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Management of corneal melting in a patient with long-standing rheumatoid arthritis – case report

Postępowanie w przypadku rozmiękania rogówki u chorego na długo trwające reumatoidalne zapalenie stawów – opis przypadku

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Summary:

Corneal melting is a rare ocular complication of rheumatoid arthritis, associated with poor prognosis. Rapid course of the disease and unpredicted treatment response, which depends on a patient general state and disease severity, make every case a challenge and requires a cooperation between ophthalmologists and rheumatologists. We present a case of a 58-year-old woman with corneal melting, who was successfully treated with systemic corticosteroids and methotrexate, along with ocular surgery.

Key words:

rheumatoid arthritis, corneal melting, corneal perforation, keratoplasty.

Streszczenie:

Rozmiękanie rogówki jest rzadkim powikłaniem reumatoidalnego zapalenia stawów, szczególnie źle rokującym. Szybki postęp choroby i nieprzewidywalna odpowiedź na zastosowane leczenie, które jest uzależnione od stanu ogólnego pacjenta i nasilenia choroby podstawowej, czynią każdy przypadek wyzwaniem dla lekarzy i wymagają współpracy okulistów i reumatologów. Prezentujemy przypadek rozmiękania rogówki u 58-letniej pacjentki z wieloletnią historią reumatoidalnego zapalenia stawów leczonej z sukcesem metodami farmakologicznymi – korykosteroidami i metotreksatem, oraz za pomocą chirurgicznej interwencji okulistycznej.

Słowa kluczowe:

reumatoidalne zapalenie stawów, rozmiękanie rogówki, perforacja rogówki, przeszczep rogówki.

Introduction

Rheumatoid arthritis (RA) is a chronic, systemic, idiopathic autoimmune condition. It mainly affects synovial joints, but may also present as extra-articular manifestations. Ocular involvement is seen in even 39% of patients with RA in the various forms, including keratoconjunctivitis sicca, keratitis, episcleritis, scleritis, uveitis and retinal vasculitis (1). Corneal melting is one of the most serious, yet, rare consequences of long-lasting eye involvement secondary to RA. This term describes a severe corneal lesion caused by collagen degradation, during prolonged exposure to inflammatory infiltration. Patients with Sjögren's syndrome secondary to RA are particularly susceptible, but corneal melting can also develop in other rheumatoid conditions, such as primary Sjögren's syndrome, enteropathic arthritis, systemic lupus erythematosus and granulomatosis with polyangiitis. Rarity of this disease and its rapid progression make every case a therapeutic challenge for both the ophthalmologist and rheumatologist. We present a case of corneal melting in a pa-

tient with long-standing RA, successfully treated with corneal scleral patch graft and penetrating keratoplasty.

Case report

Our patient was a 58-year-old woman with 16-year-old record of well-controlled, seropositive (RF and anti-CCP) rheumatoid arthritis and a secondary Sjögren's syndrome. She was severely obese (BMI – 37.5), suffered from hypertension, peptic ulcer disease, osteoporosis, spinal osteoarthritis, glucocorticoid-induced glaucoma and cataract, underwent knee arthroplasty and was treated for numerous episodes of keratitis. She complained of pain in almost all the peripheral joints and oedema affecting all joints of the right arm and the right ankle. From the onset of the RA, the patient was treated at the Department of Rheumatology, mostly as an outpatient but including four inpatient stays. Her laboratory tests results throughout the disease duration were as follows: rheumatoid factor (RF) from 55.5 to 76.2 IU/ml (NV 0-14 IU/ml), anti-cyclic citrullinated peptide

