



## Successful repair of a spontaneous scleral rupture in a patient with type VI Ehlers-Danlos syndrome

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### ABSTRACT

**Purpose:** To describe ocular findings in a patient with Type VI Ehlers-Danlos syndrome (EDS) and make ophthalmologists aware of the potential ophthalmic complications of this particular type of EDS. To briefly report the surgical technique utilized for the repair of spontaneous scleral rupture that may be associated with Type VI Ehlers-Danlos syndrome.

**Observations:** A 36-year-old female visited the Emergency Room due to sudden vision loss, edema, and redness of the right eye consistent with spontaneous scleral rupture secondary to scleral thinning due to Type VI EDS. Repair with scleral patch graft resulted in improvement in visual acuity, a decrease in hyphema, and discomfort resolution.

**Conclusions and Importance:** Spontaneous scleral perforation may occur in patients with Type VI EDS. A scleral patch graft may serve as a viable surgical repair alternative for such patients.

### 1. Introduction

Ehlers Danlos syndrome (EDS) is a group of at least ten different inherited connective tissue disorders classified based upon clinical and genetic differences.<sup>1,2</sup> The EDS comprises a heterogeneous spectrum of monogenetic conditions with multisystemic and variable clinical manifestations affecting the skin; ligaments and joints, blood vessels; and internal organs.<sup>3,4</sup>

The main ocular features of generalized connective tissue disease syndromes include blue sclera and corneal thinning. However, other findings include: epicanthal folds, ectopia lentis; glaucoma; retinal detachment; and angioid streaks have also been reported in patients with the syndrome.<sup>2,4</sup>

Following the identification of mutations in the genes encoding collagen types I, III, V, and several collagen processing enzymes, the EDS classification was made into six distinct clinical syndromes.<sup>5</sup> EDS type VI, or kyphoscoliotic type of EDS, is characterized by blue sclera with ocular fragility, joint hypermobility, and skeletal abnormalities, with an autosomal recessive mode of inheritance.<sup>2</sup> It is caused by a

lysyl-hydroxylase gene defect, affecting collagen synthesis.<sup>5</sup>

EDS type VI diagnostic criteria are scleral fragility (major criteria) and microcornea (minor criteria).<sup>6</sup> Vascular rupture is the major life-threatening complication, although it occurs less frequently than in other EDS types.<sup>7</sup> We report on a patient with EDS type VI, who had a spontaneous scleral perforation with subconjunctival uveal exposure who underwent surgical repair.

#### 1.1. Case report

A 36-year-old Hispanic female visited the local emergency room with a 1-day history of a sudden loss of vision of the right eye, after bending over to take off her shoes. This event was associated with swelling and redness of the right eye. She denied eye trauma and pain, previous eye surgery, dizziness, or headache.

Upon a comprehensive ophthalmic examination, best-corrected visual acuity was 20/400 OD and 20/25 OS. Intraocular pressure was 10 OD, and 12 OS. Slit-lamp examination of the right eye showed subconjunctival hemorrhage from 12 o'clock to 10 o'clock, and nasally, a

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round-shaped area of subconjunctival uveal exposure measuring 3 mm in diameter (Fig. 1A and B). A slit-lamp examination of the left eye revealed a superotemporal area of scleral thinning with a seemingly blue appearance. Both corneas were clear, with the right cornea measuring 10mm horizontally and 9mm vertically, and the left measuring 11mm horizontally and 10mm vertically. The right anterior chamber contained an extensive hyphema, which spared the pupillary area. The left anterior chamber was deep and quiet. The right pupil was corectopic with no afferent pupillary defect. The left pupil was round and reactive to light with no afferent pupillary defect; both lenses were clear. The right fundus was poorly visualized, yet appeared to be grossly normal. B-scan ultrasonography of the right eye did not reveal retinal detachment, scleral abnormality, or vitreous opacity. The left fundus exam was unremarkable.

Her past medical history was significant for a spontaneous left popliteal artery rupture that had been surgically repaired. Additional pertinent physical examination findings included: increased skin elasticity, pectus excavatum, joints hyperextensibility (Fig. 2A and B). A chest X-Ray showed evidence of kyphoscoliosis orthopedic surgery (Fig. 2C and D). Based on history, ocular, and physical exam findings, the patient was diagnosed with Type VI Ehlers Danlos syndrome with a secondary spontaneous right scleral rupture.

