management of retinal detachment in Osteogenesis Imperfecta

Osteogenesis imperfecta (OI) is an inherited disorder of connective tissue resulting from mutations in genes coding for type I collagen. The condition was first described in 1788 by O. J. Ekman in Sweden, and the term osteogenesis imperfecta was first used by Willem Vrolik in 1849. The disease is manifested in tissues in which the principal matrix protein is type I collagen: bone, ligaments, dentin, and sclera. Biochemical and molecular genetic studies have shown that most affected individuals have mutations in either the COL1A1 or COL1A2 genes that encode the chains of type I procollagen. Osteogenesis imperfecta is clinically characterized by increased bone fragility with a propensity to fracture, often resulting in skeletal deformity and variably associated with hearing loss, dental abnormalities, and blue sclerae.

The skeletal manifestations are usually the most prominent. There is a continuum of varying severity, ranging from asymptomatic forms with subtle osteopenia, to moderately severe forms with deformity and propensity to fracture, to a perinatal lethal form consisting of innumerable fractures in utero and at birth. For most patients, the presence of multiple fractures early in life, with or without blue sclerae, is usually sufficient to establish the diagnosis. Multiple fractures during childhood and adolescence often lead to short stature and spinal abnormalities. Thoracic scoliosis is the most common deformity, resulting from osteoporosis, compression fractures, and ligamentous laxity. Pectus planus is also a common feature.

Otologic manifestations of OI occur in approximately 50% of patients and include hearing loss, the most common problem, as well as tinnitus, vertigo, middle ear infections, and sinusitis. Dental involvement, termed dentinogenesis imperfecta, is present in 30% of patients and typically consists of soft, translucent brownish teeth. The enamel wears easily, and the teeth are carious, shortened, and susceptible to cracking. The skin is often thin, translucent, and easily distensible. Surgical scars may heal with widening and prominence. Cardiovascular involvement is less common but may include mitral valve prolapse and non-progressive aortic root dilatation. Intelligence is usually normal.

The ocular manifestations of OI are not usually sight threatening and typically consist of blue sclerae; however, the sclerae can vary in color from normal to a slightly bluish or slate color to a bright blue. The blue sclera result from thinning of the abnormal sclera, leading to the transmission of the uveal tissue to the observer. The treatment of retinal detachment in patients with OI is challenging owing to the abnormal morphologic characteristics of the sclera. In this study, we report the successful treatment of retinal detachment in 4 eyes of 3 patients with OI.

Report of Cases. Case 1. A 57-year-old man with a recent complaint of hazy vision and floaters in his left eye came to the Kresge Eye Institute (Detroit, Mich). The patient denied photopsia. His medical history was significant for OI, diagnosed when he suffered multiple bone fractures during childhood as a result of minor trauma. There was no known history of OI in the family. Best-corrected visual acuity was 20/25 OD and 20/30 OS with a –11.0-diopter correction in both eyes. Slitlamp examination was remarkable for bilateral blue sclerae. In the right eye, a posterior vitreous detachment was present with mild myopic fundus changes. In the left eye, there was a posterior vitreous detachment with vitreous hemorrhage. A funduscopy examination of the left eye showed a supertemporal retinal detachment secondary to a large retinal tear, with vitreous traction at the apex of the flap. The macula was spared. Because of the generalized thinning of the sclera, demarcation laser photoagulation was elected. Four hundred sixty-seven spots of argon green laser at 500 µm, 0.10 seconds, and 530 mW was applied.
Best-corrected visual acuity was 20/20 OD and counting fingers OS. Slitlamp examination was remarkable for mildly blue sclerae in both eyes. A fundusscopic examination of the right eye showed a break at the 7-o’clock position, with adjacent lattice degeneration and subretinal fluid. The fundusscopic examination of the left eye revealed a macula involving retinal detachment extending from the 2- to the 8-o’clock position, associated with tears at the 6- and 7-o’clock positions. The subclinical detachment in the right eye was treated with 3 rows of confluent laser photoagulation delivered at the slitlamp. Because of the extent of the detachment and inferrior location of the breaks in the left eye, surgical intervention was recommended. Intraoperatively, the breaks were treated with cryopexy. The equatorial sclera appeared to have a normal color, and scleral buckling surgery was attempted. Despite superficial placement of sutures, scleral perforation was encountered, and scleral buckling was abandoned for pars plana vitrectomy. A standard 3-port vitrectomy was performed, followed by the injection of perfluorocarbon liquid. During this procedure, the infusion bottle needed to be higher than usual, since the exchange of instruments through the sclerotomies resulted in collapse of the globe. The 3 retinal breaks were surrounded by confluent rows of endolaser photoagulation, and a fluid-air exchange was performed. The sclerotomies were closed at very high magnification, owing to the extreme thinness of the sclera. The vitreous cavity was filled with a mixture of 14% perfluoropropane gas, and the conjunctiva was closed. Two years after treatment, the retina remains attached and the visual acuity is 20/20 OD due to chronic cystoid macular edema.

