was getting worse slowly until last month. Patient has history of tumor surgery in left eye 2016 and lost to follow up until last December. The first tumor was first noticed when patient in first grade in elementary school and getting bigger. Patient was in fourth grade at the time the first tumor was operated. There was no history of eye redness and decreased visual field. The patient has no history of trauma, allergy nor similar complaint in her family (figure 1).

Physical examination revealed that she was compos mentis. Her blood pressure was 110/70 mmHg, heart rate 85 bpm, respiratory rate 18 bpm, and body temperature was 36.7º C. Ophthalmology examination revealed her visual acuity (VA) was 5/5 on both eyes. The intraocular pressure (IOP) was 14 mmHg on the right eye dan 20 mmHg on the left eye using Non-Contact Tonometry (NCT). Ocular motility (OCM) was within normal limit for both eyes.

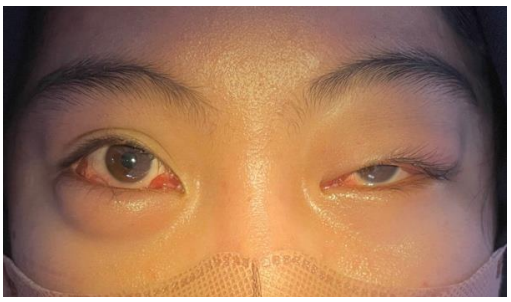

Figure 1. Clinical picture, it shows right eye (RE) palpebra inferior swelling and palpebra superior swelling, along with pseudoptosis on the left eye (LE).

Anterior segment examination for the right eye (RE) was found swelling on inferior palpebra, accompanied with solid mass throughout the inferior conjunctival palpebra, defined border, uneven surface, immobile, hyperaemia with size 21x5mm and for the left eye (LE), swelling on superior palpebra, with solid mass, defined border, uneven surface, immobile, hyperaemia with size 12x5mm in 2/3 medial and 10x10mm in 1/3 lateral of the superior conjunctival palpebra (figure 2). We found both tumors were easy to bleed. Funduscopic examination were within normal limits for both eyes (figure 3).

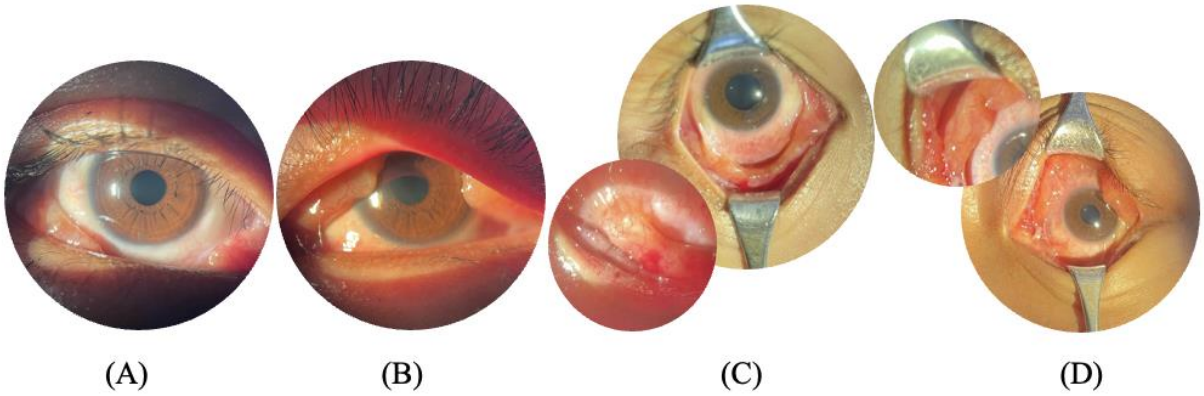

Figure 2. (A-D), Closer look for right left eye (RLE), they show solid mass throughout inferior conjunctival palpebra for RE and superior conjunctival palpebra for LE.

