in order to prevent aqueous dilution of the dye. The excess dye should then be removed from the vitreous body prior to air–fluid exchange to prevent unnecessary spreading of the dye.

The macular detachment experienced by our patient was caused by the collection of subretinal dye that occurred during the process of dye injection. This was most likely caused by the sudden ejection of a jet of dye at high speed from the cannula when the plunger became unstuck. As the cannula was pointed towards the macula and there was a lack of vitreous gel to buffer the jet of dye, the energy was sufficient to create a macula hole and force some dye through the hole into the subretinal space.

In order to prevent this from reoccurring, the following should be observed. Firstly, the cannula should be pointed away from the macula during dye injection. Secondly, a 1 ml syringe should be used, as it may allow better control of the injection process compared to higher-volume syringes. Thirdly, injection of the dye should be slow and controlled, such that the dye enters the vitreous cavity in a drip-like manner. This is probably better if carried out by an assistant. The plunger of the syringe should also be checked to ensure that it glides easily within the sleeve for a controlled injection.

It is important to remember that with any new surgical technique, a learning curve is always involved. Surgeons should therefore take the necessary precautions to minimise iatrogenic complications when trying out a new technique. This case demonstrates that even for a relatively simple procedure like injecting dye into the vitreal cavity, sight-threatening complications can occur.

References

1 Li K, Wong D, Hiscott P, Stanga P, Groenewald C, McGalliard J. Trypan blue staining of internal limiting membrane and epiretinal membrane during vitrectomy: visual results and histopathological findings. *Br J Ophthalmol* 2003; **87**(2): 216–219.
2 Melles GR, de Waard PW, Pameyer JH, Houdijn Beekhuis W. Trypan blue capsule staining to visualize the capsulorhexis in cataract surgery. *J Cataract Refract Surg* 1999; **25**(1): 7–9.
3 Feron EJ, Veckeneer M, Parys-Van Ginderdeuren R, Van Lommel A, Melles GRJ, Stalmans P. Trypan blue staining of epiretinal membranes in proliferative vitreoretinopathy. *Arch Ophthalmol* 2002; **120**(2): 141–144.

GS Ang, AJS Ang and RL Burton

Department of Ophthalmology
Norfolk & Norwich University Hospital
Norwich, UK

Correspondence: RL Burton
Tel: +1603-288511
Fax: +1603-288261
E-mail: caroline.kolyszko@nnuh.nhs.uk

Eye (2004) **18,** 759–760. doi:10.1038/sj.eye.6701312
Published online 23 January 2004

Sir,

Periorbital Oedema and epiphora as ocular side effects of imatinib Mesylate (Gleevec)

Introduction

We herein present our experience with epiphora, associated with imatinib mesylate, its causes, and management. Imatinib mesylate (Gleevec; Novartis Pharmaceuticals, East Hanover, NJ, USA) is a selective inhibitor of the bcr-abl, c-kit, and platelet-derived growth factor receptor tryrosine kinases and is a promising new targeted therapy for patients with chronic myelogenous leukaemia and gastrointestinal stromal tumours.[1–5] Imatinib mesylate is generally well tolerated, with frequent but mild side effects. Reported side effects include myalgia, fatigue, nausea, dyspepsia, diarrhoea, oedema, and liver-function abnormalities.[1] Approximately 70% of patients with chronic myelogenous leukaemia who receive imatinib mesylate develop mild to moderate regional fluid retention, usually limited to the periorbital region or legs. Rarely, fluid retention can be more generalized, with pleural or pericardial effusions, ascites, and anasarca. Treatment for most cases of imatinib mesylate-associated oedema consists of administering diuretics and decreasing the dosage.

Although periorbital oedema is a well-known side effect of imatinib mesylate and is mentioned as a common side effect in the drug insert prepared by the manufacturer and in several recently published reports of clinical trials.[6,7] To our knowledge, there are no published reports to date — aside from a report of one case of severe periorbital oedema[8]—focusing exclusively on ocular side effects associated with this medication. Here, we report a series of 12 patients treated with imatinib mesylate at our institution who reported epiphora as the main ocular side effect of this drug.

