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

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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

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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.[1] 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.[2] 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.[2] 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.[3] Corneal melting is especially associated with DES caused by systemic diseases.[4]

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

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Table 1. Blood analyses ordered by the general practice.

Test	Result	Normal range
Na^+	138 mmol/L	134–145
K^+	Sample haemolysed	
Urea	3.6 mmol/L	1.7–7.1
Creatinine	50 umol/L	45–84
eGFR	>90 mL/min/1.73m^2	
Total bilirubin	9 umol/L	0–22
Albumin	39 g/L	35–50
Alkaline phosphatases	45 U/L	38–126
Alanine transferases	10 U/L	0–50
Cholesterol	1.9 mmol/L	3.6–5.0
Haemoglobin A1c	33 mmol/mol	
Eye swab routine culture	No significant growth	

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.[5] 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 HbA1c (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 break-up time test in both eyes, the involvement was asymmetric with a more marked involvement of the left eye where a corneal melting syndrome was present. In the left eye, the tear break-up time (TBUT) was 0, and in the right eye was 1 s. Eye pressure in both eyes was 20 mm Hg. 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 leukaemia treatment; however, scarring is common after corneal melting.[6] 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 leukaemias. It was proposed that in some cases eye symptoms may be the initial mode of presentation of the systemic illness,[7] or the first manifestation of relapse after remission-inducing chemotherapy.[8] A prospective study carried out in a tertiary centre has shown that 8 of 96 (8.3%) patients with leukaemia (all types) had direct leukaemic 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

Table 2. Blood analyses ordered by ophthalmology.

Test	Result	Normal range
White cell count	6.3 × 10*9/L	4–10
Haemoglobin	105.0 g/L	120–150
Platelet count	57 × 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 × 10*12/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	^16.2%	9.9–15.5
Mean platelet volume	^12 fL	
Platelet crit	^0.070	
Platelet distribution width	^12.3%	
Manual neutrophil count	1.70 × 10*9/L	2.0–7.0
Manual lymphocyte count	2.14 × 10*9/L	1.0–3.0
Automated monocyte count	^1.24 × 10*9/L	0.2–1.0
Automated monocyte count	^1.24 × 10*9/L	0.2–1.0
Manual monocyte count	0.25 × 10*9/L	0.2–1.0
Automated eosinophil count	^0.43 × 10*9/L	0.02–0.5
Manual eosinophil count	0.13 × 10*9/L	0.02–0.5
Automated basophil count	^0.32 × 10*9/L	0.0–0.1
Manual basophil count	1.95 × 10*9/L	0.0–0.1
Metamyelocytes	0.00 × 10*9/L	0.00–0.00
Myelocytes	0.00 × 10*9/L	0.00–0.00
Promyelocytes	0.00 × 10*9/L	0.00–0.00
Blasts	0.13 × 10*9/L	0.00–0.00
Erythrocyte sed'n rate	62 mm/h	0–20
Cornea scrapings routine culture		
Bacteria	Coag. neg. staphylococci	
Yeasts and fungi	NOT isolated	
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

in myeloid leukaemias, 32/61 (52.9%), than lymphoid leukaemias, 10/35 (28.6%).

Leukaemia has many different potential ophthalmic manifestations,[9] where keratitis, DES and cornea melting are main findings related to cornea. Ocular involvements are also well-known complications of graft-versus-host disease.[10] One case report describes unilateral eyelid swelling, proptosis and diplopia as initial manifestation of AML in a 17-year-old man.[11] There are two described cases of Sjogren's syndrome associated with AML[12] and one case of

uveitis and keratoconjunctivitis sicca associated with human T-cell lymphotropic virus type 1 (HTLV-1) T-cell leukaemia/lymphoma.[13]

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.[3] This is particularly relevant in case of DES associated with systemic diseases.[4] 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'.[14] 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.[15]

The *referral criteria for patients with DES* are as follows:[14]

- 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.

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Ethical approval

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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.

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