CASE REPORT

Panuveitis simulating ocular Behçet's in cases of chronic myelogenous leukaemia in remission

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SUMMARY

We report two patients with chronic myelogenous leukaemia (CML) in remission phase who developed panuveitis simulating Behçet's disease. A 26-year-old man presented with bilateral panuveitis (hypopyon in the right eye, bilateral anterior segment inflammation, vitritis and retinitis). He was on imatinib for CML which was in remission. He gave a history of recurrent oral ulcers. The panuveitis responded to oral and topical steroids but recurred after the steroids were stopped. His ocular condition again stabilised on restarting oral steroids and azathioprine. The second patient, a 28-year-old man, presented with bilateral anterior segment inflammation, vitritis, exudative retinal detachment and hypopyon in the right eye. He was also on imatinib with the CML being in remission. The uveitis and exudative retinal detachment improved on systemic and topical steroids. The vision of this patient did not improve as optic atrophy ensued. The panuveitis seen in our patients with CML responded favourably to oral steroids/immunosuppressant therapy.

BACKGROUND

Chronic myelogenous leukaemia (CML) is a haematological malignancy of the polymorphonuclear leucocytes and its precursors, characterised by structural/functional changes and an increase in the number of neutrophils. There have been multiple reports of the occurrence of Behçet's disease (BD) in diagnosed cases of CML.^{1–6} CML has also been reported at/during follow-up of patients with BD.^{1,7} The coexistence of these diseases has been proposed to be due to the drugs used for treating CML (interferon alpha/IFN α)^{1,2} or hydroxyurea^{3,4} or both⁵. In some cases, the ulcers decreased following the withdrawal of therapy with IFN α ¹ or hydroxyurea.³ Hydroxyurea has been reported to cause leg ulcers which on histopathology showed leucocytoclastic vasculitis and perivascular infiltration by lymphocytes.⁸ We present two patients on imatinib therapy who developed a Behçet's-like autoimmune panuveitis.

CASE PRESENTATION**Case 1**

A 26-year-old man presented to us with progressive diminution of vision with mild pain in both eyes for 2 weeks. He was on imatinib for CML which was in remission. He also gave a history of recurrent oral ulcers (3–4 times in a year). There was no history of any genital ulcers or any skin lesions. On examination, the best-corrected visual acuity was

finger counting close to face in the right eye (RE), and 6/12 in the left eye (LE). The RE had a 1.5 mm hypopyon (figure 1A), and the LE had 2+ anterior chamber (AC) cells. Media was hazy in the RE due to vitritis. Areas of retinal whitening with haemorrhages were observed (figure 1B). In the LE, there were small round vitreous opacities, and small chorioretinal infiltrations (figure 2A). The fundus fluorescein angiogram revealed leakage from the optic disc, diffuse leakage and fern-like paravascular staining (figure 1C). The differentials kept were fungal metastatic endophthalmitis, CML-related panuveitis and other causes of panuveitis such as BD, tuberculosis and sarcoidosis among others.

Case 2

A 28-year-old man presented with perception of light with inaccurate projection of rays in both eyes. He was also taking imatinib for CML which was in remission. He did not give any history of oral or genital ulcers or any skin lesions. The RE had a hypopyon and the LE showed 3+ AC reaction. Both eyes revealed significant vitritis, hazily visible exudative retinal detachment, with subretinal yellowish exudates and preretinal cotton ball-like opacities. Arterial attenuation and pale discs were also evident in both eyes in this patient.

INVESTIGATIONS**Case 1**

The haemogram, chest X-ray, Mantoux, venereal disease research laboratory test for syphilis (VDRL), HIV and pathergy tests were normal. A blood culture and vitreous tap were sterile. AC tap showed typical lymphocyte cells and no lymphoma cells.

Case 2

The blood pressure, haemogram, chest X-ray, Mantoux, VDRL, HIV and pathergy tests of this patient were also normal. Optical coherence tomography revealed neurosensory detachment with cells in the vitreous and hyperintense-reflective foci throughout the retina (figure 3B).

TREATMENT**Case 1**

The patient was started on oral prednisolone 1 mg/kg and topical steroid and cycloplegic and the visual acuity improved to 6/60 (RE) and 6/12 (LE) with the clearing of the ocular media (figure 1D, figure 2B).

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Figure 1 (A) The right eye of case 1 showed hypopyon at presentation. (B) Right fundus at presentation showed vitritis and whitish retinal lesions (retinitis). (C) The fluorescein angiography showed disc leak and capillary ferning. (D) Significant improvement of media was noted in the right eye after steroids and the retinitis also responded.

Case 2

From our experience with the previous case, we empirically initiated steroids under close observation, after which the hypopyon resolved and the vitritis started subsiding. The height of the exudative detachment reduced markedly in both eyes (figure 3A). Pale disc and subretinal exudates persisted.

OUTCOME AND FOLLOW-UP

Case 1

At 1 month, visual acuity improved to 6/6 in the LE. On tapering the oral steroids, there was a recurrence with focal retinitis and intraretinal haemorrhages in the LE (figure 2C). This responded to stepping up of the steroid and addition of azathioprine (figure 2D). He is maintaining visual acuity (6/60 (RE), and 6/6

Figure 2 (A) Left eye of case 1 at presentation showed vitritis and preretinal white round vitreous opacities. (B) Significant improvement in media clarity of left eye was noted after oral steroid. (C) Recurrence of a patch of retinitis left eye was noted on tapering steroids. (D) Resolution of retinitis was evident on stepping up steroids and adding azathioprine.