Methods

We retrospectively reviewed the records of all patients who were treated in clinical trials of imatinib mesylate at our institution between January and December of 2002

and had epiphora as their primary ocular complaint. The initial dosage of Gleevec in the clinical trials was 400 mg once daily by mouth. The protocols permitted increase or decrease of the dosage or discontinuation of Gleevec as warranted in clinical judgement of the medical oncologist. All patients who had epiphora as their primary ocular complaint underwent a comprehensive ophthalmologic examination, including slit-lamp biomicroscopy, a dilated retinal examination, and probing and irrigation of all four canaliculi and nasolacrimal ducts.

Results

The mean ($\pm$standard deviation) daily dose of Gleevec was 540 ± 187 mg. In total, 12 patients who received imatinib mesylate at our institution in 2002 had epiphora as their primary ocular complaint. All of them also had periorbital oedema. Three patients had obvious conjunctival chemosis noticeable on external examination of the globes and confirmed by slit-lamp biomicroscopy. Three additional patients had conjunctivochalasis partially blocking the lower puncta. Probing and irrigation of the nasolacrimal ducts did not reveal evidence of punctal or canalicular stenosis or nasolacrimal duct blockage in any of the 12 patients with epiphora. Findings on the rest of the ocular examination were within the normal limits in all 12 patients. One patient had severe periorbital oedema that necessitated surgical removal of large festoons in the lower eyelids to restore visual function (previously reported; see Esmaeli *et al*[8]) (Figure 1). In the other 11 patients, periorbital oedema was mild to moderate and was treated conservatively. Two patients were treated with furosemide 40 mg daily and one patient was treated with topical steroids (prednisolone acetate (1%) four times a day) and reported improvement in their epiphora. The other eight patients were observed as their symptoms were not severe enough to justify treatment or they were not interested in taking any additional medications for their symptoms. Gleevec was not discontinued because of its ocular side effects in any of the patients in this study.

Discussion

Periorbital oedema is to date the most common ocular side effect associated with imatinib mesylate;[6] epiphora is so far the second most commonly reported ocular side effect of this drug.

In our series of patients with epiphora associated with imatinib mesylate, probing and irrigation of the lacrimal drainage apparatus did not reveal evidence of punctal, canalicular, or nasolacrimal duct stenosis. The mechanism for epiphora in patients receiving imatinib mesylate is probably secondary to periorbital oedema and conjunctival chalasis or chemosis.

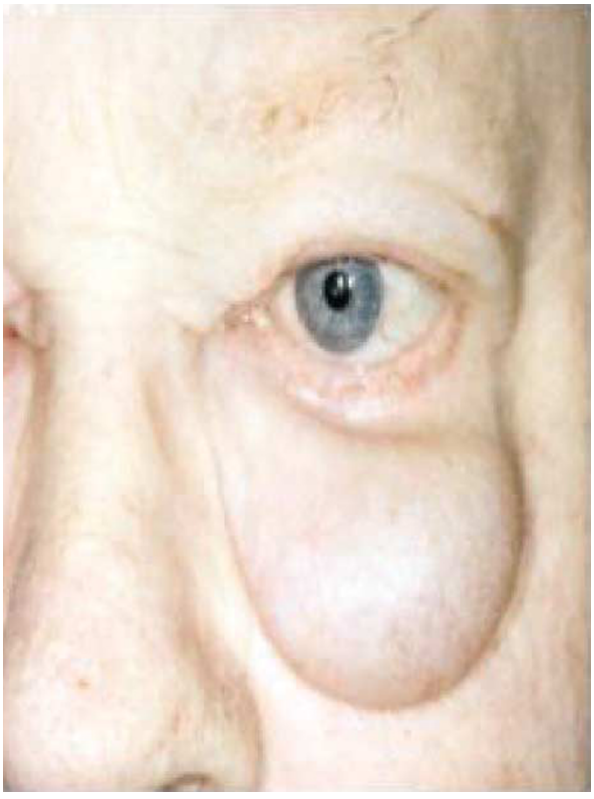

Figure 1 Severe periorbital oedema causing obstruction of vision in downgaze and inability to wear glasses in a patient treated with imatinib mesylate.

