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Intraocular lens calcification in a patient with Ehlers-Danlos syndrome

Matthew J. Maguire [a,*], Donald John Munro [b], Patrick Merz [b], Alistair Laidlaw [a], Gerd U. Auffarth [b]

[a] St Thomas' Hospital, London, UK
[b] David J Apple Laboratory, Heidelberg, Germany

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ABSTRACT

Introduction: Calcification of hydrophilic intraocular lenses (IOL) is a rare complication following cataract surgery. Secondary calcification is described as due to host factors or changes in the IOL environment and uveitis, proliferative diabetic retinopathy and sequelae of ocular surgery are recognised potentiators. The impact of systemic connective tissue disease on IOL opacification is yet to described.

Purpose: To describe the clinical presentation and management of a young patient, with a rare subtype of Ehlers-Danlos syndrome, who presented with secondary IOL calcification 14 years after primary IOL insertion.

Observations: Floret-like lesions were observed on the IOL surface. Positive staining for calcification was observed with Alizarin red and von Kossa method on laboratory analysis.

Conclusions and importance: Patients with systemic connective tissue disease, such as a subtype of Ehlers-Danlos, may present with secondary IOL calcification many years after primary lens insertion. This poses an additional consideration when implanting IOLs in these patients.

Good visual acuity can be achieved with IOL exchange.

1. Introduction

Calcification of Intraocular Lenses (IOL) is a rare complication following cataract surgery[1–3] with numerous studies attempting to establish causality of calcification in such instances. Issues with IOL manufacturing have been cited as a potential cause where whole batches have been affected with a typical pattern of lens opacification.[4] Host factors or changes to the environment of the IOL have also been cited as other potentiators, such as uveitis, proliferative diabetic retinopathy,[5] intracameral injections of gas, air or tPA.[6,7] and vitreoretinal, glaucoma, corneal surgeries.[8–10] Most cases of opacification occur within the first two years after IOL implantation.[11]

The following case report describes the presentation, management and clinicopathological features of IOL calcification in a young patient with a systemic connective tissue disease fourteen years after primary IOL insertion.

2. Case presentation

An 18-year-old male was referred to the vitreoretinal clinic complaining of progressive, painless visual deterioration in his left eye during the preceding twelve months.

The patient had undergone bilateral implantation of single-piece hydrophilic-acrylic +27D IOLs (Bausch + Lomb Akreos Fit) fourteen years previously for congenital lamellar cataracts.

These procedures were undertaken, as separate procedures, without complication and with routine recovery. No further or additional ophthalmic procedures were performed until he was referred to the ophthalmic department 14 years later.

The patient had no other ophthalmic complaint and was otherwise fit and well. He was, however, under long term review by a tertiary neurology and rheumatology department for an undiagnosed connective tissue disorder thought to be a rare subtype of EDS. This manifested with joint hypermobility and laxity with abnormal bone epiphysis and mild lumbar scoliosis. He was not undergoing any active treatment and was not on any regular medications.

Recent blood tests had been unremarkable and did not demonstrate abnormal calcium levels.

Genetic testing for the major subtypes of EDS were also negative, namely: FKBP14, collagen1A1, collagen 5A1 & 5A2, collagen 1A2, collagen 3A1 corresponding to Kyphoscoliotic, Type 1, type 5 (both classical EDS), cardiac valvular EDS, and vascular EDS respectively.

* Corresponding author. Dept Academic Ophthalmology, St Thomas' Hospital, Westminster Bridge Road, London, SE1 7EH, UK.
E-mail address: Matthew.Maguire2@nhs.net (M.J. Maguire).

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Tests for collagen 9A1, 9A2, and 9A3 which are associated with multiple epiphyseal dysplasia were also negative.

The patient was initially referred to a general ophthalmology clinic after complaining of blurred vision in his left eye, where he was noted to have opaque 'floret-like' lesions on the surface of both IOLs. The cause of these opacities was unknown, and they were resistant to Neodymium: yttrium-aluminum-garnet (Nd:YAG) laser. He was subsequently referred to the vitreoretinal clinic for consideration of IOL exchange.

