Terrien Marginal Degeneration: Clinical Characteristics and Outcomes

AARON T. CHAN, RANDALL ULATE, YAKOV GOLDICH, DAVID S. ROOTMAN, AND CLARA C. CHAN

• PURPOSE: To describe outcomes of patients with Terrien marginal degeneration.
• DESIGN: Retrospective case series.
• METHODS: Database review of 25 patients (43 eyes) seen over 10 years (2004–2013) at Toronto Western Hospital cornea clinic. Outcome measures included demographics, location of disease, topographic astigmatism, visual acuity, coexisting ocular disease, and surgical management.
• RESULTS: Mean age at presentation was 44 years (range, 20–82 years) and 54% were male. Eighteen patients (72%) had bilateral disease. Mean follow-up was 30.3 months. Mean topographic astigmatism was 4.02 diopters (D) at 5 degrees. Mean change in astigmatism 1 year from baseline was 0.75 D; at 2 years was 1.22 D; and at 3 years was 1.68 D. Mean best spectacle-corrected visual acuity (BSCVA) at presentation was 20/46 and 20/48 at last follow-up. Eyes requiring surgery (23.3%) had mean BSCVA of 20/81 at presentation and 20/106 after surgery. Five eyes perforated: 4 spontaneously, and 1 from trauma. Three eyes (6.9%) presented with pseudopterygium. Two eyes (4.7%) had intracorneal cysts. Fourteen patients (56%) presented with ocular surface inflammation.
• CONCLUSIONS: Terrien marginal degeneration is a slow-progressing, bilateral but asymmetric degeneration of the peripheral cornea. Men over 40 are more commonly affected. Stromal thinning, vascularization, lipid deposition, and against-the-rule astigmatism are classic signs. Though typically noninflammatory, a variant form characterized by prominent inflammation exists. Surgery (lamellar graft) can preserve corneal integrity and is indicated when conventional options fail to maintain vision or if perforation is imminent. Perforations are rare but can result in significant vision loss. (Am J Ophthalmol 2015;160(5):867–872. © 2015 by Elsevier Inc. All rights reserved.)

TERRIEN MARGINAL DEGENERATION WAS FIRST described by Terrien in 1990 as a bilateral, marginal ectasia of the cornea.[1,2] This not-uncommon condition is now characterized as a slow-progressing, noninflammatory degeneration, initially presenting in the superonasal cornea.[1–7] Though any age can be affected, literature suggests it appears primarily above the age of 40 and more commonly in men.[3,5] Disease progression is classically slow, taking several years to develop. Patients are usually asymptomatic until continued thinning results in increased astigmatism and subsequent diminution of visual acuity.[6] Perforations, either spontaneous or with minor trauma, are a serious consequence, but they are rare, with only a handful of reported cases.[2,5,6]

Clinical hallmarks of Terrien marginal degeneration include ectasia and furrowing of the peripheral cornea with associated lipid deposition, as well as vascularization. Initial findings present as fine, white-yellow, punctate, stromal opacifications that appear similar to arcus senilis.[4,7] Subsequent stromal thinning is heralded by the formation of a circumferential, gutter-like cavitation parallel to the limbus.[7] In later stages, lipid deposition, visible as a solid white line, develops along the anterior edge (Figure 1). This leading edge is steeply sloped, in contrast to the gradual slope of the posterior lip.[4] Vascularization stems radially from the limbus and is located within the anterior stroma.[4] An area of clear cornea can often be visualized between the leading edge of the gutter and the limbus.[4–7] Pseudopterygia, at positions other than 3 o'clock and 9 o'clock, grow obliquely onto the cornea in approximately 20% of Terrien cases[8] (Figure 2). These pseudopterygia are thought to be characteristic of this condition and may occur in the earlier stages of disease, before marked thinning.[8] Terrien degeneration typically presents bilaterally but can be very asymmetric between the 2 eyes. The superior cornea is primarily affected, but as the disease progresses, inferior cornea can also be involved.[7]

The majority of patients with Terrien marginal degeneration lack signs and symptoms of inflammation. However, a variant form of the disease with prominent inflammatory findings has been identified by a number of investigators.[7,9,10] Histopathologic examinations reveal an intact epithelium throughout the course of the disease, despite degeneration of the basal epithelial cells, and an abnormal appearance to the basement membrane.[11] The Bowman layer and anterior stromal lamella are lost and replaced by vascularized connective tissue. Histiocytes that line the blood vessels have evidence of increased lysosomal activity and collagen deposition, consistent with a degenerative etiology.[11] The Descemet membrane and endothelium are typically intact, though a number of

