

Case Report

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Bilateral Visual Loss in a Patient with Chronic Myelogenous Leukemia after Initiation of Imatinib Therapy

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Abstract

Objective and importance: Imatinib—the principle treatment currently available for chronic myeloid leukemia (CML)—may be implicated in neovascular glaucoma (NVG) pathogenesis.

Clinical presentation: A 64 year old diabetic female develops CML and receives imatinib treatment develops aggressive bilateral neovascular glaucoma within 1 month of initiation of treatment. The left eye is lost and the right eye was hardly salvaged through panretinal photocoagulation and substitution of imatinib therapy to dasatinib therapy.

Intervention: Systemic imatinib therapy for CML.

Conclusion: Imatinib may be implicated in the causation of NVG in CML patients, who should thus receive regular thorough ophthalmic evaluation as long as imatinib therapy continues.

Keywords: Chronic; Myeloid; Leukemia; Imatinib; Glaucoma; Neovascularisation

Introduction

Chronic myelogenous leukemia (CML) is a pluripotent stem cell disease characterized by anemia, extreme blood granulocytosis and granulocytic immaturity, basophilia, often thrombocytosis, and splenomegaly. It is associated with a reciprocal chromosomal translocation t(9; 22) (q34; q11) resulting in a BCR-ABL fusion gene (Philadelphia chromosome). This translocation results in a new hybrid protein (bcr-abl) with overactive tyrosine kinase activity and is implicated in the development of CML. The first tyrosine-kinase inhibitor imatinib was introduced to clinical practice about 10 years ago and it radically improved the outcome of CML patients.

Case Report

A 64 year old female presented to the outpatient clinic of Damanhour Oncology center complaining of easy fatigability, tiredness and headache. She had been diabetic (type 2) for the preceding 7 years. Clinical examination showed moderate splenomegaly. Laboratory investigations were ordered (Table 1). Owing to the relatively high cost of the laboratory investigations, not all necessary tests (e.g. quantitative bcr/abl analysis, ratio of Ph chromosome positive cells) could be ordered freely from the patient. The patient's diabetic state was relatively well controlled at presentation and remained so throughout the treatment and follow up period. The preliminary diagnosis was CML and cytoreductive therapy was initiated with hydroxyurea capsules. Laboratory investigations were repeated one week later (Table 1). Imatinib therapy (Imatinib mesylate, CIPLA, India), 400 mg per day was then instituted, 1 month after which she reported headache, bilateral ocular pain and gradual progressive diminution of vision. Though no data is available about the pre-imatinib vision and IOP of the patient, yet the patient reportedly had -at least apparently- a level of vision that was judged by the patient as normal allowing free full mobility and independence in life tasks. The patient was lost for follow up for approximately 3 months after which she presented with bilateral

visual complaints. Laboratory investigations were repeated (Table 1) and Imatinib therapy was stopped.

Ophthalmic consultation elsewhere revealed a diagnosis of glaucoma in the right eye for which an operation was performed. The results of an ophthalmic assessment conducted 1 month later are shown in table 2 and figure 1.

The diagnosis of bilateral neovascular glaucoma (NVG) was confirmed.

The patient was prescribed brimonidine eye drops (ED) TID, brinzolamide ED TID and a prostaglandin analogue/beta blocker combination once daily. A follow up visit 1 month later revealed an IOP of 19 mmHg (OD), and a visual acuity of CF at 50 cm. Pan retinal photocoagulation (PRP) was performed. Quantitative PCR analysis for the bcr-abl gene revealed 31% positive cells upon which imatinib mesylate (Gleevec® Novartis Pharm AG) therapy at a daily dose of 400 mg was restarted. The patient was self medicating and stopped all topical treatment and presented 1 month later with a VA of hand motion (HM), a 2 mm hyphema, with rubeosis iridis, corneal oedema and an IOP of 35 mmHg. Full IOP lowering medications were restarted and a review 1 week later showed a visual acuity of HM, hyphema and an IOP of 6 mmHg. Throughout this period, she was monitored by regular complete blood pictures which revealed hematological remission. Imatinib therapy was stopped and the patient was shifted to Sprycel