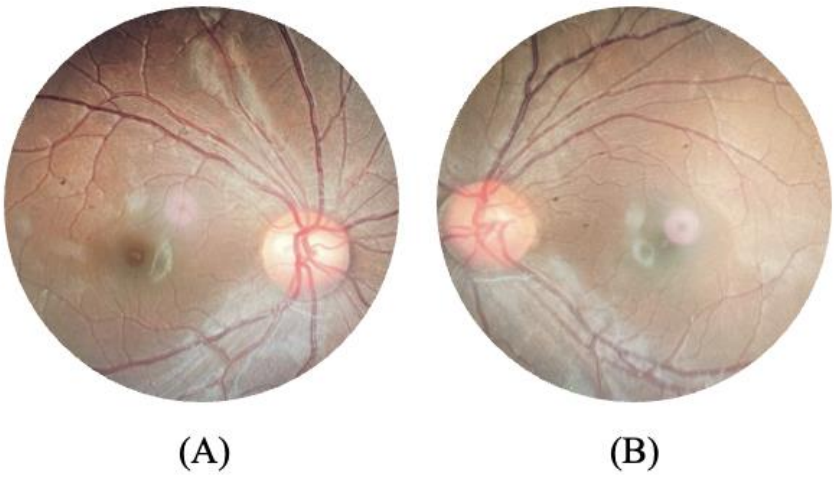

Figure 3. Funduscopic examination show no sign of abnormality or optic nerve compression, and no vitreous opacity. (A) right eye, (B) left eye

The patient's blood ancillary tests were done to evaluate systemic disease, results were within normal limits. Pathology anatomy result for the first surgery in 2016 was found chronic inflammations. The patient had undergone imaging study, Computed Tomography (CT) Scan result in December 19th 2022 were right and left orbital cellulitis pre-septal, right and left orbital lymphoproliferative lesion, left inferior concha nasalis hypertrophy with septum nasi deviation to the right side +/- 0.8cm from midline, no sign of infarction, haemorrhage, infection process nor metastasis on brain parenchyme. Therefore, our early diagnosis for patient was RLE benign conjunctival tumors with differential diagnosis (DD) Orbital Adnexal Lymphoma (OAL) DD conjunctival lymphoproliferative.

Initial planning, we planned excisional biopsy for LE accompanied with RLE cryotherapy, but during the operation we decided to change to LE excisional biopsy (debulking) anterior orbitotomy approach, RE incisional biopsy, RLE cryotherapy, and RLE Amniotic Membrane Transplant (AMT) installation. Post operation medication we gave Methylprednisolone 500mg injection in 100 cc PZ intravenously per day for three days followed with prednisone 20mg orally three times a day for eleven days, ketorolac 30 mg and paracetamol 500mg orally three times a day for painkillers, RLE levofloxacin eye drop and fluorometholone eye drop six times a day. Patient was discharged after third injection of Methylprednisolone 500mg. We followed up our patient routinely (figure 4 and 5).