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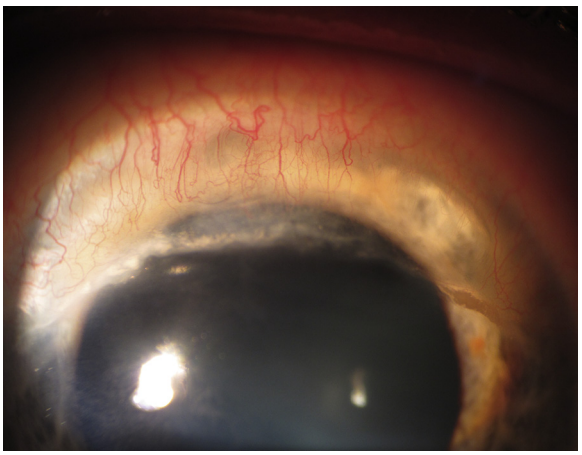

FIGURE 1. Clinical features of Terrien marginal degeneration. Classic findings including peripheral thinning, superficial vascularization, and a leading edge of lipid deposition.

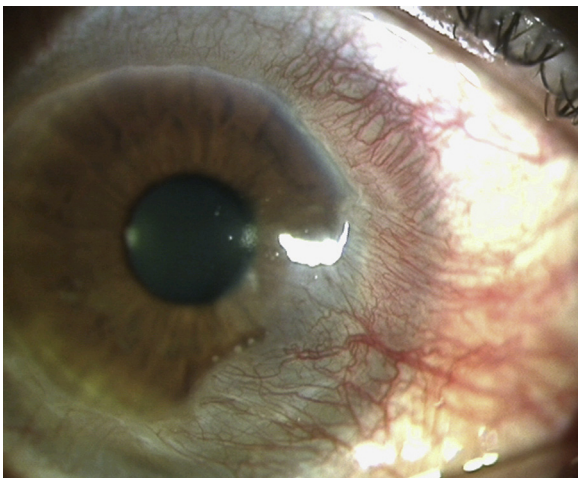

FIGURE 2. Pseudopterygium in case of Terrien marginal degeneration with ocular surface inflammation. Note the conjunctival injection in the area of the pseudopterygium.

reports have observed spontaneous ruptures in these layers, resulting in intralamellar dissection and intracorneal cysts[12,13] (Figure 3).

Although the clinical and histopathologic manifestations of Terrien degeneration are well documented, the literature on this condition is relatively sparse, and the exact etiology of the condition remains obscure. Herein we present a larger, retrospective study describing the clinical characteristics and outcomes of patients diagnosed with the condition in a tertiary corneal clinic at the Toronto Western Hospital from 2004 to 2013. The purpose of the study is, in part, to confirm reported findings with a larger, more robust population, and to draw on any new conclusions that may help the practicing ophthalmologist understand this disease better.

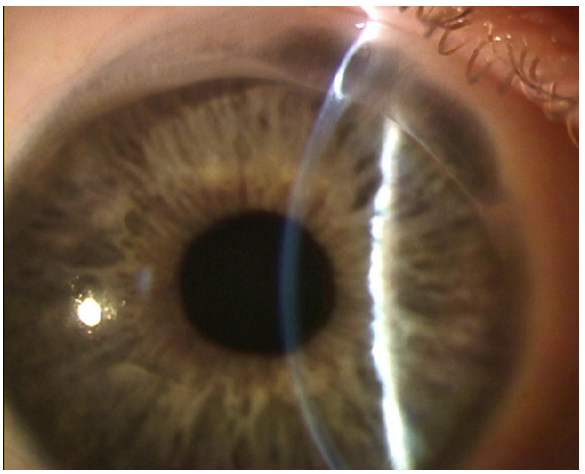

FIGURE 3. Intracorneal cyst in Terrien marginal degeneration, as a result of a break in the Descemet membrane.

METHODS

THIS RETROSPECTIVE OBSERVATIONAL CASE SERIES WAS approved by the Research Ethics Board of the University Health Network (Approval #14-7486-C). This study was conducted in compliance with the tenets of the Declaration of Helsinki. A database search of patients seen over a 10-year period (2004–2013) with a diagnosis of Terrien marginal degeneration was conducted at a specialty cornea clinic at the Toronto Western Hospital, Toronto, Ontario, Canada. The charts of 43 eyes of 25 patients were reviewed retrospectively. Patients were excluded if they did not fit the diagnostic criteria of Terrien marginal degeneration, defined primarily by evidence of peripheral corneal thinning, superficial vascularization, and lipid deposition (Figure 1). Patient demographics and clinical characteristics including location and laterality, visual acuity, topographic astigmatism, coexisting ocular disease, and need for surgical treatment were analyzed.

