Henoch-Schönlein Purpura Associated with Adult Human Immunodeficiency Virus Infection: Case Report and Review of the Literature

Dear Editor,

Henoch-Schönlein purpura (HSP) is an immunoglobulin (Ig) A–mediated small vessel vasculitis that occurs uncommonly among adults and even more rarely in individuals infected with the human immunodeficiency virus (HIV). There are overlapping clinical features between HIV-associated nephropathy, HSP and secondary IgA nephropathy. However the systemic associations of HSP are uncommon in the other 2 conditions. The management is also very different. We report a case of a Singaporean man with HIV infection, who presented with classical signs and symptoms as well as pathologic findings consistent with adult HSP.

Case Report

A 59-year-old Chinese Singaporean man was diagnosed with HIV infection with a CD4 count of 64 cells/mm^3 in a tertiary hospital. His hepatitis B and C serologies (HBsAg, total antiHBc Ab, antiHCV Ab) were negative. He was also diagnosed to have diabetes mellitus, hypertension and hyperlipidemia. He was started on combination antiretroviral therapy (cART) with stavudine, lamivudine and efavirenz. On initial follow-up, his CD4 count remained low at 83 cells/mm^3 but he achieved viral suppression (HIV-1 RNA <40 copies/mL) 6 months later. However, he was subsequently lost to follow-up and discontinued cART due to financial difficulties. He next presented to our hospital with a week of non-colicky abdominal pain, diarrhoea and blood streaked stools associated with vomiting a year after stopping cART. He had no fever, headache nor respiratory symptoms. Physical examination was remarkable for the presence of multiple pinhead size petechiae over the dorsum of both feet (Fig.1a) and periumbilical area (Fig. 1b). Initial investigations showed normal platelet counts, coagulation

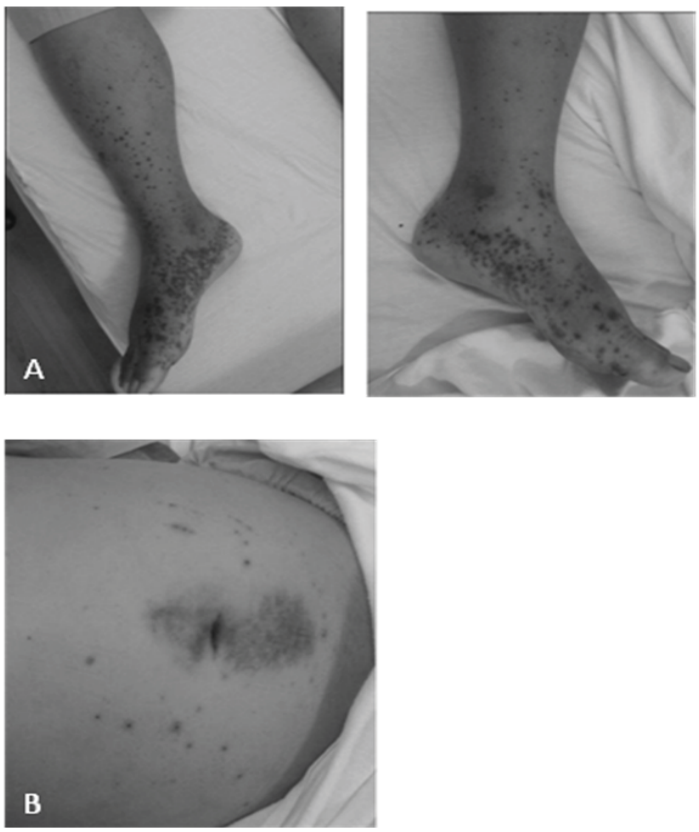

Fig. 1 (a) (Top) Initial petechial rash that progressed in size and numbers into palpable purpura in the lower limbs, and (b) (bottom) initial petechial rash over periumbilical area.

and liver profile. However, renal panel showed an acute kidney injury (urea 19.9 mmol/L, creatinine 130 mmol/L) with hyponatremia (sodium 127 mmol/L) and hypokalemia (potassium 3.0 mmol/L).

