A case of severe dry eye disease with corneal melting as presenting complaint of acute myeloid leukaemia

Dmitri Pchejetski1,2, Heba Alshaker2, Radomir Babovic1 and Kyaw Maw1

Abstract
Dry eye syndrome is a common multifactorial disorder of the tear film and ocular surface. In rare cases, it may be caused by systemic diseases. Corneal melting is a complication of dry eye syndrome and is a potentially blinding condition. Here we report a case of a 67-year-old patient who attended her general practitioner for a year complaining of persistent dry eyes. Ophthalmological assessment showed severe dry eye syndrome with cornea melting in left eye. Blood test revealed anaemia and thrombocytopenia with circulating blasts. Bone marrow biopsy showed 15% myeloblasts with monosomy 7, compatible with acute myeloid leukaemia. Patient was started on intensive chemotherapy regime and was a candidate for allogenic bone marrow transplant. To our knowledge, this is the first case report demonstrating dry eye syndrome with sterile corneal melting as the possible presenting complaints of acute myeloid leukaemia. This case will serve as a useful reminder to general practitioners and accident and emergency doctors about the current guidelines regarding referral of persistently symptomatic patients with dry eye syndrome for further investigation in secondary care.

Keywords
dry eye syndrome, corneal melting, sicca syndrome, acute myeloid leukaemia, autoimmune complications

Date received 24 June 2020; accepted: 21 January 2021

Introduction
Dry eye or dry eye syndrome (DES) (also known as keratoconjunctivitis sicca, or more recently dysfunctional tear syndrome) is a multifactorial disorder of the tear film and ocular surface which is associated with symptoms of ocular discomfort. DES occurs due to dysfunction of the lacrimal functional unit that consists of lacrimal glands, ocular surface, including cornea, conjunctiva, eyelids, meibomian glands, ocular nerves and goblet cells. DES is accompanied by increased osmolarity of the tear film and inflammation of the ocular surface. Symptoms usually affect both eyes and often include dryness, grittiness or soreness progressively worsening throughout the day, conjunctival erythema and sticky eyelids.

The prevalence of DES may range between 8% and 34% depending on the criteria used. It is more common with increasing age with around one-third of people over 65 years affected. Treatment usually consists of lubricating eye drops and anti-inflammatory medication. The two main complications associated with DES are conjunctivitis and keratitis. Common causes of DES include being out in hot or windy weather; wearing contact lenses; blepharitis; side effect of antihistamines, antidepressants, beta-blockers and diuretics; and hormonal changes in women. In rare cases, DES may be caused by autoimmune diseases such as rheumatoid arthritis or vasculitides. Corneal melting is a potentially blinding condition and it has been reported that severe DES can lead to sterile corneal melt and perforation. Corneal melting is especially associated with DES caused by systemic diseases.

Acute myeloid leukaemia (AML) is a cancer of the myeloid lineage of blood cells. It is characterized by the rapid growth of immature white blood cells that build up in the bone marrow and interfere with the production of normal blood cells. AML is the most common acute leukaemia
affecting adults, and its incidence increases with age. AML can present with many different symptoms including weight loss, fatigue, fever, night sweats, recurrent infections and bleeding. Autoimmune complications of AML are very rare, but cases of autoimmune haemolytic anaemia have been reported. There is no literature to date describing DES as the presenting manifestation of AML. This case report highlights two key aspects of DES management – identifying a potential cause of a refractory DES and referring to secondary care for management of potential DES complications such as corneal melting.

**Case**

**General practice**

A 67-year-old woman attended her general practitioner (GP) for a year complaining of persistent gritty eye pain, intermittent redness and mild decrease in visual acuity.

She had a background history of hypertension, type II diabetes mellitus, previous traumatic ankle injury with limitation of mobility and recurrent mouth ulcers. Her medications included prednisolone mouthwash, tramadol, spironolactone, furosemide and metformin.

