Spinal Cord (2002) 40, 48–49

www.nature.com/sc

Letter to the Editor

Clopidogrel and recurrent severe haematuria in a patient with paraplegia

Individuals with spinal cord injury (SCI) are more likely to die from heart disease, and at an earlier age, than the able-bodied population, and a clustering of risk factors associated with ischaemic heart disease (including hyperlipidemia, hypertension and diabetes mellitus) has been demonstrated in them.[1] It is therefore likely that some people with SCI will be taking anti-platelet drugs, including glycoprotein IIb/IIIa (GP IIb/IIIa) inhibitors such as clopidogrel.

Clopidogrel inhibits platelet aggregation by selectively blocking the binding of adenosine diphosphate (ADP) to its platelet receptor, and subsequent ADP-mediated activation of the GP IIb/IIIa complex. Because it irreversibly modifies the platelet ADP receptor, platelets exposed to clopidogrel are affected for the remainder of their life span. Repeated doses of 75 mg per day of clopidogrel produce substantial inhibition of ADP-induced platelet aggregation from the first day. After stopping clopidogrel, platelet aggregation and the bleeding times gradually return to baseline values, usually within 5 days. The overall incidence of bleeding in the patients taking clopidogrel is 9.3%; gastrointestinal bleeding occurs in 2.0%, and 0.7% need hospitalisation.[2]

We report a patient with paraplegia, who was taking clopidogrel and who developed severe recurrent haematuria following cystoscopy, removal of bladder stones and bladder biopsy.

Case report

A 56-year-old male developed paraplegia following aortic aneurysm repair. He also suffered from transient ischaemic attacks, for which he was prescribed aspirin 75 mg and clopidogrel 75 mg. Bladder drainage was by a long-term indwelling urethral catheter, and he subsequently developed bladder stones. Cystoscopy revealed highly congested bladder mucosa. The stones were flushed out and a cold cup biopsy of bladder mucosa was performed, the biopsy site being fulgurated with diathermy. Urine was noted to be clear at the end of the procedure. About 9 h later, the patient developed haematuria, which became progressively severe over the next few days, requiring continuous bladder irrigation through a 22 Fr. three-way Foley catheter.

Histology of the bladder biopsy showed moderate chronic inflammation with an acute inflammatory component. Although the biopsy section showed presence of blood vessels, it did not contain any blood vessel of sufficient size to explain such marked post-biopsy bleeding (Figure 1). Clopidogrel was stopped and haematuria subsided over the next 5–7 days, following which clopidogrel was then recommenced. Seven weeks later, he again developed severe haematuria. Clopidogrel was discontinued once again and he was instead prescribed dalteparin sodium (2500 units subcutaneously once a day). Haematuria subsided gradually during the course of next week.

On an abdominal computerised tomography (CT) scan and ultrasound examination, the right kidney was normal while the left contained a parapelvic cyst measuring 4 cm in diameter, with some calcification but no irregular thickening

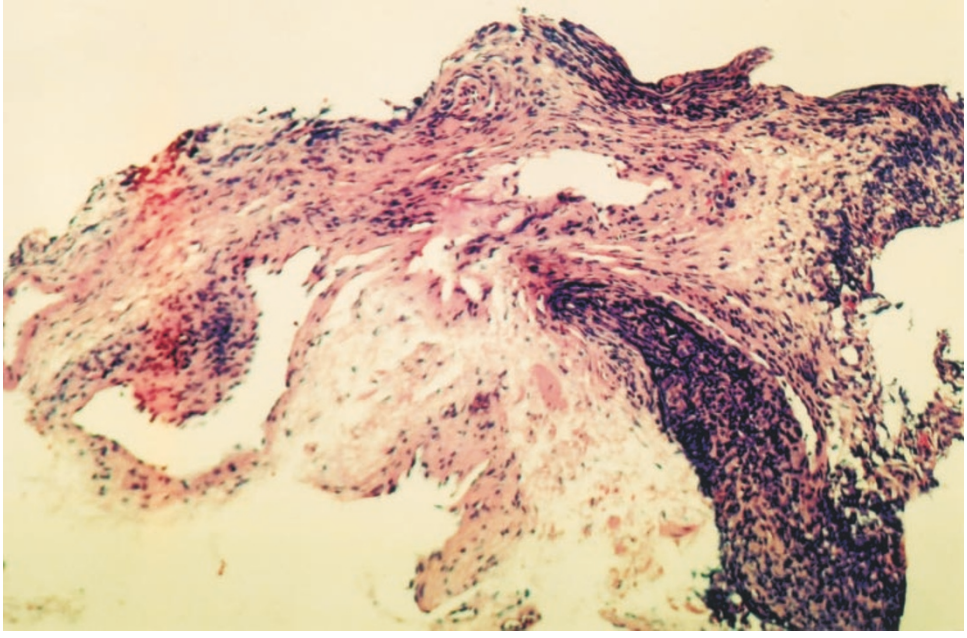

Figure 1 Photomicrograph of bladder biopsy showing moderate chronic inflammation with a minor acute inflammatory component. Two or three vessels of moderate size are included. The urothelium is largely denuded in this section