Visual acuity (VA) was recorded as 6/9 in the right eye and 6/18 in the left. Floret-like lesions across the surface of both IOLs were noted once again, although more numerous in the left eye and closer to the central axis. Throughout, the patient did not complain of visual symptoms in his right eye. A plan was made for left IOL exchange and post-explanted lens analysis.

The patient underwent uncomplicated left IOL exchange: the calcified IOL optic was cut in half and the 2 halves of the IOL were explanted through an enlarged corneal section. Sufficient capsular support remained for the implantation of a 3-piece hydrophobic sulcus IOL. Two weeks later his left VA was 6/10 with good post-operative recovery. There are no immediate to plans to operate on his asymptomatic fellow eye.

3. Histopathological analysis

Light microscopic images were captured at different light magnifications. The IOL was histologically stained to identify possible causes of opacification. Deposits of calcium on the surface of the IOL can be stained with alizarin red, deposits inside the IOL with the von Kossa method.[6,12]

4. Results of IOL analysis

Gross Light-microscopy showed a complete opacification of the IOL including the haptics (Fig. 1).

4.1. Histopathological staining

One half of the lens was stained using Alizarin red and demonstrated diffuse staining across the anterior and posterior lens surface and both haptics (Fig. 2).

The second lens specimen was stained with the von Kossa method and demonstrated calcium phosphate deposits beneath the whole IOL surface (Fig. 3).

5. Discussion

Intraocular lens calcification is rare complication of cataract surgery and can be classified according to their morphological features. 3 major groups have been identified: primary, secondary and false-positive (pseudo-calcification)[11,13]

Primary calcification demonstrates a pattern of calcification that is largely attributable to a manufacturing event such as improper polymer formation, forceps impressions, viscoelastic substances, and faulty packaging. In primary calcification, calcium typically permeates into the lens and there is no pre-existing or concurrent eye disease. Primary calcification, therefore, is due to an anomaly with the IOL itself.

Secondary calcification occurs due to host factors affecting the environment of the IOL, such as diseases or conditions causing dysfunction of the blood-aqueous-barrier, (BAB) or intraocular surgeries. The typical pattern of secondary IOL calcification is with lens surface calcium deposits. Pseudo-calcification is not calcification, but a misdiagnosis due to tissue artefacts or misuse of special stains.[11]

The calcification pattern seen in our patient was typical of secondary calcification, with crystalline deposits under the anterior and posterior optical lens surfaces which stained positive for Alizarin red and the von Kossa method; suggesting a high calcium content without penetrating deep into the lens matter itself, as is typical of primary calcification.

This report discusses a case of bilateral IOL calcification. Two independent and separate manufacturing issues affecting a single patient seems less likely as an explanation than an abnormality with the lens environment, such as an alteration of BAB.