A diagnosis of DES was made and she was treated with artificial tears. Her symptoms, however, did not resolve. Her GP ordered investigations, which included serum urea and electrolytes (U&E), liver function tests (LFTs), eye swab for bacterial culture, cholesterol and Haemoglobin A1c (Table 1) and were all normal and showed good diabetes control. Of note, full blood count was not ordered. In a view of unresolved symptoms, she was referred to the ophthalmology department.

**Ophthalmology**

Ophthalmology assessment showed DES with reduced tear break-up time (TBUT) was 0, and in the right eye was 1s. Eye pressure in both eyes was 20mmHg. On the conjunctival swab, HSV1, HSV2, varicella zoster and adenovirus were not detected. Patient was started on lubricating eye treatment, steroid drops and prophylactic antibiotic drops. To investigate potential causes, the ophthalmologist ordered blood tests, including complete blood count (Table 2), which revealed anaemia and thrombocytopenia with 2% circulating blasts and significant basophilia. The patient was referred to haematology.

**Haematology**

On further questioning the patient denied any significant constitutional symptoms, bone pain weight loss, recurrent infections or bleeding history, although she reported easy ecchymosis. She had no significant family history of malignancy or haematological problems.

On examination, her Eastern Cooperative Oncology Group (ECOG) performance status was 1; she showed mild pallor, but no jaundice. There was no palpable lymphadenopathy. On abdominal examination, the liver was not palpable, but a fullness over left hypochondrial area was present. Ultrasound scan confirmed splenomegaly with no focal lesions.

Bone marrow aspirate and trephine biopsy showed 15% blasts with monocytoid features. BCR ABL test was negative. Trephine was hypocellular with myeloid prominent features, CD117 positive and CD34 staining 10%–20% increased. Cytogenetic analysis showed myeloblasts with monosomy 7. These results could not differentiate de novo AML from progression from myelodysplastic syndrome; however, patient’s full blood count test 2 years before presentation was normal, which indicates no evidence of myelodysplastic syndrome at that time. Patient was started on intensive chemotherapy regime and is a candidate for allogenic bone marrow transplant. Patient’s dry eye symptoms have improved after leukemia treatment; however, scarring is common after corneal melting. No systemic rheumatological condition was detected.

**Discussion**

This is the first case of DES and associated corneal melting as the potential initial presentation of AML. There is limited literature on ocular manifestations of AML and other leukemias. It was proposed that in some cases eye symptoms may be the initial mode of presentation of the systemic illness, or the first manifestation of relapse after remission-inducing chemotherapy. A prospective study carried out in a tertiary centre has shown that 8 of 96 (8.3%) patients with leukemia (all types) had direct leukemic infiltration. Secondary or indirect involvement due to anaemia, thrombocytopenia, hyperviscosity, total body irradiation and immunosuppression was seen in 42 (43.8%) subjects. Ocular changes were present in 37/79 (46.8%) adults and 5/17 (29.4%) children. The ocular manifestations were significantly more frequent.
in myeloid leukaemias, 32/61 (52.9%), than lymphoid leu-
kaemias, 10/35 (28.6%).

Leukaemia has many different potential ophthalmic
manifestations, where keratitis, DES and cornea melting
are main findings related to cornea. Ocular involvements
are also well-known complications of graft-versus-host
disease. One case report describes unilateral eyelid swell-
ing, proptosis and diplopia as initial manifestation of AML
in a 17-year-old man. There are two described cases of
Sjogren’s syndrome associated with AML and one case of

