CASE REPORT

Myeloid sarcoma presenting as an unusual limbal mass

Rachna Meel,¹ Arjun Desai,² Nripen Gaur,² Sameer Bakhshi³

¹Department Of Oculoplastics and Ocular Oncology, Dr Rajendra Prasad Centre for Ophthalmic Sciences, All India Institute of Medical Sciences, New Delhi, India

²Ophthalmology, Dr Rajendra Prasad Centre for Ophthalmic Sciences, All India Institute of Medical Sciences, New Delhi, India

³Department of Medical Oncology, Institute Rotary Cancer Hospital, All India Institute of Medical Sciences, New Delhi, New Delhi, India

Correspondence to

Dr Rachna Meel,
dr.rachnameel@gmail.com

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SUMMARY

A 19-year-old woman presented to the outpatient department with occasional ocular pain and redness and a perilimbal mass, which she noticed 5 months ago in her left eye. She had no systemic complaints. Ultrasound biomicroscopy of the mass showed a hypoechoic lesion with uniform reflectivity. The patient underwent an excision biopsy and a histopathological analysis revealed features suggestive of a granulocytic sarcoma/myeloid sarcoma. Further haematopathological evaluation confirmed concurrent acute myeloid (myelomonocytic) leukaemia French American British classification M4. There was complete remission of the ocular surface lesion and leukaemia with systemic chemotherapy. At the last follow-up of 18 months post-treatment the patient is free of disease.

BACKGROUND

Ocular and adnexal involvement in leukaemia is well known and has been found to occur in 80% of patients with acute leukaemia.¹ Ophthalmic involvement may be secondary to haematological derangements like anaemia, hyperviscosity and thrombocytopenia, clinically evident as Roth's spots, vitreous/retinal haemorrhages and ischaemic retinal changes on fundus examination. Direct infiltration of ocular and adnexal tissues by leukaemic cells is less common. Schachat *et al* in a study of 120 eyes with acute leukaemia reported leukaemic infiltrates in 3% cases at the time of diagnosis.² It may also present as diffuse infiltration of ocular/orbital tissues, which is more commonly observed in acute lymphocytic leukaemia and involves choroid, retina and optic nerve in decreasing order of frequency. Tumour formation with extramedullary leukaemic blast cells—known as myeloid sarcoma, is more frequently encountered in acute myeloid leukaemia (AML) and manifests most commonly in the orbit followed by the lacrimal glands or extraocular muscles. Conjunctival infiltration by tumour cells is highly unusual in leukaemia.³ Herein, we describe the clinical findings, imaging and treatment outcome in a young patient who presented to us with a limbal mass, as an unfamiliar initial manifestation of AML.

CASE PRESENTATION

A 19-year-old woman presented with a reddish mass over the surface of her left eye, which she noticed 5 months ago. The mass had gradually increased in size. The patient also had occasional

pain and redness in the affected eye. She had no systemic symptoms.

On examination, she had a best corrected visual acuity of 20/20 (6/6) in both eyes. In the left eye, a pink violaceous conjunctival mass was noted, extending for about 8 clock hours (9–5 clock hours) around the limbus. The conjunctiva overlying the mass was stretched out with prominent superficial vascularisation (figure 1). The mass was firm and non-tender on touching with a sterile cotton swab. An anterior segment examination on a slit lamp biomicroscope revealed no abnormalities. A dilated fundus examination using a binocular indirect ophthalmoscope was unremarkable. Right eye was within normal limits. Systemic examination was found to be normal. A clinical differential diagnosis of scleral cyst or inclusion cyst of conjunctiva was considered.

INVESTIGATIONS

On ultrasound biomicroscopy, the mass was found to be hypoechoic and limited to the conjunctiva with uniform reflectivity (figure 2). A routine blood smear done preoperatively showed findings suggestive of microcytic hypochromic anaemia.

An excision biopsy of the mass was done. Histopathological analysis revealed features of a malignant round cell tumour. H&E stained sections revealed a discohesive population of pleomorphic round to oval cells, a few with angulated nuclei and scant cytoplasm (figure 3). Immunohistochemical stains were strongly positive for myeloperoxidase (MPO), leukocyte common antigen (LCA) and MIC2, suggestive of a myeloid sarcoma (figure 4).