Furthermore, the IOL-manufacturer reported that a thorough review

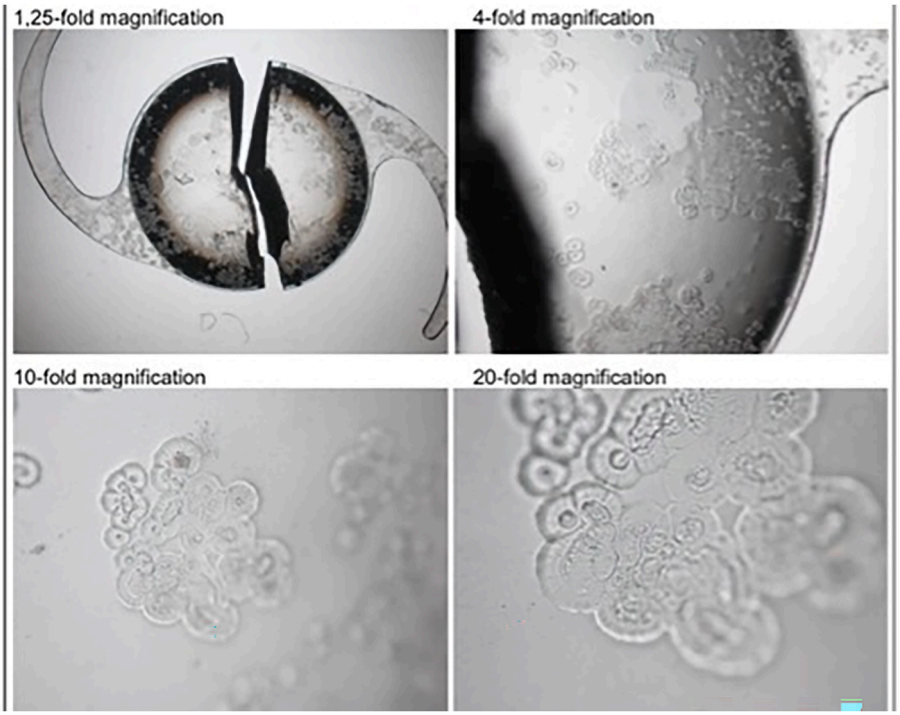

Fig. 1. Overview images of the opacified IOL and 'floret-like' lesions.

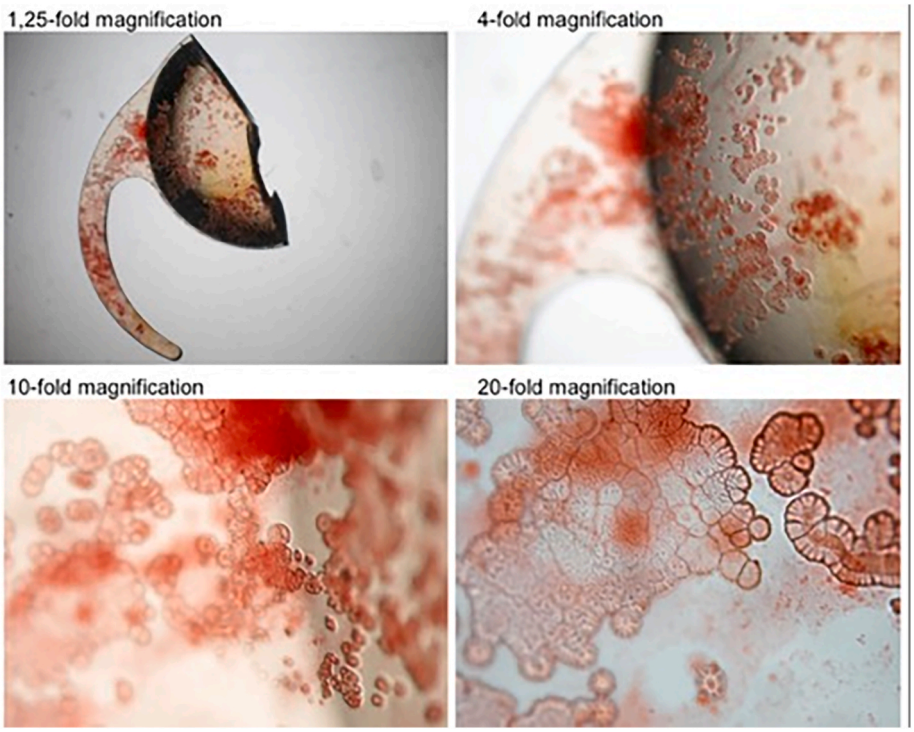

Fig. 2. Alizarin red staining of the explanted IOL at different magnifications. Diffuse staining, and therefore calcification, is visible across the anterior and posterior lens surface and both haptics. (For interpretation of the references to colour in this figure legend, the reader is referred to the Web version of this article.)

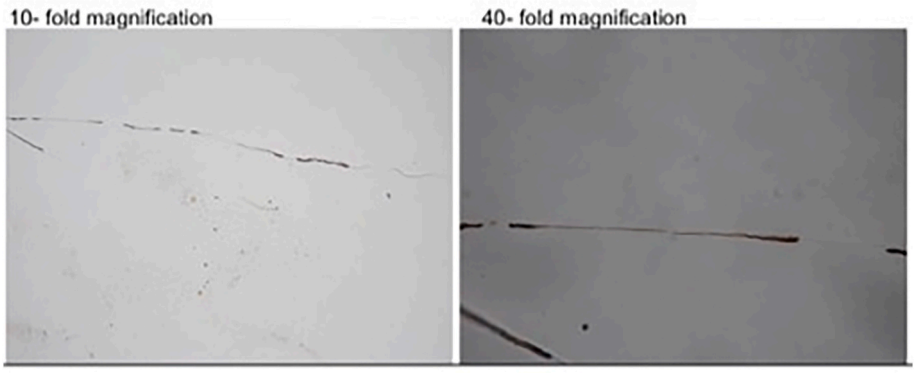

Fig. 3. Von Kossa staining method of the explanted IOL at different magnifications demonstrating calcium phosphate deposits beneath the lens surface.