| Test                                      | Result       | Normal range |
|-------------------------------------------|--------------|--------------|
| White cell count                          | $6.3 \times 10^9/L$ | 4–10         |
| Haemoglobin                               | 105.0 g/L    | 120–150      |
| Platelet count                            | $57 \times 10^9/L$ | 150–410      |
| Haematocrit                               | 0.304        | 0.36–0.46    |
| Mean cell volume                          | 95.6 fL      | 83–101       |
| Red cell count                            | $3.18 \times 10^9/L$ | 3.8–4.8     |
| Mean cell haemoglobin                     | 33.0 pg      | 27–32        |
| Mean cell haemoglobin conc.               | 345.0 g/L    | 316–349      |
| Red cell distribution width               | $\leq 12.2\%$ | 9.9–15.5     |
| Mean platelet volume                      | $\leq 12.8\%$ |              |
| Platelet crit                             | $\leq 0.070$ |              |
| Platelet distribution width               | $\leq 12.3\%$ |              |
| Manual neutrophil count                   | $1.70 \times 10^9/L$ | 2.0–7.0   |
| Manual lymphocyte count                   | $2.14 \times 10^9/L$ | 1.0–3.0   |
| Automated monocyte count                  | $\leq 1.24 \times 10^9/L$ | 0.2–1.0   |
| Automated monocyte count                  | $\leq 1.24 \times 10^9/L$ | 0.2–1.0   |
| Manual monocyte count                     | $0.25 \times 10^9/L$ | 0.2–1.0   |
| Automated eosinophil count                | $\leq 0.43 \times 10^9/L$ | 0.02–0.5  |
| Manual eosinophil count                   | $0.13 \times 10^9/L$ | 0.02–0.5  |
| Automated basophil count                  | $\leq 0.32 \times 10^9/L$ | 0.0–0.1   |
| Manual basophil count                     | $1.95 \times 10^9/L$ | 0.0–0.1   |
| Metamyelocytes                            | $0.00 \times 10^9/L$ | 0.00–0.00 |
| Myelocytes                                | $0.00 \times 10^9/L$ | 0.00–0.00 |
| Promyelocytes                             | $0.00 \times 10^9/L$ | 0.00–0.00 |
| Blasts                                    | $0.13 \times 10^9/L$ | 0.00–0.00 |
| Erythrocyte sediment rate                 | 62 mm/h      | 0–20         |
| Cornea scrapings routine culture          |              |              |
| Bacteria                                  | Coag. neg. staphylococci | NOT isolated |
| Yeasts and fungi                          |              |              |
| BLOOD EBV antibodies EB virus serology    |              |              |
| EBV VCA IgG antibodies                    | DETECTED     |              |
| EBV EBNA IgG antibodies                   | DETECTED     |              |
| EBV VCA IgM antibodies                    | Not detected |              |
| BLOOD CMV serology                        |              |              |
| CMV IgG antibodies                        | DETECTED     |              |
| Swab Herpes simplex virus type 1          | DNA NOT detected |              |
| Swab Herpes simplex virus type 2          | DNA NOT detected |              |
| Swab varicella zoster                     | DNA NOT detected |              |
| Adenovirus                                | DNA NOT detected |              |
| Hepatitis B core total antibody           | Not detected |              |
| Hepatitis B surface antigen               | Not detected |              |
| Hepatitis C antibodies                    | Not detected |              |
| HIV 1 and 2 antigen/antibody              | NOT detected |              |
| Antinuclear antibody (ANA) ELISA screen including dsDNA, RNP, Ro, La, centromere, Scl-70, Sm, Jo-1, fibrillarin, RNA Pol III, Rib-P, PM-Scl, PCNA, Mi-2 proteins | 0.1 | 0.0–1.0 |
| ANCA set PR3 ELISA                        | 0.10 iu/mL | 0.00–3.00     |
| ANCA set MP0 ELISA                        | <0.10 iu/mL | 0.00–5.00     |
| Rheumatoid factor                         | <20 iu/mL | <30           |
uveitis and keratoconjunctivitis sicca associated with human T-cell lymphotropic virus type 1 (HTLV-1) T-cell leukaemia/lymphoma.  

The main take-home message of this case is that non-resolving DES may be a manifestation of more serious conditions and should be investigated in case of persistent symptoms. Importantly DES can have significant side effects such as corneal melting and perforation which is a potentially blinding condition. This is particularly relevant in case of DES associated with systemic diseases. National Institute for Health and Care Excellence (NICE) recommends that after the initial treatment, doctors may attempt to ‘identify underlying medical or surgical conditions associated with DES’. Quite often these are benign conditions such as allergic conjunctivitis or blepharitis. However, rheumatological disorders and vasculitides are known to cause DES and these should be investigated. All severe cases are usually managed in the secondary care.