RESULTS

THE AVERAGE AGE AT DIAGNOSIS IN THIS COHORT OF PAtients was 44 years (standard deviation [SD], 18 years; range, 20–82 years). Men were slightly more affected than women (54%, 14/25). Eighteen patients (72%) presented with bilateral involvement. Mean follow-up was 30.3 months (SD, 35.3 months; range, 0–114 months).

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TABLE. Clinical Characteristics of Patients With Terrien Marginal Degeneration Requiring Surgical Treatment

Case	Patient	Sex	Age	Eye	Ocular Comorbidities	Symptoms		Topographic Astigmatism		BSCVA	BSCVA	Other Findings	Perforation	Surgical Treatments
						Decreased Vision	Redness/ Soreness	Cyl (D)	Axis	Pre-op	Post-op			
1	1	M	34	OD	Cataract	+		6.67	175	20/100	20/70	Ghost vessels		LK, P&IOL
2	2	M	50	OD	Blepharitis, cataract		+	2.57	41	20/25	20/25	Pseudopterygium		SK, AMG
3	2	M	50	OS	Blepharitis, cataract		+	10.82	32	20/25	20/200	Pseudopterygium	+	LK, P&IOL, AMG
4	3	M	58	OD	Blepharitis, cataract	+	+	5.59	6	20/40	20/200	Rosacea	+	Rupture repair, aphakia + IOL, iridoplasty
5	3	M	58	OS	Blepharitis, cataract	+	+	8.59	148	20/50	20/70	Rosacea		LK
6	4	M	47	OD	Glaucoma	+		N/A	N/A	20/400	20/400		+	PKP, AMG
7	5	F	67	OD	Scleral thinning	+		13.4	8	20/400	20/80			LK
8	6	F	45	OD	Blepharitis	+	+	20.68	93	20/400	20/80			LK, P&IOL
9	7	F	20	OS	Blepharitis	+		8.47	139	20/50	20/200	Intracorneal cyst	+	LK
10	8	M	20	OS				1.67	59	20/25	20/70		+	LK

AMG = amniotic membrane graft; BSCVA = best spectacle-corrected visual acuity; Cyl = cylinder; D = diopters; IOL = intraocular lens; LK = lamellar keratoplasty; N/A = not available; P&IOL = phacoemulsification and intraocular lens; PKP = penetrating keratoplasty; Post-op = postoperative; Pre-op = preoperative; SK = superficial keratectomy.

Twenty-eight eyes (65%) had either a superior or superior-nasal pattern of disease on initial presentation. The other 15 eyes (35%) presented initially with 360 degrees or >180 degrees of involvement. Topographic analysis was available in 29 eyes of 16 patients. Mean astigmatism at presentation was 4.02 diopters (D) at 5 degrees (SD, 3.49 D; range, 0.22–20.68 D). Data on change in topographic astigmatism were available in 1-year, 2-year, and 3-year intervals for 11 eyes, 7 eyes, and 6 eyes, respectively. In our cohort, astigmatic power increased by a mean of 0.75 D (SD, 1.09; range, −0.04 to 2.98 D) at 1 year, 1.22 D (SD, 3.02; range, −0.78 to 6.86 D) at 2 years from baseline, and 1.68 D (SD, 3.16; range, −0.64 to 7.64 D) by the third year of follow-up.

Surgery was required in 10 of 43 eyes (23.3%), and a corneal lamellar graft was performed in 7 of these cases. Corneal perforation occurred in 5 eyes (11.6%, 5/43), 4 of which perforated spontaneously, and 1 owing to trauma. Individual and ocular details for patients requiring surgery are shown in the Table.

Eighteen patients (72%, 18/25) presented with vision loss at initial consultation with decreased best spectacle-corrected visual acuity (BSCVA) to a mean of 20/46 (0.36 logMAR). BSCVA on last recorded follow-up was mean 20/48 (0.38 logMAR). Eyes requiring surgical intervention were worse off, presenting with mean BSCVA 20/81 (0.61 logMAR) at initial visit and 20/106 (0.73 logMAR) at last follow-up. Five eyes that did not perforate but that required surgery saw an improvement in BSCVA from mean 20/115 (0.76 logMAR) to 20/60 (0.48 logMAR). Perforated corneas had a BSCVA decrease from an average of 20/57 (0.46 logMAR) to 20/187 (0.97 logMAR), despite surgical treatment.