Case 3. A 54-year-old man had a recent onset of blurry vision in the left eye. His medical history was significant for OI, diagnosed in childhood because of multiple fractures he had sustained. There was no known history of OI in the family. Best-corrected visual acuity is 20/200 OU. Refraction was −2.00+0.75/−5.25+1.00×110° OD and −5.25+1.00×029° OS. Slitlamp examination was remarkable for blue sclerae in both eyes and pseudophakia in the right eye. A fundusoscopic examination of the right eye revealed a retinal detachment from the 7- to the 9-o’clock position, associated with tears at the 7- and 9-o’clock positions. The detachment extended posteriorly to the temporal arcade, sparing the macula. There was also a supranasal retinal break at the 1-o’clock position, without subretinal fluid. Because of the location of the breaks, the extent of the detachment, and the generalized thinning of the sclera, pars plana vitrectomy was elected. A standard 3-port vitrectomy was performed, followed by the injection of perfluorocarbon liquid. During this procedure, the infusion bottle needed to be higher than usual, since the exchange of instruments through the sclerotomies resulted in collapse of the globe. The 3 retinal breaks were surrounded by confluent rows of endolaser photoagulation, and a fluid-air exchange was performed. The sclerotomies were closed at very high magnification, owing to the extreme thinness of the sclera. The vitreous cavity was filled with a mixture of 14% perfluoropropane gas, and the conjunctiva was closed. Two years after treatment, the retina remains attached and the visual acuity is 20/20 OD and 20/25 OS.

Comment. Osteogenesis imperfecta is a genetic disorder of connective tissue characterized by increased bone fragility and usually associated with hearing loss, abnormalities of dentition, and blue sclerae. This phenotypically and genotypically heterogeneous disorder involves tissues such as bone, ligaments, dentin, and sclera, in which the principal matrix protein is type I collagen. Clinically, OI is grouped with other heritable disorders of connective tissue, including Ehler-Danlos syndrome, Marfan syndrome, homocystinuria, Weill-Marchesani syndrome, cutis laxa, pseudoxanthoma elasticum, fibrodysplasia ossificans progressiva, and the chondrodysplasias.

The main ocular finding in OI is blue sclerae; however, similar to the other phenotypic features of the disease, the color of the sclera is extremely variable and ranges from normal to slightly bluish to bright blue. In a clinical study of 46 patients with OI, ocular rigidity was reduced in patients compared with controls. Furthermore, among patients with OI, the blueness of the sclera was inversely related to ocular rigidity (the association persisted after adjusting for refractive error and corneal thickness). In most patients, no other ocular abnormalities are noted, and vision is not affected. One report describes an ocular form of OI in a South African family of Indian ancestry consistent with autosomal recessive inheritance. The 6 affected family members had severe skeletal abnormalities and blindness due to corneal opacity, secondary glaucoma, and hyperplasia of the vitreous. The sclerae in these patients were white. In an additional report, retinal diastasis with retinal detachment was described in a 13-year-old girl with OI. The patient underwent external drainage of subretinal fluid, intravitreal gas injection, cryopexy, and barricade laser, with successful long-term anatomic and visual results. The authors proposed that patients with OI are more susceptible to retinal detachment because decreased scleral rigidity leads to increased tractional forces on the peripheral retina.