of the manufacturing records did not reveal any issues or discrepancies, nor identify any failure to meet its manufacturing specifications. Production was reported to be within the ISO tolerances and the manufacturers claimed not to have received any report of adverse events associated with other lenses of the same model manufactured in that batch of production. (Bausch and Lomb, Global Device Complaint Management Department, Written Communication, January 22nd, 2019).

Cao et al. have reviewed the reported cases of Akreos Adapt IOL opacification, however all reports are in the context of recognised predisposing factors, namely: complex proliferative diabetic retinopathy; intracameral gas and air and vitreoretinal, corneal and glaucoma surgeries.[14] The patient presented in this case report was not exposed to any of these potentiators.

Ehlers-Danlos syndrome (EDS) constitutes a heterogenous group of inherited connective tissue diseases[15] of which 13 subtypes are recognised. The typical symptoms of joint hypermobility and laxity recognised in our patient are typically due to a genetic defect in the synthesis and structure of collagen and connective tissue. However, other typical symptoms include joint dislocations, skin fragility, easy bruising and vascular issues such as arterial rupture. Incidence is approximately 1:5000 and inheritance can be autosomal dominant, recessive, or X-linked recessive and there is no preponderance for gender or race.[16]

The typical ocular presentation of EDS is as brittle corneal syndrome where genetic defects cause thin corneas (<400 μm) which may or may not rupture. Patients often have keratoconus or keratoglobus with areas of thinned and blue looking sclera. Our patient did not present with any of these ocular symptoms.

EDS is known to affect the vasculature in certain subtypes and known to be heterogenous in its presentation.[16] This could feasibly have led to disturbance of the BAB in our patient which may have affected the metabolic environment of the anterior chamber permitting an influx of proteins and cell aggregates responsible for secondary calcification seen in both IOLs.

EDS is known to be associated with abnormal calcification, with, amongst others, reports of abnormal joint, breast, soft tissue and tooth

calcification[17,18,19]. It is possible, therefore, that within the scope of the EDS disease process the environment of the anterior chamber in our patient was altered such that made it conducive to lens calcification. The BAB is maintained by an epithelial barrier with tight junctions which helps maintain and regulate the intraocular fluids.[20] EDS is also known to affect the vasculature which may offer an explanation for an altered anterior chamber environment.

It is worth reinforcing the message that Nd:YAG laser in these patients should also be avoided as it will not resolve the patient's symptoms and may compromise or complicate future surgical management.

6. Conclusion

We present a single case report of secondary IOL calcification in a patient with a rare subtype of Ehlers-Danlos syndrome fourteen years after initial IOL insertion that has been successfully managed with surgical IOL exchange. The exact cause for the bilateral lens calcification in our patient remains unknown and perhaps is due to a combination of factors, but clinicians should be aware of IOL opacification as a potential complication. We demonstrated that a good visual outcome can be achieved in these patients, following explanation. This case contributes to the literature on IOL calcification and it highlights an additional consideration when implanting IOLs in patients with systemic connective tissue disease.

Patient consent

Written consent to publish personal information and case details has been obtained from the patient.

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All authors attest that they meet the current ICMJE criteria for Authorship.

CRediT authorship contribution statement

Matthew J. Maguire: Conceptualization, Investigation, Methodology, Project administration, Writing – original draft, Writing – review & editing. **Donald John Munro:** Investigation, Methodology, Writing – original draft, Writing – review & editing. **Patrick Merz:** Conceptualization, Formal analysis, Investigation, Methodology, Project administration, Writing – original draft, Writing – review & editing. **Alistair Laidlaw:** Conceptualization, Investigation, Methodology, Supervision, Writing – original draft, Writing – review & editing. **Gerd U. Auffarth:** Formal analysis, Methodology, Project administration, Supervision, Writing – original draft, Writing – review & editing, Conceptualization.

Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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