of the cyst wall. No other lesion was demonstrated that could account for the haematuria.

He was discharged home on aspirin and dalteparin sodium. He now takes warfarin and wears a penile sheath for drainage of his neuropathic bladder; he is doing very well. Follow-up CT scan of the kidneys showed no subsequent changes in size of the left parapelvic cyst (which appeared benign), no alteration in the associated calcification and no evidence of any related soft tissue abnormality.

Discussion

As this case illustrates, significant bleeding can occur in the patients who continue to take anti-platelet drugs during invasive operative procedures. For this reason, Zhu and associates from Denmark[3] recommended stopping aspirin 1 week prior to all invasive urological procedures. On the other hand, patients who stop taking such drugs risk developing thrombotic or embolic phenomena. In our case, we were indeed concerned that our patient might develop just such a major ischaemic episode if he were to stop taking his anti-platelet drugs before the procedure, and we therefore did not advise him to do so. Such risks are not merely theoretical: when anticoagulant therapy was stopped prior to dental surgery, five patients out of 526 (0.95%) suffered serious embolic complications, and four of these died.[4] Furthermore, Ardekian and associates[5] showed that aspirin therapy can safely be continued during oral surgery, as local haemostasis is sufficient to control bleeding. Opinion and practice vary widely between radiologists and urologists in the United Kingdom with regard to stopping aspirin and warfarin before prostate biopsy: 52% of radiologists compared with 27% of urologists advocate stopping such drugs before the biopsy.[6]

Thus the potential complication of bleeding after an invasive urological procedure must be balanced against the risk of developing a thrombotic episode when anti-platelet drugs such as clopidogrel are discontinued, particularly in those (including SCI patients) who are already at high risk of developing heart disease. It may be that the chronically inflamed neuropathic bladder is somwhat more prone to post-biopsy haemorrhage than the healthy bladder. As is often the case in medicine, a therapeutic tightrope must be walked, and in the end each case must be decided on its own merits.

S Vaidyanathan[1], BM Soni[1], G Singh[1], PL Hughes[2] and P Mansour[3]

[1]Regional Spinal Injuries Centre, District General Hospital, Southport PR8 6PN, UK; [2]Department of Radiology, District General Hospital, Southport PR8 6PN, UK; [3]Department of Cellular Pathology, District General Hospital, Southport PR8 6PN, UK

Acknowledgements

Our gratitude to Pannone & Partners, Solicitors, (cathy.leech@pannone.co.uk), 123 Deansgate, Manchester, M3 2BU, UK, for kindly sponsoring the printing of the colour illustration. Pannone & Partners (www.pannone.com) are delighted to be able to support this publication in *Spinal Cord*.

References

1 Bauman WA, Kahn NN, Grimm DR, Spungen AM. Risk factors for atherogenesis and cardiovascular autonomic function in persons with spinal cord injury. *Spinal Cord* 1999; **37:** 601 – 616.

2 The Association of the British Pharmaceutical Industry (ABPI) Compendium of Data Sheets and Summaries of Product Characteristics 1999 – 2000; pp 252 – 254.

3 Zhu JP, Davidsen MB, Meyhoff HH. Aspirin, a silent, risk factor in urology. *Scand J Urol Nephrol* 1995; **29:** 369 – 374.

4 Wahl MJ *et al*. Myths of dental surgery in patients receiving anticoagulant therapy. *J Am Dent Assoc* 2000; **131:** 77 – 81.

5 Ardekian L *et al*. Does low-dose aspirin therapy complicate oral surgical procedures? *J Am Dent Assoc* 2000; **131:** 331 – 335.

6 Connor SE, Wingate JP. Management of patients treated with aspirin or warfarin and evaluation of haemostasis prior to prostatic biopsy: a survey of current practice amongst radiologists and urologists. *Clin Radiol* 1999; **54:** 598 – 603.