antibodies (anti-CCP) – always > 200.0 U/ml, C-reactive protein (CRP) concentration between 2.05 and 18.27 mg/l, presence of anti-nuclear antibodies (ANA) – 1: 320 and anti-PM-Scl antibodies. No anti-Ro/SS-A and anti-La/SS-B antibodies were found. Our patient has been treated with oral methotrexate, prednisone and sarilumab – with dosage modification if needed. The diagnosis of the Sjögren's syndrome was confirmed by the biopsy of the labial gland. The histopathological examination of the sample revealed Focus Score (FS) > 1. She was first admitted to the Department of Ophthalmology 1.5 years ago, due to blurred vision, photophobia and dry eye symptoms in her left eye that persisted for 5 days. Upon assessment, the visual acuity in the left eye was significantly reduced to counting fingers at 1 meter, while the visual acuity in the right eye was 20/20. The slit lamp examination revealed a massive peripheral corneal perforation at the 3 o'clock position, with an iris plugging in the left eye caused by a process known as a corneal melting. No fundus abnormalities were found in both eyes. DAS28 score was 3.5, indicating low activity of RA. An allogenic scleral patch graft was used to facilitate ulceration healing. Postoperatively, dexamethasone, tobramycin and levofloxacin were administered topically. After 10 days, penetrating keratoplasty was performed due to graft leakage and iris prolapse. Corneal graft dimensions were 7.75/8.25 mm – adequate to cover the temporal perforation located 3.0 mm from the corneal limbus. Because of location of the perforation, the graft was decentered. The full-thickness corneal transplant was secured in place using nineteen 10–0 nylon sutures. During post-operative period, no signs of transplant rejection or ocular inflammation were observed; the anterior chamber remained deep and quiet, transplant was clear and ocular pressure was 18 mmHg. No fundus abnormality was found, either. The visual acuity in the left eye markedly improved and the patient, in good general condition, was discharged from the hospital. Directly after the surgery, patient started her treatment with tobramycin, dexamethasone, levofloxacin and tropicamide used topically as well as methotrexate 25.0 mg per week, methylprednisolone 8.0 mg/d and sarilumab 200.0 mg every 14 days s.c for systemic immunosuppression. After 9 uneventful months, she was admitted to the Department of Ophthalmology for the second time, because of persistent, severe pain and decreased visual acuity in her left eye. Ocular exam revealed further visual acuity reduction to seeing hand movements with uncertain light perception in the left eye and full visual acuity in the right eye. The slit lamp exam showed a leakage along graft margin at the 6 o'clock position, caused by transplant maceration. Seven additional sutures were used to re-seal the transplant. Dosage of the systemic immunosuppressive medications was increased. The patient's condition improved within a few days after the reoperation (Fig. 1.). Half year ago, she underwent phacoemulsification of cataract in her left eye caused by the long-term use of corticosteroids. For the time being, the left eye remains stable, without any signs of disease progression while the right eye presents with mild opacity in the peripheral cornea consistent with the features of dry eye disease. The best corrected visual acuity in the right eye is 20/25.

The patient is still treated at our Ophthalmology Clinic with tear substitutes to relieve dry eye symptoms and preser-

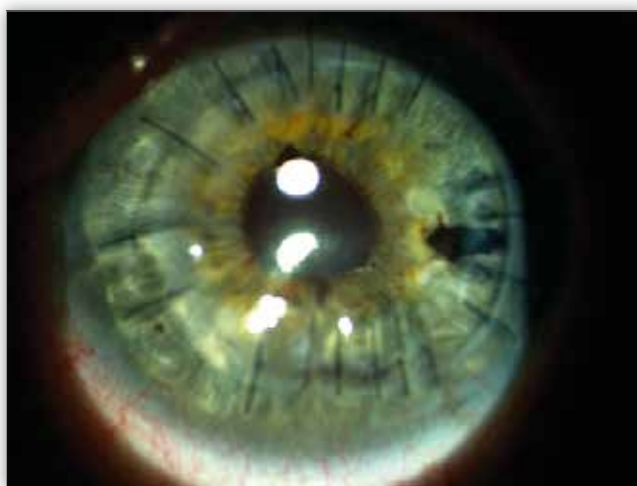


Fig. 4. The patient's cornea 12 months after keratoplasty.

Ryc. 4. Stan rogówki pacjentki po 12 miesiącach od keratoplastyki.

vative-free dexamethasone eye drops, twice a day, to lower the risk of transplant rejection.

Discussion

Rheumatoid arthritis is a chronic, autoinflammatory disease affecting 0.5% to 1% of population in developed countries worldwide, with annual incidence of 5–50 per 100.000 adults. There is an apparent female preponderance, women suffer from RA 3 times more often than men (2). It mainly affects synovial joints, but may also have extra-articular manifestations. The ocular involvement affects 39% of patients with RA, and its most severe complications are corneal melting and necrotizing scleritis. Corneal melting is usually associated with the presence of the RA-related dry eye disease (RA-DED), which affects almost 90% of patients, and secondary Sjögren's syndrome, but may also occur without these underlying conditions. Additionally, patients with both secondary Sjögren's syndrome (that is, 11% to 31% of RA patients) and RA-DED may experience more severe DED symptoms and accelerated progression of corneal ulcerations (3). There is visible correlation between duration of the disease and presence of the DED, but none between the severity of the DED and the activity of RA. The exact pathogenesis of corneal ulceration secondary to rheumatoid diseases has not been completely understood yet. Various factors which may simultaneously affect the cornea predisposing to ulceration have been described. Corneal melting is thought to be an effect of a massive inflammatory corneal infiltration. This concept is supported by a fact that ulcerative keratitis tends to develop more frequently within the peripheral cornea due to its denser vasculature which facilitates the infiltration of the inflammatory cells, as compared to the central avascular cornea. Upregulation of proinflammatory cytokines (TNF- α , IL-6) was found in keratocytes of RA patients with corneal ulceration, which according to Prada et al. may alter the production of metalloproteinases and result in keratocyte collagen damage (4). According to many authors investigating this medical condition, the effect of the shift in metalloproteinases (MMP) and its inhibitor (TIMP) equilibrium is one of possible causes of corneal ulceration (4, 5). Smith et al. suggested that overproduction of MMP-2 in the corneal stroma and MMP-9 in lacrimal glands