The following day, the patient was taken to the operating room for surgical repair of the scleral defect (Fig. 1B). General endotracheal anesthesia was administered. The patient was placed in a supine position and was prepped and draped in the usual sterile fashion. An eyelid speculum was placed on the right eye. An anterior chamber paracentesis was performed at 10 and 2 o'clock, and acetylcholine chloride intraocular solution was instilled. A conjunctival peritomy from 12 to 6 o'clock was done, and a scleral defect measuring 3mm in diameter, with uveal prolapse was identified. A scleral patch measuring twice the diameter of the defect was sutured directly to the uninvolved sclera surrounding the defect, without any prior scleral dissection. Interrupted 9-0 nylon sutures were used for the bulbar sclera, and 10-0 nylon suture was used in the limbal area. The anterior chamber was reformed, and the water-tightness was verified. Conjunctiva was closed with interrupted 8-0 Vicryl sutures. Cefazolin and dexamethasone were injected at the nasal bulbar subconjunctival space. Tobramycin-dexamethasone ointment was applied, and the eye was patched overnight with a safety shield. No complications occurred during the surgery.

On the first postoperative day, the best-corrected visual acuity was 20/50 in the operated eye. The scleral patch was in place, and the resolution of the hyphema was observed (Fig. 1C). Prednisolone acetate 1% and ofloxacin 0.3% ophthalmic solution, four times daily, were prescribed, and the patient was discharged home. On the fourth postoperative day, the visual acuity was 20/60 (20/40 with pinhole) in the operated eye. The scleral patch remained in place, and there was no evidence of infection. On the twelfth postoperative day, the patient reported improvement in visual acuity and had no discomfort. Her visual acuity was 20/40 in the operated eye. The scleral patch remained in place (Fig. 1D). A corneal dellen was noted near the scleral patch, for which preservative-free lubricant at least four times a day was recommended. On a follow-up appointment two months after surgery, visual

acuity was 20/80 (20/40 with pinhole) in the operated eye. Loose sutures were removed, and the patient was instructed to continue her follow-up with an ophthalmologist near her hometown.

## 2. Discussion

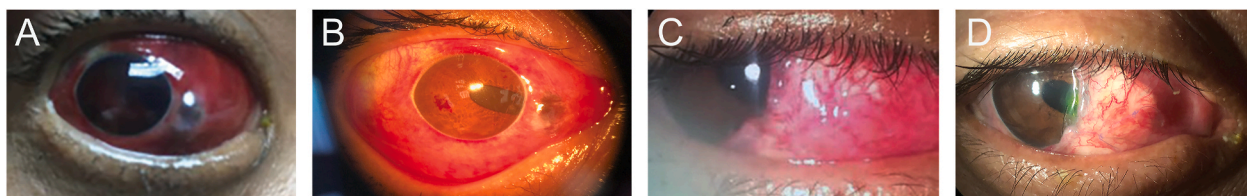
Patients with Type VI EDS tend to display muscular hypotonia at birth.<sup>7</sup> Additional findings include severe kyphoscoliosis, joint hypermobility, subluxation, skin hyperelasticity, and in some cases, arterial rupture.<sup>7</sup> Our patient had these clinical characteristics. Features that distinguish kyphoscoliotic EDS from other types of EDS are its ocular manifestations, particularly scleral fragility and ocular globe rupture, which our patient developed during her third decade.

Type VI EDS is due to deficiency of lysyl hydroxylase, an enzyme that plays a role in collagen cross-linking formation.<sup>7</sup> Collagen is a component of the sclera, and defects in its structure place patients at an increased risk for scleral rupture both spontaneously or after minimal trauma.<sup>2</sup>