Figure 3 (A) Right eye of case 2 showed resolving vitritis (hazy media), pale disc, arterial attenuation, subretinal exudates (after 1 week of oral steroids). The media of the left eye of patient 2 cleared significantly after 1 week of oral steroids, revealing a pale disc, arterial attenuation and subretinal exudates. (B) Optical coherence tomogram still showed persisting retinal detachment with cells in vitreous (after 1 week of oral steroids).

(LE)) till the last follow-up of 1 year on 5 mg oral prednisolone and 150 mg oral azathioprine.

Case 2

The vision of this patient did not improve likely due to associated optic atrophy. The uveitis is currently in remission on a low dose of oral steroids.

DISCUSSION

The panuveitis seen in the first patient resembles the ocular involvement seen in cases of BD to a great extent. This patient also had a history of oral ulcers. The other patient did not give a history of oral ulcers but presented with a hypopyon uveitis in one eye which can be typically seen in cases of Behçet's disease. Both the cases responded to immunosuppression. The ferning appearance in fluorescein angiogram is also typically seen in BD.

Differential diagnosis of the presentation seen in our patients includes ocular involvement in tuberculosis, sarcoidosis, endogenous endophthalmitis, primary intraocular lymphoma and viral retinitis. In both our patients, a diagnosis of tuberculosis and sarcoidosis was ruled out using relevant investigations. In the first case, endogenous endophthalmitis was excluded by the sterile vitreous tap. Primary intraocular lymphoma is a rarity considering the young age of both the patients, and in the first case, the aqueous tap showed typical lymphocytes and no lymphoma cells. Viral retinitis, especially acute retinal necrosis,^{9 10} may clinically cause a panuveitis. However, acute retinal necrosis is a clinical diagnosis and was clinically ruled out by the absence of typical peripheral⁹ retinitis patches and prominent occlusive arteriolitis. Our patient had only a patch of posterior focal retinitis.

In the second case, a vitreous tap could not be performed as the patient denied for the same. However, in such cases of panuveitis, the workup may also have included diagnostic vitrectomy, flow cytometry and viral PCR. The authors did not plan a diagnostic vitrectomy in either of the patients due to good clinical response to steroid, ocular inflammation clinically simulating BD, an absence of consent, invasive nature of the procedure, known complications of vitrectomy and financial constraints of the patients.

BD is an autoimmune systemic disorder diagnosed by the presence of recurrent oral aphthous ulcers occurring at least three times a year with at least two of the following symptoms—recurrent genital ulcers, ocular inflammation, skin lesions and positive pathergy test.¹¹ Our patients could not afford for human leucocyte antigen-B51 (HLA-B51); however, the diagnosis of BD is based on clinical criteria, and positivity of HLA-B51 is not required for diagnosis.¹¹ Morphologically, the panuveitis seen in our patients closely resembled the panuveitis described in cases

of BD, though the full diagnostic criteria¹¹ of BD were not met in either of the cases.

The final common pathway of tissue damage in BD seems to be predominantly mediated by the polymorphonuclear leucocytes (neutrophils) and cytotoxic T cells.¹² Histological analysis of the BD lesions reveals extensive perivascular infiltration by neutrophils resulting in the proposal to classify BD as 'neutrophilic vasculitis'¹³ or 'neutrophilic phlebitis'.¹⁴ The neutrophils in BD are primed and are activated rapidly following exposure to a proper trigger.¹² These cells express various neutrophil activation markers (CD10, CD11a and CD14). Also, the Th17 cells may upregulate the neutrophil activation along with the cytokine milieu (interleukin (IL) 8, tumour necrosis factor alpha (TNF α) and IFN γ). Neutrophils show increased chemotaxis, phagocytosis and a rise in reactive oxygen species and myeloperoxidase in BD. In animal studies, the HLA-B51 transgenic mice show hyperactive peripheral blood neutrophils.¹⁵ The lifespan of the neutrophils is also increased in BD. Overall, it may be said that neutrophil is a key player in the pathogenesis of BD.¹²

Considering the past reports of BD developing in treated cases of CML and our cases which also developed a BD-like autoimmune uveitis following treatment of CML with imatinib, we propose that the development of autoimmune phenomenon in treated cases of CML may be due to an alteration induced in neutrophils of such patients immaterial of the drug used. Neutrophil function analysis and IL analysis is beyond our resources and scope. Nevertheless, our cases imply that it is important to recognise that patients with CML in remission may present with

panuveitis. Such panuveitis may respond well to systemic immunosuppression if recognised and treated early.

Contributors RC was involved in clinical management of the patients. Both the authors acquired the images, drafted the manuscript and have approved the final version of the manuscript. RC and KT agree to be accountable for the work.

Competing interests None declared.

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Learning points

- Patients with chronic myelogenous leukaemia in remission may present with visual loss due to panuveitis simulating Behçet's disease.
- Response to systemic steroid and immunosuppressives is good if initiated early.
- Early detection and management are crucial as visual recovery may be limited by multiple factors including optic atrophy and macular pigmentary changes in cases who present late.

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