may cause keratocyte collagen degradation (5). Additional factor which may predispose to corneal ulceration is corneal thickness reduction. In a recent publication from 2015, Gunes et al. examined 58 patients with RA to assess the impact of the disease on corneal parameters and dry eye syndrome. This study revealed that the central corneal thickness (CCT) and peripheral corneal thickness (PCT) were decreased in RA patients as compared to the control group, but it did not correlate significantly with RA activity. According to Gunes et al., changes in corneal parameters may be especially important in RA patients whose eligibility to ocular surgery is assessed (6). This study confirmed previous reports of decreased corneal thickness in patients with rheumatoid arthritis. Limited number of reports on RA-related corneal melting makes it extremely difficult for the physician to choose the optimum treatment. A review paper published in 2012 discussing peripheral ulcerative keratitis stated that aggressive treatment of underlying, systemic disease using disease-modifying anti-rheumatic drugs (DMARDs) is crucial for effective treatment of corneal melting (7). Based on own experience, Knox Cartwright et al. developed a simple therapeutic scheme for patients with RA-related corneal ulceration. They recommend systemic corticosteroids for acute control of the disease. In patients treated with methotrexate, its dose should be maximized. If the response is inadequate and patient articular manifestations remain inactive, mycophenolate mofetil should be added. If active inflammation still persists, biological treatment with antitumor necrosis factor agent should be considered (8). Treatment with infliximab (antibody anti TNF- α) proved to be beneficial in patients described by Silva et al. (9). As for the topical treatment, cyclosporin was reported to contribute to favorable outcomes in patients with clinically silent rheumatoid disease and corneal ulcers (10). Furthermore, the non-preserved artificial tear substitutes can provide temporary relief and should be used by patients with symptoms of dry eye syndrome. Surgical intervention, along with proper medical treatment are often needed in patients with non-infectious corneal perforation. The review of corneal perforation management strategies suggest 3 appropriate surgical approaches: corneal gluing, amniotic membrane transplantation and its variants, and corneal transplantation, from which the first two are used as a temporary solution (10). Additionally, amniotic membrane, because of its natural anti-inflammatory properties, could be used as a patch or graft to promote ulcer healing (7).

Summary

Corneal melting is an uncommon, dangerous complication secondary to rheumatoid arthritis. As it is exceptionally rare,

the treatment becomes a challenging task for the physicians, who need to rely on case reports or studies conducted in small patient samples. Multicenter, collaborative research in a large group of patients is much needed to develop a standard treatment algorithm. Also, improvements in RA pharmacotherapy, especially further development in the field of disease-modifying anti-rheumatoid drugs, are likely to reduce future incidence of corneal melting.

At present, cooperation between rheumatologist and ophthalmologist is crucial, because aggressive medical treatment along with proper surgical intervention are the best management options in RA-related corneal melting.

References:

1. Vignesh AP, Srinivasan R: *Ocular manifestations of rheumatoid arthritis and their correlation with anti-cyclic citrullinated peptide antibodies*. Clin Ophthalmol. 2015; 9: 393–397.
2. Scott DL, Wolfe F, Huizinga TW: *Rheumatoid arthritis*. Lancet. 2010; 376(9746): 1094–1108.
3. Fox RI, Stern M, Michelson P: *Update in Sjögren syndrome*. Curr Opin Rheumatol. 2000; 12(5): 391–398.
4. Prada J, Noelle B, Baatz H, Hartmann C, Pleyer U: *Tumour necrosis factor alpha and interleukin 6 gene expression in keratocytes from patients with rheumatoid corneal ulcerations*. Br J Ophthalmol. 2003; 87(5): 548–550.
5. Smith VA, Hoh HB, Easty DL: *Role of ocular matrix metalloproteinases in peripheral ulcerative keratitis*. Br J Ophthalmol. 1999; 83: 1376–1383.
6. Gunes A, Inal EE, Tok L, Tok O: *Evaluation of central and peripheral corneal thicknesses in patients with rheumatoid arthritis*. Arq Bras Oftalmol. 2015; 78(4): 236–240.
7. Yagci A: *Update on peripheral ulcerative keratitis*. Clin Ophthalmol. 2012; 6: 747–754.
8. Knox Cartwright NE, Tole DM, Georgoudis P, Cook SD: *Peripheral ulcerative keratitis and corneal melt: a 10-year single center review with historical comparison*. Cornea. 2014; 33(1): 27–31.
9. Silva BL, Cardozo JB, Marback P, Machado FC, Galvão V, Santiago MB: *Peripheral ulcerative keratitis: a serious complication of rheumatoid arthritis*. Rheumatol Int. 2010; 30(9): 1267–1268.
10. Jhanji V, Young AL, Mehta JS, Sharma N, Agarwal T, Vajpayee RB: *Management of corneal perforation*. Surv Ophthalmol. 2011; 56(6): 522–538.

The paper was originally received 16.03.2016 (KO-00062-2016)/
Praca wpłynęła do Redakcji 16.03.2016 r. (KO-00062-2016)
Accepted for publication 06.08.2016/
Zakwalifikowano do druku 06.08.2016 r.

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