Autopsy studies were performed on eyes obtained from patients with OI congenita, a lethal form of OI. Light and electron microscopy indicated decreased collagen fiber diameter and cross striation periodicity within the cornea and sclera. The authors of these studies concluded that collagen fibrils have characteristics of immature collagen, which is more translucent than normal, so that the underlying...
ing uveal pigment and blood become clinically visible, resulting in the blue appearance of the sclera.

We report the treatment of rhegmatogenous retinal detachment in 4 eyes of 3 patients with OI. Scleral buckling surgery, pneumatic retinopexy, and primary vitrectomy are the standards for repair of uncomplicated rhegmatogenous retinal detachments. In patients with OI, however, the thin sclera provides an increased risk of scleral perforation during the buckling procedure. In our first patient, demarcation laser photoagulation was applied (5 years ago) and proved to be successful in preventing extension of the detachment. It has been reported that demarcation laser photoagulation may be an effective method to manage acute or chronic macula-sparing shallow retinal detachments without proliferative vitreoretinopathy. Laser photoagulation rapidly enhances retinal adhesion to 140% of normal in 24 hours and twice normal between 3 days and 4 weeks. For laser treatment to be effective, confluent laser photoagulation burns should surround the entire detachment.

In the left eye of our third patient, the presence of multiple inferior breaks and the extent of the detachment presented the options of scleral buckling or pars plana vitrectomy. Early in the procedure, it became evident that performing a scleral buckle was not possible. In our experience, the lack of blue discoloration of the sclera in the buckling area may be misleading when considering suture placement. In patients with OI, the sclera has an abnormal consistency, which may lead to inadvertent needle perforation, even with conservative suture depth. Pars plana vitrectomy in these patients may also be challenging. During vitrectomy, increased infusion pressure may be needed to prevent collapse of the globe during instrument exchange. This is secondary to the laxity of the sclera and its lack of rigidity. At the end of surgery, closure of the sclerotomy wounds with partial-thickness scleral sutures requires care to prevent perforation.

Based on a MEDLINE search, this is the first report of treating retinal detachment in patients with OI with demarcation laser photoagulation or pars plana vitrectomy. There are challenges facing the surgeon during vitrectomy surgery because of decreased scleral rigidity. The thin sclera in patients with OI makes the scleral buckling procedure a less desirable choice of treatment, even when the sclera appears white.

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Pseudotumor Cerebri Induced by All-trans Retinoic Acid Treatment of Acute Promyelocytic Leukemia

In acute promyelocytic leukaemia (APML), a chromosomal translocation (t(15;17)) gene rearrangement fuses the retinoic acid receptor (RAR) gene from chromosome 17 and the promyelocytic leukaemia (PML) gene from chromosome 15, forming the basis for production of a chimeric (fusion) protein that causes a block in cell differentiation. Molecular diagnosis and follow-up after treatment is now possible with detection of PML/RAR fusion messenger RNA.

Normally, the RAR gene encodes a member of the nuclear hormone receptor family of transcription factors. After binding retinoic acid, the retinoic acid receptor can promote expression of a variety of genes. However, in APML, the PML/RAR fusion protein tends to suppress gene transcription and blocks differentiation of the promyelocytes. Treatment with the RAR ligand, all-trans retinoic acid (ATRA), relieves the block and promotes differentiation and is associated with an 80% complete remission rate. This report describes the occurrence of pseudotumor cerebri induced by ATRA treatment of APML.

Report of a Case. A 30-year-old man with APML being treated with ATRA had had headaches and diplopia within 2 weeks of the initiation of ATRA treatment. Examination disclosed a visual acuity of 20/15 OU, a left abducens palsy, and a blood pressure of 120/92 mm Hg. The fundus picture is shown in the Figure. The right fundus was similar in appearance. Spontaneous venous pulsations were absent.