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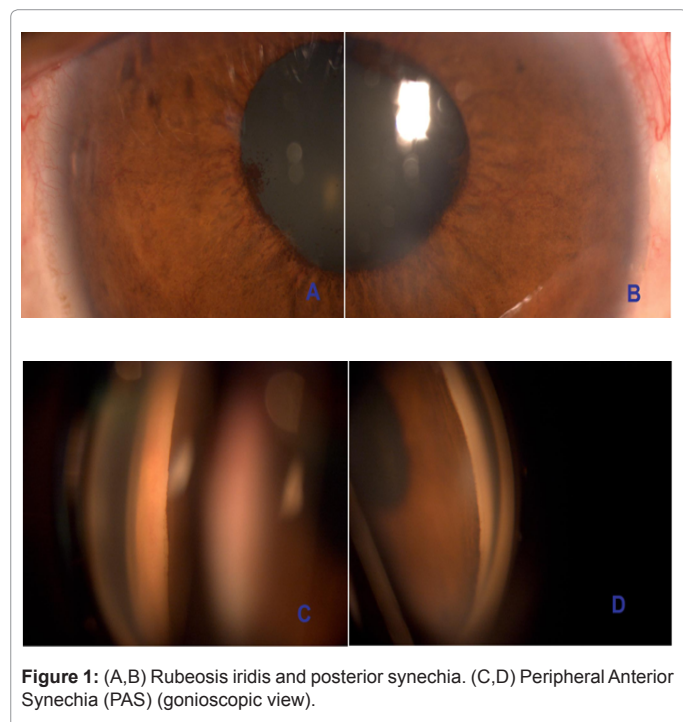
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Lab parameters on presentation		Lab parameters 1 week later		Lab parameters 3 months later	
Lab parameter	Results	Lab parameter	Results	Lab parameter	Results
WBC	122×10 ⁹ /L	WBC	70.6×10 ⁹ /L	WBC	12.1×10 ⁹ /L
PLT	1,254×10 ⁹ /L	PLT	782×10 ⁹ /L	PLT	115×10 ⁹ /L
Hb	11.1 g/dL	Hb	11 g/dL	Hb	13.7 g/dL
Differential WBC count	Shift to the left with absolute basophilia	Qualitative PCR analysis for bcr-abl fusion gene	Positive		
Liver & kidney functions	Normal	JAK2V617F mutation	Negative		
Serum uric acid	6.4 mg/dL				

Table 1: Lab parameters before and 1 week and 3 months after initiation of therapy.

	OD	OS
Visual acuity	Counting fingers (CF) at 10 cm	No Perception of Light
IOP (mmHg)	26	62
Cornea	Clear cornea	Bullous keratopathy
Anterior Chamber	Normal depth and content	Normal depth and content
Iris	Extensive rubeosis iridis and posterior synechia	Extensive rubeosis iridis and posterior synechia
Gonioscopy	360 degrees of peripheral anterior synechia (PAS) with neovessels in the angle	Not possible
Fundus	- Totally cupped optic disc with neovascularization of the disc (NVD) - Retinal hemorrhages along the vascular arcades - A large—almost one disc diameter sized— hard exudate patch in the macula - Numerous dot hemorrhages all over the posterior pole and retinal periphery	Totally cupped optic disc with neovascularization of the disc (NVD)
Remarks	Superonasal scarred flat bleb	End stage neovascular glaucoma (NVG)

Table 2: Ophthalmologic examination on presentation.



(Dasatinib, Bristol Myers Squibb) tablets, 100 mg daily. Monthly CBCs were normal thereafter.

Discussion

The ophthalmic manifestations of CML are quite variable and include intraretinal hemorrhages, Roth spots, nerve fiber layer infarcts, subhyaloid and vitreous haemorrhages and papilloedema secondary to raised intracranial pressure [1]. There are various reports on the ocular

side effects of imatinib therapy, most reporting periorbital oedema [2], besides others including epiphora, recurrent subconjunctival hemorrhage and optic neuritis. There are variable reports about glaucoma developing in CML patients with imatinib therapy [3,4], even the drug information leaflet points this out as a rare possibility. However, the reports are inconsistent and do not demonstrate the exact type of glaucoma. In our case, the type of glaucoma was neovascular, possibly due to retinal ischemia. We recognise that our patient—being originally diabetic—was already prone to develop glaucoma, especially neovascular glaucoma (as a result of retinal ischemia), yet the imatinib therapy may have aggravated the condition. We hypothesize that the very high WBC and PLT counts induced a hyperviscosity state that initiated or aggravated retinal ischemia. In such a situation, the imatinib therapy may actually have protected the remaining eye from visual loss by improving the haematologic parameters of the patient. Alternatively, imatinib may have aggravated retinal ischemia, or induced neovascularization by another mechanism as recently reported by Gulati and Saif [5]. Wherever the true situation is regarding the relationship between CML, Imatinib and vision loss, it is worth noting that CML patients on Imatinib therapy should have regular thorough ophthalmic evaluations, especially if diabetic. Better still, it may be advisable to avoid imatinib therapy in a patient with a known risk factor for glaucoma, and possibly resort to a safer drug, like nilotinib, for which no ocular side effects are reported so far.

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