Figure 1 Preoperative clinical photograph of the left eye of the patient showing limbal mass extending from 9 to 5 clock hours.

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Figure 2 Ultrasound biomicroscopy demonstrating a uniform hypoechoic conjunctival mass.

The patient was referred to a medical oncologist for further evaluation. A bone marrow biopsy was done which showed a cellularity of 95%–100% which predominantly comprised of immature cells (blasts) and a cellular touch preparation showed approximately 30% blasts which were MPO positive suggestive of AML with bone marrow aspirate findings suggestive of AML M4 (acute myelomonocytic leukaemia). Flow cytometric analysis of bone marrow revealed approximately 40% blasts which were CD45+, CD34+, cMPO+, CD117+, CD33dim+, HLADR+, CD38+, CD13dim+, CD19dim+, CD15–, CD11b–, CD56–, CD36–, CD14–, CD64–, CD4–, CD65–, CD2–, CD7–, CD9–, cCD3– and cCD79a–, indicating AML. She was found to have a karyotype of 46, XX with no abnormal polymorphic variation from the general population. A cytogenetic analysis with reverse transcription-PCR was positive for AML-ETO fusion transcript but negative for FLT3-ITD and nucleophosmin (NPM) mutations.

TREATMENT

The patient received chemotherapy. The 3+7 protocol was used for induction—60 mg/m² of daunorubicin for 3 days and 100 mg/m² of cytarabine for 7 days. This was followed by consolidation therapy with 2 cycles of high dose cytarabine (Ara-C) (HiDAC)—18 gm/m² given over 5 days (day 1, 3 and 5), in two divided doses (3 gm/m² each) a day as a slow infusion—over the

Figure 3 Microphotograph showing pleomorphic round to oval cells seen with scant cytoplasm and angulated nuclei (H&E stain).

Figure 4 Microphotograph showing positive staining for myeloperoxidase stain.

next 2 months. As a consequence of chemotherapy, the patient developed febrile neutropenia and fungal pneumonia, which was managed with antifungals (amphotericin B) and broad-spectrum antibiotics (meropenem, piperacillin-tazobactam, teicoplanin, linezolid, cefoperazone-sulbactam). She also required a total of 4 units of packed red blood cells over the course of treatment.

The third dose of HiDAC was deferred as the patient developed severe chemotherapy-related toxicities after each cycle of therapy.

OUTCOME AND FOLLOW-UP

There was a complete regression of the limbal granulocytic sarcoma with systemic disease remission. On the last follow-up of 18 months post-treatment the patient was free of disease (figure 5).

DISCUSSION

Myeloid sarcoma also known as granulocytic sarcoma is an uncommon manifestation of AML. It is an extra medullary tumour of immature granulocytic cells and is more commonly seen in the paediatric population. It can manifest at the onset of disease, during remission or as a relapse. It has been found to predate the onset of systemic disease in about a quarter of

Figure 5 Clinical photograph of the left eye of the patient at one last follow-up.

cases.⁴ Myeloid sarcoma most commonly involves skin, lymph nodes and bones.⁵ Ocular and adnexal involvement has been variably reported.⁶ In at least two prospective studies in medical literature, none of the patients with AML had leukaemic infiltrates involving the eye.^{7,8} While another study reported ocular involvement as high as 66.7% in AML.⁹ With regard to ocular involvement, the most common site to be involved is the orbit. The leukaemic cells have a predilection for bone and periosteum which are the sites of active haematopoiesis and present as an orbital mass. Less commonly they may arise in the lacrimal glands and extraocular muscles.¹⁰ Involvement of conjunctiva as an extramedullary site for leukaemic infiltrate has been reported to occur in only 2%–4% of cases of acute leukaemia.³ Conjunctival involvement may be unilateral or bilateral and present as diffuse or focal lesion—as an ocular surface, palpebral or caruncular mass. Diffuse palpebral involvement can mimic, giant papillary hyperplasia.^{6,10–15}

In a review of literature of the last 30 years, we could find only seven reported cases of conjunctival myeloid sarcoma (table 1).