Three eyes (6.9%, 3/43) presented with pseudopterygia at oblique angles. Two eyes (4.7%) had intracorneal cysts. Fourteen patients (56%, 14/25) showed signs of ocular inflammation, which included signs of conjunctival injection, edema, and stromal infiltration. Meibomian gland dysfunction was the most common comorbidity, present in 10 patients (40%). Systemic and/or ocular rosacea was observed in 5 patients (20%).

DISCUSSION

CONSISTENT WITH PRIOR LITERATURE,[1–7] OUR STUDY confirms that Terrien marginal degeneration emerges at any age (range, 9–82 years), but on average manifests after the age of 40 (mean, 44 years) and affects men more than women (54%). Terrien[1] himself described the condition as being bilateral, and Suveges and associates[11] describe it as being one that may progress asymmetrically between the eyes. Eighteen of the 25 patients (72%) in our study presented bilaterally, which is comparable to prior reports. The 7 patients with unilateral presentation

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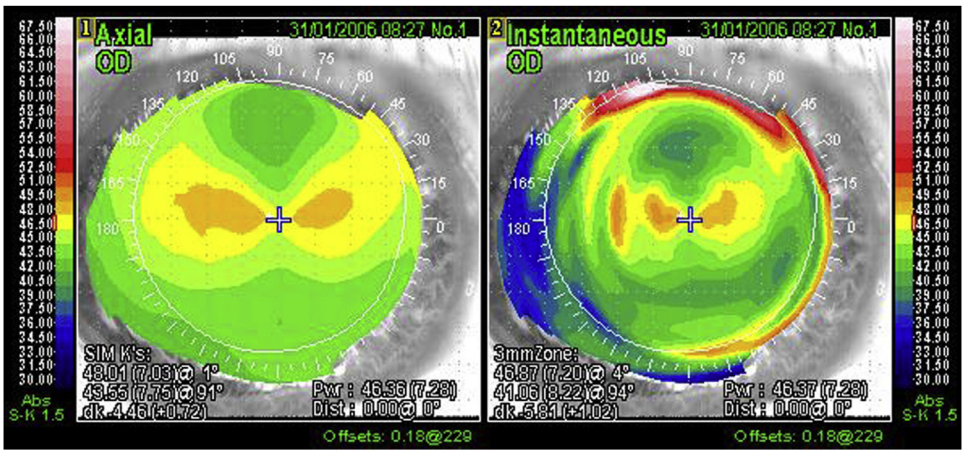

FIGURE 4. Topographic map showing against-the-rule astigmatism in a patient with Terrien marginal degeneration.

had a mean age of 30 years (SD, 11 years; range, 20–47 years), below the expected age for Terrien degeneration, suggesting that perhaps the bilateral nature of the disease had not yet manifested itself clinically.

Corneal topographic alterations account for the majority of the symptoms in Terrien marginal degeneration. The peripheral furrowing, which typically begins superiorly, leads to flattening of the vertical meridian and the characteristic "against-the-rule" astigmatism, described by Wilson and associates.[14] This is confirmed in our study, as 65% of our patients presented initially with a superior or superior-nasal distribution and those with decreased vision had an average against-the-rule astigmatism of 4.02 diopters at 5 degrees. Figure 4 is an example of a typical topographic map of a patient with Terrien marginal degeneration. Classically, the condition is slow-progressing and asymptomatic, often taking 30 years to unfold.[2] In contrast, we found that 18 of our patients (72%) were symptomatic, with vision loss on initial presentation to our clinic. We also found a relatively rapid progression in topographic astigmatism from year to year, with a mean progression of 1.68 D in astigmatic power for patients with 3 years of follow-up. These observations may be due to a selection bias, as there is a propensity for our specialty cornea clinic to receive more advanced cases, suggesting that milder and asymptomatic cases of Terrien disease are excluded from this study, as they may not necessitate referral.

In this study, 10 of 43 eyes (23.3%) received surgical treatment, verifying that for the most part, Terrien degeneration is slow and can be managed conservatively. A corneal lamellar keratoplasty was the predominant treatment choice, representing 7 of 10 surgical cases. The technique for lamellar keratoplasty is described as follows. Conjunctival peritomy is performed in the area of thinned cornea. The epithelium over the host area to be patched is gently debrided. A cadaver corneoscleral rim is prepared with the central 6–7 mm of central or eccentric cornea removed by trephination such that approximately 3 mm of cornea and 3 mm of sclera is available for patching. The graft endothelium and epithelium is removed with a 64 beaver blade (Becton Dickinson, Franklin Lakes, New Jersey, USA). The lateral and posterior borders of the lamellar corneoscleral graft are cut freehand to match the number of clock hours of host tissue requiring patching and the posterior stroma thinned using vannas scissors. Then, 10-0 nylon interrupted sutures are used to secure the lamellar corneal graft into place, and 8-0 vicryl sutures are used to close the conjunctiva. Other options for Terrien disease include full-thickness crescenteric keratoplasty and, rarely, full-thickness penetrating keratoplasty. One patient in the present study required such an intervention and underwent a limbus-to-limbus penetrating keratoplasty with a large-diameter 13 mm graft sewn into the sclera. The patient had approximately 3 clock hours of intact peripheral cornea and such a significant level of astigmatism that topography was not measurable.