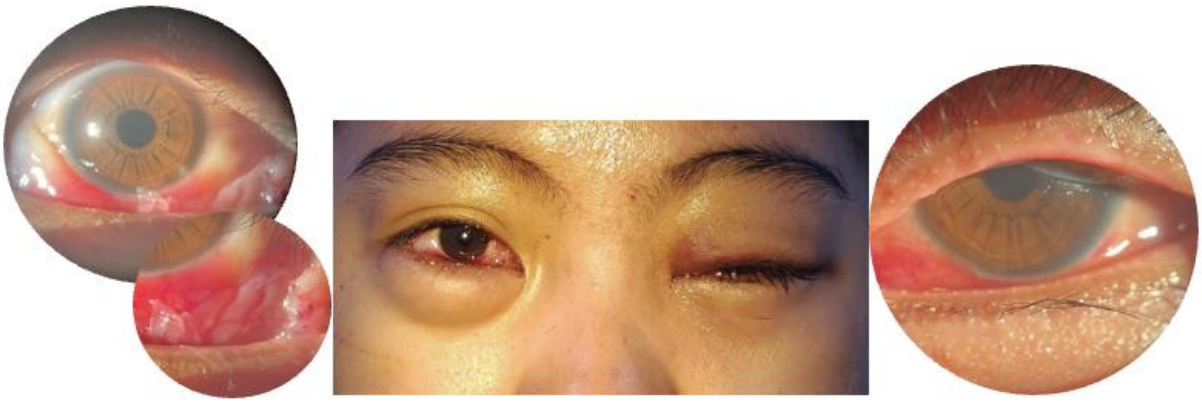

Figure 4. Day 1 after operation, ophthalmology examination showed, RE swelling on inferior palpebra, accompanied with hyperaemia conjunctiva, subconjunctival bleeding at the inferior, mild chemosis 180 degree inferior, also AMT intact on the conjunctival palpebra inferior. LE showed, pseudoptosis, superior palpebra swelling, accompanied with hyperaemia conjunctiva, AMT intact on the conjunctival palpebra superior, also contact lens (CL) intact on the cornea.

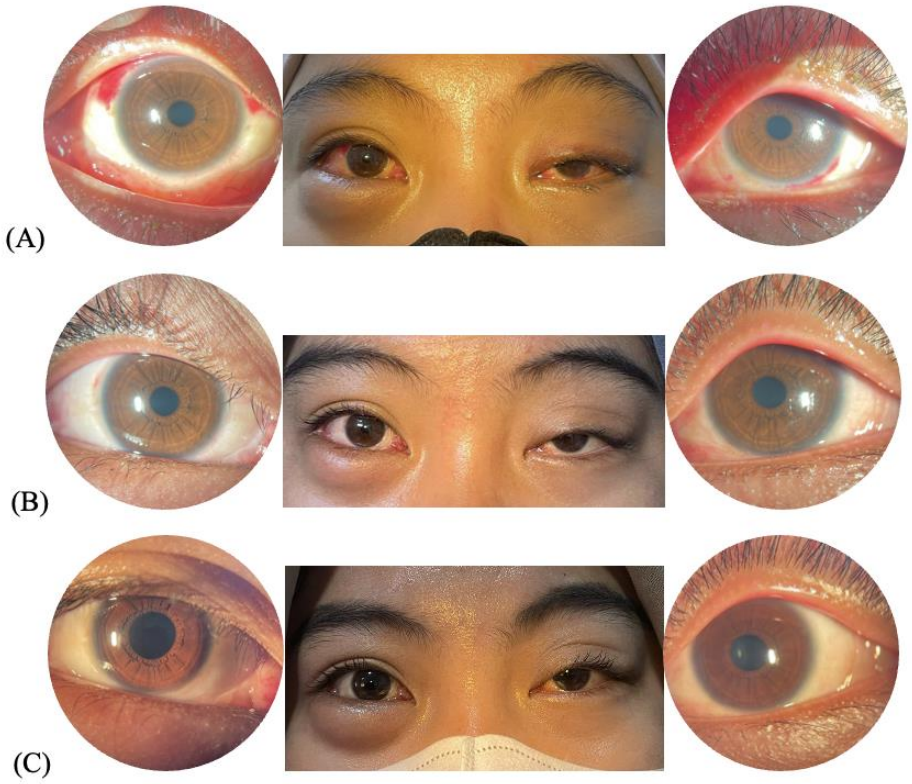

Figure 5. Follow up after surgery, (A) A week, (B) A month, (C) 3 months.

Histopathologic result, came after 28 days, after meticulous review from pathology anatomy department (figure 7), it came out with Amyloidosis and on congo red painting with polarization: positive (a picture of apple green birefringence is obtained). We then consult our patient to Internal Department (dept.) for any sign of systemic amyloidosis and systemic treatment. Patient got Methotrexate 4 tablets once a week for a month, she felt no improvement. Internal dept. then gave another treatment, mycophenolate sodium twice a day for a month. In two weeks during new regimen, patient complaint, the tumor on her left inferior palpebra was getting bigger. Patient continue the medication and showed no improvement. The Internal dept. then changed the medication to myfortic for a month, and still no sign of improvement. After discussions with Internal dept. they conclude that its more to primary Amylodosis rather than secondary Amyloidosis.