In the current case, the conjunctival involvement presented as a perilimbal lesion, clinically similar to that reported by Font *et al.*¹¹ To the best of our knowledge, this is only the fourth case of (acute myelomonocytic leukaemia) AML M4 reported in the literature to manifest as a conjunctival myeloid sarcoma. Of the seven cases of AML reported to have conjunctival myeloid sarcoma, summarised in table 1, it is interesting to note that three patients had—AML M4, similar to the current case. Thus, it appears that conjunctival involvement may be more common in this subgroup of AML. This group of leukaemia is characterised by extensive skin involvement, which however was absent in the current case.

Also, it is notable that like in our case, six of the seven cases of conjunctival myeloid sarcoma were reported in adult patients. It is thus likely that conjunctival involvement may perhaps be more common in adults with AML.

There is no consensus on the treatment protocol for myeloid sarcoma due to a lack of prospective randomised studies. Like with the central nervous system, there is poor penetration of the chemotherapeutic agents into the eye and therefore, some authors recommend irradiation in cases of ocular infiltration like that in the uvea along with systemic chemotherapy. Similarly, optic nerve infiltration, which is considered as an ophthalmic emergency due to its devastating effect on vision, is treated with urgent irradiation, though the doses as per various studies vary from 700 to 2000 rads.¹⁶ Orbital myeloid sarcoma portends a poor prognosis. In patients presenting with isolated myeloid sarcoma or myeloid sarcoma with AML, conventional AML chemotherapeutic regimens are followed. Treatment outcome and survival in patients with myeloid sarcoma are reported to be poorer in cases presenting with leukaemia than those without. Complete treatment response and 2-year event-free survival rates have been found to be 69% vs 57% and 43% vs 32% in patients of myeloid sarcoma without leukaemia versus those with leukaemia, respectively.¹⁷ Conjunctival infiltrates tend to show good resolution with systemic chemotherapy.¹⁶

However, there is a lack of long-term follow-ups in the cases reported in medical literature. The current case showed complete resolution of conjunctival myeloid sarcoma and patient was free of disease at last follow-up.

To conclude, myeloid sarcoma should be considered as a differential diagnosis for conjunctival ocular surface tumours, especially in adults. Haematological investigations may detect AML in such systemically asymptomatic cases.

Table 1 Summary of review of literature for cases of conjunctival myeloid sarcoma

	Author (Year)	Age/Sex	Laterality	Conjunctival lesion	AML type	Temporal association	Treatment	Outcome	Follow-up
1	Font <i>et al</i> (1985) ¹¹	28/F	Bilateral	Perilimbal	Acute monocytic	Relapse	CT and local RT (2000 rads)	CR	Disease free at 7 months
2	Lee <i>et al</i> (1985) ¹²	57/M	Bilateral	Palpebral, diffuse (giant papillary reaction)	Acute myelomonocytic leukaemia	Initial manifestation	NA	NA	NA
3	Mansour <i>et al</i> (1985) ¹³	28/M	Bilateral	Caruncular and diffuse palpebral mass	Acute myelomonocytic leukaemia	Relapse	NA	NA	NA
4	Tsumura <i>et al</i> (1991) ¹⁴	29/F	Left	Focal bulbar	Acute myelomonocytic leukaemia	Relapse	Gyc. dauno, vin, eno and prednisolone	CR of conjunctival lesion	Died at 2 months
5	Douglas <i>et al</i> (2002) ⁶	42/F	Right	Focal limbal	Acute myelogenous leukaemia	Initial manifestation	Induction -ida and ara-c CT	CR	Disease free at 1 month
6	Fleckenstein <i>et al</i> (2003) ¹⁵	73/F	Bilateral	Diffuse bulbar	Acute myelogenous leukaemia	Initial manifestation	Local radiation and low dose CT with ara-C	CR	Died at 5 months
7	Hong <i>et al</i> (2011) ¹⁰	10/F	Right	Fleshy, bulbar, local	Acute monocytic leukaemia M5	Relapse	CT and STC	CR	Disease free at 16 months
8	Current case	28/F	Left	Perilimbal mass	Acute myelomonocytic leukaemia M4	Initial manifestation	CT	CR	Disease free at 18 months

AML, acute myeloid leukaemia; CR, complete regression; CT, chemotherapy; F, female; -ida, idarubicin; M, male; NA, not available; RT, radiotherapy; STC, stem cell transplant.

Learning points

- Ocular surface mass may be a manifestation of asymptomatic acute myeloid leukaemia.
- Cases of ocular surface mass should be carefully investigated to rule out the same.

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