Apart from the one previously reported case of severe periorbital oedema that necessitated surgical intervention for restoration of visual function,[8] periorbital oedema was mild to moderate in this cohort.

In summary, epiphora in patients receiving imatinib mesylate appears to be caused in part by periorbital oedema and can be managed conservatively in most cases. In patients with epiphora whose symptoms do not resolve spontaneously, the use of oral diuretics and topical steroids may be helpful in improving the symptoms and signs of epiphora and periorbital oedema. In patients with unusually severe periorbital oedema, surgical excision of periocular soft tissues may be necessary to improve function.

References

1 Druker BJ, Sawyers CL, Kantarjian H, Resta DJ, Reese SF, Ford JM *et al*. Activity of a specific inhibitor of the BCR-ABL tyrosine kinase in the blast crisis of chronic myeloid leukemia

and acute lymphoblastic leukemia with Philadelphia chromosome. *N Engl J Med* 2001; **344**: 1038–1042.
2 Druker BJ, Talpaz M, Resta Debra J, Peng B, Buchdunger E, Ford JM *et al*. Efficacy and safety of a specific inhibitor of the BCR-ABL Tyrosine Kinase in Chronic Myeloid Leukemia. *N Engl J Med* 2001; **344**: 1031–1037.
3 Heinrich MC, Griffith DJ, Druker BJ, Wait CL, Ott KA, Zigler AJ. Inhibition of c-kit receptor tyrosine kinase activity by STI571: targeting BCR-ABL as therapy for CML. *Oncologist* 2000; **6**: 925–932.
4 Mauro MJ, Druker BJ. STI571: Targeting BCR-ABL as Therapy for CML. *Oncologist* 2001; **6**: 233–238.
5 Van Oosterom AT, Judson I, Verweij J, Stroobants S, Di Paulo ED, Dimitrijevic S *et al*. Safety and efficacy of imatinib (STI571) in metastatic gastrointestinal stromal tumors: a phase I study. *Lancet* 2001; **358**: 1421–1423.
6 Demeetri GD, von Mehren M, Blanke CD, Van Den Abbeele AD, Eisenberg B, Roberts PJ *et al*. Efficacy and Safety of Imatinib Mesylate in advanced gastrointestinal stromal tumors. *N Engl J Med* 2002; **347**: 472–480.
7 Hasselbalch HC. STI571 (Gleevec), a new drug for the treatment of chronic myeloid leukemia. *Ugeskr Laeger* 2002; **164**: 2914–2917.
8 Esmaeli B, Prieto VG, Butler CE, Kim SK, Ahmadi MA, Kantarjian HM *et al*. Severe periorbital edema secondary to ST1571 (Gleevec). *Cancer* 2002; **95**: 881–887.

B Esmaeli[1], R Diba[1], MA Ahmadi[1], HG Saadati[1], MM Faustina[1], TR Shepler[1], M Talpaz[2], R Fraunfelder[3], MB Rios[4] and H Kantarjian[4]

[1]Section of Ophthalmology
Department of Plastic Surgery
Box 443, The University of Texas
MD Anderson Cancer Center
1515 Holcombe Blvd, Houston TX 77030, USA

[2]Department of Bioimmunotherapy
The University of Texas
MD Anderson Cancer Center
1515 Holcombe Blvd, Houston
TX 77030, USA

[3]Department of Ophthalmology
Oregon Health Sciences Center OR, USA

[4]Department of Leukemia
The University of Texas
MD Anderson Cancer Center
1515 Holcombe Blvd
Houston TX 77030, USA

Correspondence: B Esmaeli
Section of Ophthalmology
Department of Plastic Surgery, Box 443
MD Anderson Cancer Center, 1515 Holcombe Blvd
Houston TX 77030, USA
Tel: +1 713 794 1247
Fax: 713 794 5492
E-mail: besmaeli@mdanderson.org

Eye (2004) **18,** 760–762. doi:10.1038/sj.eye.6701315
Published online 23 January 2004