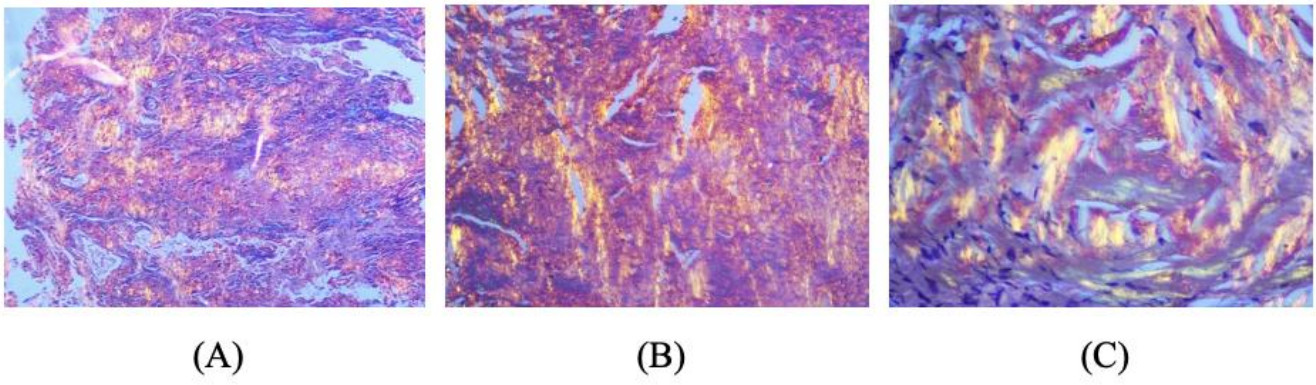

Figure 6. Histopathologic presentation from our Pathology Anatomy dept. shows tissue fragments of extensive eosinophilic amorphous material covered with polygonal squamous epithelium, round-oval nuclei, smooth chromatin, ample cytoplasm, eosinophilic. Intak basement membrane. In the stroma, lymphocytes and histiocytes were seen. There was no specific process or signs of malignancy. (A) Magnification 40x, (B) Magnification 200x, (C) Magnification 400x.

Six month after the surgery, we then underwent a follow up surgery to right eye inferior palpebra. In two years follow up. We found no sign of enlargement (figure 7).

Figure 7. Two years follow up. No sign of enlargement amyloidosis..

Their ages at initial diagnosis and management varied among the patients. Each patient has a unique clinical presentation both before and after surgery. Their visual acuity also differed when they returned two years later. The family history and genetic pattern of congenital cataract in this family are depicted in Figure 6.

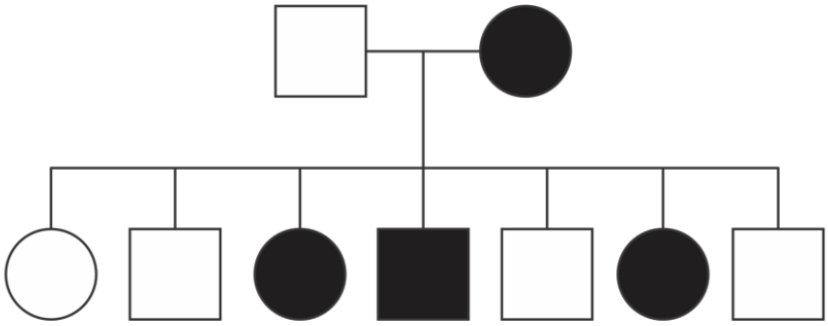

Figure 6. A family pedigree of this family. The black in colour were affected individual. The mother and three of seven child are affected.

DISCUSSION

Like other cancers, conjunctival tumors are characterized by how they originated and whether they are benign or malignant. Due to unique histological characteristics, features, and tumor cell location, subtypes of tumors within groupings of malignancies may appear or behave differently despite being produced from the same cell[7]. Melanocytic, epithelial vascular, and lymphoid tumors are the most common, but choristomatous, fibrous, neural, xanthomatous, myxomatous, lipomatous, lacrimal, metastatic/leukemic, secondary, inflammatory, infectious, degenerative, and non-neoplastic simulators are also encountered[8].