The referral criteria for patients with DES are as follows:

- Moderate to severe eye pain or photophobia, marked redness in one eye, or reduced visual acuity – same day referral;
- Uncontrolled symptoms despite appropriate treatment for about 4 weeks;
- Deterioration of visual acuity;
- Suspected corneal damage or ulcers;
- Diagnosis that requires specialist assessment;
- Presence of an underlying disease that requires specialist management, for example, Sjögren’s syndrome, eyelid deformities.

In conclusion, this is the first case report demonstrating DES and corneal melting as the possible sole manifestation of AML and underlying the necessity to refer persistently symptomatic patients with DES for further investigation in secondary care.

Author Contributions
D.P. managed the patient, reported the case, collected background information, wrote the manuscript. R.B. and K.M. managed the patient, reported the case, edited the manuscript. H.A. collected background information, wrote the manuscript.

Declaration of conflicting interests
The author(s) declared no potential conflicts of interest with respect to the research, authorship and/or publication of this article.

Ethical approval
Our institution does not require ethical approval for reporting individual cases or case series.

Funding
The author(s) received no financial support for the research, authorship and/or publication of this article.

Informed consent
Written informed consent was obtained from the patient for publication of this case report and any accompanying images. A copy of the written consent is available for review by the Editor-in-Chief of this journal.

ORCID iD
Dmitri Pchejetski https://orcid.org/0000-0003-1074-9261

References
1. Research in dry eye: report of the research subcommittee of the international dry eye workshop (2007). Ocul Surf 2007; 5(2): 179–193.
2. Phadatare PMM, Nighojkar P, Askarkar S, et al. A comprehensive review on dry eye disease: diagnosis, medical management, recent developments, and future challenges. Adv Pharmaceut 2015; 2015: 704946.
3. Harada K, Mohamed YH, Uematsu M, et al. Three cases of acute sterile corneal melt after cataract surgery. Am J Ophthalmol Case Rep 2019; 13: 62–65.
4. Mimier M, Janczak D, Hill-Bator A, et al. Management of corneal melting in a patient with long-standing rheumatoid arthritis – case report. Klin Oczna 2016; 118(3): 235–237.
5. Tamura H, Ogata K, Yokose N, et al. Autoimmune hemolytic anemia in patients with de novo acute myelocytic leukemia. Ann Hematol 1996; 72(1): 45–47.
6. Hossain P. The corneal melting point. Eye 2012; 26(8): 1029–1030.
7. Gordon KB, Rugo HS, Duncan JL, et al. Ocular manifestations of leukemia: leukemic infiltration versus infectious process. Ophthalmology 2001; 108(12): 2293–2300.
8. Kincaid MC and Green WR. Ocular and orbital involvement in leukemia. Surv Ophthalmal 1983; 27(4): 211–232.
9. Sharma T, Grewal J, Gupta S, et al. Ophthalmic manifestations of acute leukemia: the ophthalmologist’s role. Eye 2004; 18(7): 663–672.
10. Koch KR, Joussen MA and Huber KK. Ocular involvement in chronic graft-versus-host disease: therapeutic approaches to complicated courses. Cornea 2011; 30(1): 107–113.
11. Chaudhry IA, Alaraj AM and Alkatan HM. Unilateral eyelid swelling, proptosis and diplopia as initial manifestation of acute myeloid leukemia. Saudi J Ophthalmol 2012; 26(2): 241–244.
12. Brault C, Gourguechon C, Chehimi M, et al. Unusual association of two cases of acute myeloblastic leukemia and possible Sjögren’s syndrome and review of literature. Hematol Leukemia 2017; 5(1): 2.
13. Liu MM, Furusato E, Cao X, et al. Ocular manifestations and pathology of adult T-cell leukemia/lymphoma associated with human T-lymphotropic virus type 1. Rare Tumors 2010; 2(4): e63.
14. Drug Therapeutics Bulletin. The management of dry eye. BMJ 2015; 353: i2333.
15. Malik MU and Sim F. Management of dry eye syndrome. GPonline, 2011, https://www.gponline.com/management-dry-eye-syndrome/ophthalmology/ophthalmology/article/1050178