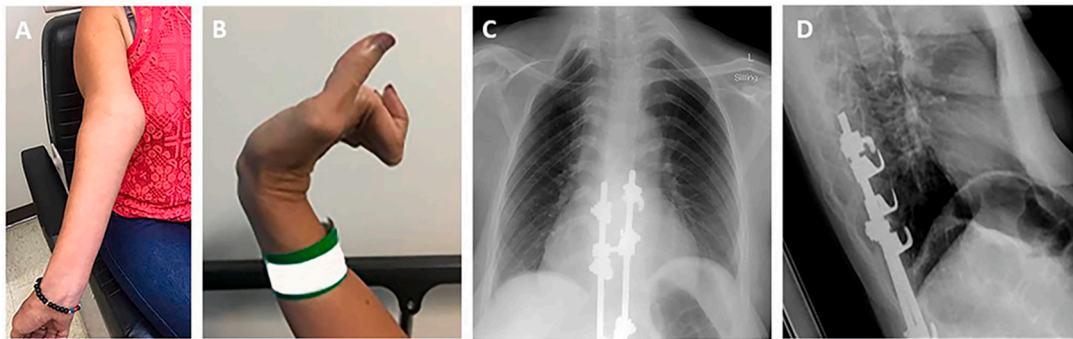
Thin or ruptured sclera must be repaired, as this can both prevent prolapse of ocular contents and infection.<sup>8</sup> Repair of scleral defects using scleral patch graft offers a series of advantages. Grafts are readily available, made of flexible tissue that possesses adequate tensile strength, can be preserved for long periods, and have favorable cosmetic results, as they tend to blend with the host sclera.<sup>8,9</sup> Since scleral tissue is avascular, there is little risk of host rejection.<sup>8</sup> A disadvantage of this same characteristic, however, is that scleral grafts may fail due to lack of vascularization leading to subsequent tissue necrosis.<sup>8</sup> Indications for surgical repair, with scleral patch graft, are scleral thinning with uveal exposure, impending globe perforation, and corneoscleral perforation.<sup>8,9</sup>

Patients who are candidates for scleral patch graft tend to present with redness, pain, soreness, and irritation.<sup>8,9</sup> A case series found a scleral patch graft to be effective for treating spontaneous and traumatic corneoscleral perforations, with nine out of fifteen patients achieving a stable ocular surface.<sup>9</sup> Only three patients faced complications, which included phthisis bulbi and evisceration in a patient who had late-onset endophthalmitis.<sup>9</sup> Another case series found adequate epithelialization and vascularization in ten out of thirteen patients who required a scleral patch graft for repair of scleral defects.<sup>8</sup> Visual acuity was stable in nine out of thirteen patients. Complications included endophthalmitis, graft necrosis, and graft dehiscence with uveal prolapse.

While the use of scleral patch graft for repair of globe perforation has been reported for a variety of conditions, there are few reported cases about its use in the repair of spontaneous scleral rupture in patients with Type VI EDS. A recent case report described the use of a 360-degree scleral patch graft in a patient with Type VI EDS who developed re-detachments and scleral rupture during vitrectomy for retinal detachment repairs.<sup>4</sup> In 1986, Nakazawa and colleagues reported the use of preserved scleral graft for the management of a post-traumatic staphyloma in a patient with Type VI EDS.<sup>10</sup> Trabeculectomy with a scleral patch graft has also been reported for the management of a patient with Type VI EDS and advanced glaucoma.<sup>11</sup> Our patient had extensive scleral thinning, and a scleral patch graft resulted in a viable option.



**Fig. 1.** External color photographs of the right eye. A. At presentation revealing hyphema, extensive subconjunctival hemorrhage, and a nasal area of scleral perforation with uveal exposure. B. Prior to surgery, revealing the extent of corectopia and residual hyphema. Postoperative days 1 and 12, C and D, respectively, showing resolution of the hyphema, as well as a well-positioned scleral patch that is well covered with the conjunctiva. On the later, a small corneal dellen is noted in association with the graft. (For interpretation of the references to color in this figure legend, the reader is referred to the Web version of this article.)



**Fig. 2.** Physical examination findings included hyperextensibility of the elbow and wrist joints, as depicted in A and B, respectively. Chest X-Ray posteroanterior and lateral, C and D, respectively, revealed evidence of prior scoliosis repair surgery.

Our patient had sudden onset loss of visual acuity, swelling, and redness of the right eye without pain or history of trauma. Upon examination, subconjunctival hemorrhage and a round-shaped, 3mm area of subconjunctival uveal exposure of the right eye were noted. Along with a history and physical exam findings significant for increased skin elasticity, pectus excavatum, hyperextensibility of joints, history of kyphoscoliosis, infantile hypotonia, and popliteal artery rupture, a clinical diagnosis of Type VI EDS was made. A scleral patch graft was chosen as the method of repair due to the advantages it offers availability, adequate cosmetic results, and minimal risk of host rejection. No intraoperative complications occurred. Postoperatively, the patient's visual acuity improved from 20/400 on initial preoperative evaluation to 20/80 on the most recent follow-up appointment two months after surgery. The patient denied pain or discomfort, and the scleral patch remained in place. The only postoperative complication noted was a corneal dellen on a follow-up appointment on post-op day 12, which was successfully treated with preservative-free lubricant.