The conjunctiva, a thin layer of tissue that covers the eye and lines the eyelids, can also generate a conjunctival tumor. These benign or malignant tumors can form anywhere on the conjunctiva. Papillomas, melanomas, squamous cell carcinomas, and lymphomas are common conjunctival tumors. Diagnose a conjunctival tumor with a complete eye exam, including a slit-lamp and perhaps a sample. Treatment depends on tumor kind, size, location, and metastasis to other regions of the eye or body. After surgery, radiation or chemotherapy may treat the tumor[9,10].

The conjunctiva contains specialized lymphoid tissue and acts as an antigen barrier as part of the MALT system. An incisional biopsy for histological and cytological testing is the best conjunctival lymphoma diagnosis. The pathologist may perform immunoprofiling by immunohistochemistry or flow cytometry and/or molecular studies[11]. Conjunctival MALT system stimulation by antigen causes reactive lymphoid hyperplasia. RLH affects men and women equally and is more common in youth. Morphological, immunohistochemical, and molecular genetic characteristics reveal that the lesion contains polyclonal B- and T-lymphocytes in about equal numbers. B-cell NHL can arise in this conjunctival MALT system. Four B-NHL subtypes dominate conjunctival lymphoma[5,12].

Conjunctival RLH and B-NHL appear as'salmon patch'-like enlargements with no symptoms. According to another study, RLH can occur anywhere, but typically in the nasal part of the conjunctiva, 4mm from the limbus, non-pigmented, 10mm in size, and 1-1.5mm thick. B-NHL is usually in the forniceal region, 4mm from the limbus, inferior conjunctiva. Average lesion size is 20mm, thickness is 2mm[5,12].

Pyogenic granuloma, another conjunctival tumor. Conjunctival pyogenic granuloma (PG) is a benign vascular development of immature capillaries caused by inadequate surgical or traumatic wound healing. It is usually observed after surgery or other insults at a traumatic wound site or suture line. A vascularized tumor protrudes from the conjunctiva, despite an unknown cause. Zehra F. et al. also reported that PG is a common vascular abnormality that affects the skin and occasionally the mucosa, presenting with solitary, bright red, rapidly expanding papules after conjunctival surgery or trauma like chalazion, strabismus, or enucleation[13,14].

Amyloidosis is a group of diseases that cause significant morbidity and mortality and are on the rise. Imaging findings are generic and heterogeneous, which is concerning. Amyloidosis is highly related with, and often coexists with, many other chronic disease states, each with its own imaging findings, which reduces its specificity. It might appear as a localized, tumor-like lesion or infiltrative process in any organ. It should be considered a possible cause of worsening or new symptoms or imaging abnormalities in chronic inflammatory disease patients, especially multiple myeloma patients. The radiologist can help the patient when radiologic data precede clinical findings. To improve patient care, the radiologist must be familiar with amyloidosis' multiple imaging abnormalities and the patient's clinical history, which may raise suspicion[15]. Amyloidosis is a group of diseases that deposit hyaline extracellular material in many tissues, including the eye and ocular adnexa. Amyloidosis has been seen in almost every eye area, adnexa, and orbit. Patients may suspect amyloidosis, but tissue biopsy can confirm it with characteristic histological findings. Due to amyloidosis type-specific treatment regimens, terminology standardization has been emphasized.

Another study defined "amyloidosis" as a group of quite different diseases caused by dynamic misfolding of proteins that form insoluble fibrillary clumps. These aggregates injure organs when extracellularly deposited. These "chameleon" proteins, which produce amyloid fibrils in human tissues, have the following properties despite their structural and functional diversity: a) Pink staining with hematoxylin and eosin, methyl violet, or crystal violet; b) High Congo red dye binding affinity; c) Apple-green, yellow, or orange birefringence and dichroism under polarized light microscopy; d) Rigid, non-branching fibrils 7.5-10 nm in diameter; e) X-ray diffraction pattern of β-sheet fibrillary proteins.[3,16].

Ocular symptoms are the most prevalent but the sole sign of gelsolin-, keratoepithelin-, and lactoferrin-related amyloidosis. Ocular involvement may be the first symptoms of a clinical condition that the ophthalmologist and internist would diagnose as systemic amyloidosis after a comprehensive workup. A patient with established systemic amyloidosis, with or without subjective visual problems, is frequently referred to an ophthalmologist for ocular morbidity[3].

