a single founder. However, our patient differed from them, in that she exhibited an absence of hypocalciuria and enhanced proximal tubule salt reabsorption, and was from a different geographical region in Japan.

Conflict of interest statement. None declared.

1Department of Medicine Yasuyuki Mizumori1
Public Muraoka Hospital Hyogo Shigeaki Muto2
2Department of Nephrology Shin-ichi Uchida3
Jichi Medical School Tochigi Sei Sasaki1
3Department of Nephrology Eiji Kusano2
Tokyo Medical and Dental University Tokyo, Japan
Email: smuto@jichi.ac.jp


doi:10.1093/ndt/gfl361

Advance Access publication 25 July 2006

The use of lepirudin in haemodialysis complicated with heparin-induced thrombocytopenia type II (HIT II)—dosage monitoring

Sir,

Heparin-induced thrombocytopenia type II (HIT II) is an unpredictable prothrombotic, immune-mediated life-threatening complication that occurs following administration of unfractionated heparin (UFH) or low-molecular weight heparin (LMWH) for a variety of prophylactic or therapeutic applications [1]. The mainstay of HIT treatment consists of the immediate cessation of all forms of heparin therapies and the simultaneous initiation of non-heparin, rapidly acting anticoagulant therapies with direct thrombin inhibitors (DTIs) [1]. DTIs bind directly to thrombin, thus preventing fibrin formation and clotting. The three available DTIs are lepirudin, argatroban and bivalirudin, with only lepirudin and argatroban being currently approved by the U.S. Food and Drug Administration for use in HIT [1].

The major challenges of lepirudin treatment, given by any route, are the lack of an antidote and the extreme care needed when treating patients with any degree of renal insufficiency as it is primarily eliminated through the kidneys. Therefore, dosing must be reduced in patients with impaired renal function [1]. Moreover, its use is currently not indicated in patients requiring haemodialysis [2]. Only anecdotal reports are available on the usage of lepirudin as anticoagulant in haemodialysis [3–5].

Adding one more anecdotal case, we report a 23-year-old female who developed HIT following pre-emptive, living related donor, renal transplantation. The patient was pre-operatively exposed to both UFH and LMWH heparin during five haemodialysis sessions. HIT (diagnosed on the basis of both clinical and serological grounds) caused right common and external iliac vein and renal graft artery and vein thrombosis, resulting in graft loss. Heparin-free haemodialysis was continued using the DTI lepirudin as anticoagulant for both thromboses and haemodialysis. The dose of lepirudin (given as repetitive intravenous bolus) was titrated based on the activated partial thromboplastin time (aPTT) in order to maintain an aPTT value of 70–80 s [1]. In detail, the patient received 0.005 mg/kg/h of lepirudin the first day, 0.0024 mg/kg/h the second day, 0.0016 mg/kg/h the third day and for the subsequent 7 days 0.0012 mg/kg/h as a maintenance dose. She was then switched to oral anticoagulation treatment with acenocoumarol after a combined anticoagulation period of 5 days. aPTT values were evaluated every 3 h in the first day and every 4 h thereafter. The patient underwent four haemodialysis sessions post-operatively without any bleeding complications. Finally, she was accepted into the continuous ambulatory peritoneal dialysis (CAPD) programme.

It should be noted that although lepirudin dose for normal renal function is 0.15 mg/kg/h and for patients with creatinine clearance of 15–29 ml/min is reduced to 0.0225 mg/kg/h, the appropriate dose for patients requiring haemodialysis is almost 125 and 19 times less, respectively, suggesting that extremely cautious dosing adjustments at shorter intervals (i.e. every 4 h) should be made in such cases.

Recently, Haase et al. [6] successfully used fondaparinux as an anticoagulant in a dialysis patient with symptomatic HIT II. The pentasaccharides seem to have a promising role in treatment and/or prevention of HIT, since they do not appear to interact with platelets or platelet factor 4. However, fondaparinux, as lepirudin, is eliminated primarily through the kidneys (it is contraindicated in patients with creatinine clearance <30 ml/min), thus leaving the issue of appropriate dosing in dialysis patients in pendency.

We conclude that lepirudin can be used with safety in patients requiring short-term haemodialysis, providing aPTT is closely monitored, especially on the first day of treatment.

Conflict of interest statement. None declared.
The significance of cicatricial conjunctivitis in Wegener’s granulomatosis

Sir,

Wegener’s granulomatosis exhibits large heterogeneity in clinical expression. The spectrum of ocular disease can occur at any stage in its natural history. Cicatricial conjunctivitis, a fibrotic conjunctival scarring response is rare and associated with subglottic stenosis.

Case

A 70-year-old man was referred to the ophthalmology department with symptoms of ocular discomfort and abnormal conjunctival appearances. He had no previous ophthalmic history. He was recently clinically diagnosed with Wegener’s granulomatosis (WG) with inflammation involving his kidneys, nose and lungs with positive c-ANCA (EIA) levels of 7.6 units (<2.0). Nasal mucosa biopsy revealed mixed inflammatory infiltrate. He was too ill to undergo a renal biopsy.

Ocular examination revealed bilateral sub-tarsal conjunctival fibrosis with symblephara appearing as vertical folds between bulbar and palpebral conjunctiva (Figure 1) representative of conjunctival cicatrization. Conjunctival biopsy demonstrated minimal inflammation with no specific C3, IgA or IgG distribution as occurs with mucous membrane pemphigoid (MMP), an important differential. Serum indirect immunofluorescence for both IgG and IgA were also negative, excluding MMP.

Discussion

Our case demonstrates the heterogeneity in clinical expression of WG. Conjunctival disease has been reported in 4–16% of patients with ocular manifestations [1–4]. This can vary from conjunctival hyperaemia to granulomatous lesions, tarsal conjunctival necrosis, active fibrovascular proliferation or inactive scar tissue. Cicatricial conjunctivitis in WG is extremely rare [4]. An important differential diagnosis is MMP, an autoimmune disease whose target antigen is the β2 peptide of the α6β1-integrin of the basement membrane zone of conjunctiva and epidermis [5]. The conjunctival autoantigen in WG is currently unknown.

Chronic inflammation and fibrosis of the conjunctiva can induce dry eyes via occlusion of the ducts of the lacrimal and accessory glands, eyelid and eye lash abnormalities (entropion, lagophthalmos, trichiasis and dystrichiasis). The aetiology of fibrosis is unknown but these changes can lead to corneal scarring, infection, perforation and loss of vision.

The location of conjunctival disease predominantly at the eyelid borders may further the understanding of the pathogenesis of WG. The eyelids are supplied by terminal branches of the marginal and peripheral arcade vessels [6]. An occlusive vasculitis of these peripheral vessels, branches or both may lead to ischaemia or infarction [4].

Physicians should be aware that ‘conjunctivitis’ may represent serious eye involvement from WG and liaison with an ophthalmologist is desirable. Mucous membrane pemphigoid is an important differential diagnosis and should be excluded in all cases. A significant association exists between conjunctival disease and subglottic stenosis [4]. Subglottic stenosis can rapidly progress, leading to laryngeal obstruction and respiratory failure [7]. Our patient continues to be closely monitored and is currently stable.

Conflict of interest statement. None declared.


References


doi:10.1093/ndt/gfl352

Advance Access publication 5 July 2006