Surgery is indicated when conservative alternatives, such as glasses and contact lenses, inadequately manage the increasing astigmatism, or if the risk of perforation is imminent. Five eyes received surgery for these reasons, and BSCVA improved on average by 3.5 lines, from 20/115 to 20/60. This improvement, however, may be confounded by the vision-improving effects of cataract surgery, which was performed in combination with the lamellar keratoplasty on a number of occasions. A total of 5 eyes perforated (11.6%, 5/43), 4 spontaneously and 1 owingto mild trauma. This is comparable to Austin and Brown,[9] who report corneal perforation rates at approximately 15%. Perforated corneas had worse visual outcomes in our cohort, with an average decrease in BSCVA from 20/58 to 20/187 before and after perforation, regardless of surgical intervention. It is thus crucial for ophthalmologists to recognize and offer surgical intervention *before* the patient perforates. Careful counseling and education on protective

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measures are warranted for Terrien patients who have severe thinning or participate in activities that have a tendency toward trauma (certain sports, etc).

In this study, 14 patients (56%) with Terrien marginal degeneration presented with signs of ocular inflammation. This brings up an interesting trend in the literature that is worth exploring. The argument for an inflammatory type of Terrien marginal degeneration has been previously made and is strongly supported by Iwamoto and associates,[10] who distinguish 2 forms of the condition based on histopathology: quiescent and inflammatory; and by Austin and Brown,[9] who describe recurrent bouts of episcleritis, scleritis, and ocular inflammation with clinical alterations consistent with Terrien degeneration in 6 patients. In addition to obvious and signs of ocular surface inflammation, subclinical manifestations have also been observed and may play an important role in understanding this disease. Pouliquen and associates[2] and Ceresara and associates,[4] respectively, observed inflammatory cell infiltration and activated keratocytes in the stroma via confocal and electron microscopy. Some authors hypothesize that inflammatory changes contribute to the pathologic process of Terrien marginal degeneration, and cases of systemic inflammation can further accelerate the process.[13] Indeed, Terrien has been associated with a number of systemic inflammatory diseases such as rheumatoid arthritis,[15] juvenile idiopathic arthritis,[13] and erythema elevatum diutinum[16] in isolated cases.

In our study, the most common comorbidity was meibomian gland dysfunction, present in 10 of 25 patients (40%). Meibomian gland dysfunction is a known sequela of rosacea (present in 20% of our patients) and can lead to severe ocular surface damage and chronic inflammation of the lids if not treated appropriately. To our knowledge, this is the first study associating meibomian gland dysfunction to inflammatory Terrien marginal degeneration, as hypersensitivity reactions have been postulated in the pathogenesis of both conditions.[10] Further research is needed to discern whether severe lid disease and chronic ocular surface inflammation from meibomian gland dysfunction can precipitate Terrien marginal degeneration, or whether these findings are merely incidental.

Weaknesses of this study include its retrospective nature, and thus its inability to control for variables such as the concomitant cataract surgery mentioned before. Also, selection bias likely accounts for the higher incidences of severe and symptomatic versions of Terrien marginal degeneration in this series. This conceivably explains the high proportion of the inflammatory variant as seen in this study, and may not truly reflect its prevalence in the general population. Nevertheless, general ophthalmologists should be aware of this subtype and of how to distinguish it from inflammatory peripheral ulcerative keratitis cases related to autoimmune conditions.

This study is the largest series reported in the literature of Terrien marginal degeneration and, to our knowledge, is the first reporting on changes in topographic astigmatism. We were able to verify many of the findings presented in published reports from multiple past decades. The practicing ophthalmologist should note that Terrien marginal degeneration is generally slow-progressing, is bilateral but asymmetric, and may present with or without ocular inflammation. In cases with ocular inflammation, it is important to distinguish from autoimmune- or infectious-related cases of peripheral ulcerative keratitis. For advanced cases with prominent thinning, we advocate earlier surgery to be important for preserving visual function and corneal integrity. Perforation, though rare, remains a serious complication that results in significant vision loss. It is advisable to discuss with all Terrien patients the risks of spontaneous and trauma-related perforation, and to educate on the need for protective eyewear.

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Biosketch

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