Amyloidosis with ocular symptoms is rare. They are mostly diagnosed histopathologically and the differential diagnosis of conjunctival neoplasms. Amyloidosis can affect any ocular and periocular structure and have several clinical symptoms, making diagnosis difficult. Slow-progressing periocular and orbital amyloidosis can cause eye issues. Ptosis and visible or palpable periocular mass or tissue infiltration are the most typical symptoms. Rare symptoms include periocular pain, repeated subcutaneous hemorrhages, keratoconjunctivitis sicca, ocular motility disorders, pupillary abnormalities, proptosis, and globe displacement. A restricted orbital mass or extensive amyloid infiltration might trigger proptosis. Ocular amyloidosis is distinguished from idiopathic inflammatory pseudotumor by mild or no pain[17].

Localized amyloid plaque deposition in the conjunctiva's substantia properia is a common form of amyloidosis in healthy young and middle-aged adults of any gender. Two types of localized orbital amyloidosis exist. Progressive proptosis, ocular movement limitation, and bilateral nodular infiltration of extraorbital muscles and adnexal tissues describe one kind. The second kind, amyloidoma, appears seldom near the lacrimal glands in the front orbit. In an orbital CT scan, these yellow waxy amyloidomas show calcification due to their fragility. Periocular involvement can cause ptosis and ophthalmoplegia, which may arise weeks or months later. Extraocular muscle infiltration and necrosis, particularly the levator and Muller's Muscles[17], cause several disorders.Our patients fit that description. Gradual progression, palpable mass, ptosis. Localized amyloidosis most often occurs on conjunctivas in young and middle-aged people. We suspected amyloidoma due of its waxy appearance, delicate consistency, and easy bleeding, which was confirmed during surgery.

The conjunctiva may be involved alone or with the orbicularis occuli or levator muscles. Salmon patch nodules and blephariptosis can result from amyloid accumulation in these structures. Tansal conjunctiva and fornixes (superior more than inferior) are common sites of conjunctival amyloidosis. Amyloid deposits can be unilateral or bilateral, rubbery or waxy[17]. Several pathways can cause ptosis in ocular amyloidosis. The levator aponeurosis from the tarsal plate is strained and dehisced due to repeated eyelid expansion from hemorrhages. Large amyloid masses might burden the lid, causing mechanical ptosis. Direct muscle amyloid infiltration may cause myogenic ptosis[18].

Management of ocular amyloidosis varies by instance. Many conjunctival lesions are treated conservatively with observation or artificial tears or gels. Local excision or surgical debulking may be done for stubborn patients. Demirci et al. found 27% recurrence after surgical debulking. Fraunfelder wrote about liquid nitrogen cryotherapy for conjunctival amyloidosis. Cryotherapy causes amyloidotic conjunctival ischemia by destroying small blood vessels. No systemic amyloidosis was found in the four study subjects. Three patients had surgical debulking before liquid nitrogen cryotherapy at the excision site[19,20].

Sultana et al. found that amyloidosis debulking is usually treated with surgery. Some surgeries are difficult. Recurrence is well-documented due to amyloid accumulation in aberrant tissues. Orbital disease recurrence is 29% higher than conjunctival involvement (15%). At 12-month follow-up, all patients were stable with no recurrence or progression. Conservative management for orbital amyloidosis, especially conjunctival, is important. If the patient is happy with the mass and amyloidosis is stable, observation without surgery is appropriate[21]. Dermarkarian et al. said debulking was the most common treatment[22].

According to Leibovitch et al., observation and surgical debulking were the main treatments. In their 39-month mean follow-up, 21% showed considerable improvement after treatment, while 79% were stable or had no recurrence[23]. Despite only 3 months of follow-up, it helped our patient's left eye. We will monitor the patient. Primary localized conjunctival amyloidosis remains for this patient.

CONCLUSIONS

Although we can suspect Amyloidosis through examination, histopathologic examination is necessary for definite diagnosis. There are no definite management for Amyloidosis, but we can relief patient discomforts depend on the complaint.

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