Patients with a clinical Type VI EDS diagnosis and other connective tissue disorders should undergo an ophthalmologic assessment to detect ocular features early in their course and manage them appropriately.<sup>6</sup>

### 3. Conclusions

Although rare, patients with Type VI EDS may develop spontaneous scleral perforation as a result of scleral fragility from defects in collagen synthesis. Our case suggests that scleral patch graft may result in the improvement of visual acuity, hyphema, and pain in patients who present with similar symptoms. Scleral patch graft appears to be a successful technique to repair a spontaneous scleral rupture in patients with the syndrome.

Further research is warranted to establish long-term outcomes in patients with the type VI EDS who undergo spontaneous scleral rupture repair by scleral patch graft, as well as for co-management measures to prevent and cope with this ocular complication in patients with the syndrome.

#### Patient consent

Written consent to publish the case report was obtained from the patient. This report does not contain any personal information that could lead to the identification of the patient.

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#### Research ethics

We further confirm that any aspect of the work covered in this manuscript that has involved human patients has been conducted with the ethical approval of all relevant bodies and that such approvals are acknowledged within the manuscript.

#### Authorship

All listed authors meet the ICMJE criteria. We attest that all authors contributed significantly to the creation of this manuscript, each having fulfilled criteria as established by the ICMJE.

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#### References

- Pollack JS, Custer PL, Hart WM, Smith ME, Fitzpatrick MM. Ocular complications in Ehlers-Danlos syndrome type IV. *Arch Ophthalmol.* 1997;115(3):416–419. <https://doi.org/10.1001/archoph.1997.01100150418018>.
- Cameron JA. Corneal abnormalities in Ehlers-Danlos syndrome type VI. *Cornea.* 1993;12(1):54–59. <https://doi.org/10.1097/00003226-199301000-00009>.
- Giunta C, Baumann M, Fauth C, et al. A cohort of 17 patients with kyphoscoliotic Ehlers-Danlos syndrome caused by biallelic mutations in FKBP14: expansion of the clinical and mutational spectrum and description of the natural history. *Genet Med.* 2018;20(1):42–54. <https://doi.org/10.1038/gim.2017.70>.
- Whitlow S, Idrees Z. RD repair using 360-degree scleral graft for extensive scleral ectasia in a patient with Ehlers Danlos syndrome. *Am J Ophthalmol Case Reports.* 2020;17. <https://doi.org/10.1016/j.ajoc.2019.100554>.

5. Mao JR, Bristow J. The Ehlers-Danlos syndrome: on beyond collagens. *J Clin Invest*. 2001;107(9):1063–1069. <https://doi.org/10.1172/JCI12881>.
6. Gharbiya M, Moramarco A, Castori M, et al. Ocular features in joint hypermobility syndrome/Ehlers-Danlos syndrome hypermobility type: a clinical and in vivo confocal microscopy study. *Am J Ophthalmol*. 2012;154(3). <https://doi.org/10.1016/j.ajo.2012.03.023>.
7. Rohrbach M, Vandersteen A, Yi U, et al. Phenotypic variability of the kyphoscoliotic type of Ehlers-Danlos syndrome (EDS VIA): clinical, molecular and biochemical delineation. *Orphanet J Rare Dis*. 2011;6(1):1–9. <https://doi.org/10.1186/1750-1172-6-46>.
8. Sangwan VS, Jain V, Gupta P. Structural and functional outcome of scleral patch graft. *Eye*. 2007;21(7):930–935. <https://doi.org/10.1038/sj.eye.6702344>.
9. Article O, Sultan S, Siyal NA, Ashraf NN, Khokhar AR. Scleral patch graft in spontaneous and traumatic. *Corneoscleral Perforations*. 2018;34(3):184–189.
10. Nakazawa M, Tamai M, Kiyosawa M, Watanabe Y. Homograft of preserved sclera for post-traumatic scleral staphyloma in Ehlers-Danlos syndrome. *Graefes Arch Clin Exp Ophthalmol*. 1986;224(3):247–250. <https://doi.org/10.1007/BF02143064>.
11. Cheriya D, Bharathi S, Raman G. Trabeculectomy with scleral patch graft for advanced glaucoma in ehler-danlos syndrome. *Kerala J Ophthalmol*. 2016;28(2):142. [https://doi.org/10.4103/kjo.kjo\\_32\\_16](https://doi.org/10.4103/kjo.kjo_32_16).