His CD4 lymphocyte count was 51 cells/mm^3 and HIV-1 RNA was 4.71 x 10^5 copies/mL (log 5.67). Septic workup including blood, urine and stool cultures was negative. Urine analysis was remarkable for microscopic haematuria with dysmorphic red blood cells 524 cells/HPF, and proteinuria with a urine protein-to-creatinine of ratio 0.17 g/mmol. C-reactive protein was elevated at 75 mg/L. Additional blood investigations including anti-nuclear antibody, anti-double stranded DNA, anti-myeloperoxidase, anti-PR3, PCR for DNA of cytomegalovirus, parvovirus B19, cryoglobulin and myeloma panel were all negative. His serum complement component C3 was mildly reduced to 46 mg/dL (normal range 85 to 185 mg/dL) and C4 was within normal range.

His vital signs were stable initially and his renal profile slightly improved with hydration (urea 16 mmol/L, creatinine 124 mmol/L). The palpable purpura increased in number and sizes after 5 days, appearing on the dorsum of his hands. A skin biopsy was done revealing leucocytoclastic vasculitis involving small vessels with antibodies to IgA and C3 deposition in the dermal blood vessels on direct immunofluorescence which were consistent with a diagnosis of HSP. His platelet and coagulation profile remained within normal limits.

Haemodialysis was initiated due to severe metabolic acidosis and worsening renal profile. Renal ultrasound revealed normal kidneys with no obstruction. He was started on intravenous hydrocortisone 100 mg every 6 hours when his abdominal pain recurred. His previous cART was restarted to improve his immune status. Subsequently, he developed severe gastrointestinal bleeding. He underwent plasma exchange as his abdominal symptoms and renal failure did not respond to steroids. Gastroduodenoscopy and colonoscopy showed ulcers in the duodenum and rectosigmoid. Abdominal computed tomography angiography showed diffuse enterocolitis with active intraluminal bleeding. He was also treated for *Clostridium difficile* colitis with intravenous metronidazole and oral vancomycin as well as cytomegalovirus (CMV) colitis which was treated with intravenous ganciclovir based on immunohistochemical evidence of CMV in a small bowel biopsy. Unfortunately, he died from severe bleeding despite repeated embolisation 5 weeks after admission.

Discussion

A clinical diagnosis of HSP was made in this case based on the appearance of a palpable purpuric rash in the typical adult distribution following a week of gastrointestinal symptoms and was confirmed histologically by skin biopsy. This has been described in adult onset HSP in which rash predominates with arthritis, gastrointestinal (GI) disease and renal disease.[1] Adult HSP is generally more severe, and the risk of progression to renal impairment including end stage renal failure has been reported to be around 30%.[2] GI symptoms may be the first symptoms as in our patient due to submucosal haemorrhage and oedema.

Although HIV is common worldwide, rheumatic manifestations of HIV including HSP are not well reported. The aetiology and pathogenesis of HSP in HIV is not very well understood. HIV may have direct effect on the vascular endothelium or by causing immune activation resulting in hypergammmaglobulinemia and high circulation of immune complexes. Our patient had advanced HIV disease with very low CD4 count when he presented with symptoms of HSP, similar to a cohort of HIV patients with rheumatological manifestations reported from China.[3] He had however, been previously treated with cART and achieved virologic suppression before his treatment was interrupted. This has been reported to be associated with HSP in one case report.[4]

The use of glucocorticoids is controversial in the management of HSP. Although results are conflicting, Methylprednisolone pulse therapy and prednisone are widely used as are other immunomodulating agents.[5,6] Our patient received plasma exchange with haemodialysis when he developed life-threatening gastrointestinal haemorrhage that was thought to be due to vasculitic lesions of HSP.[7] However, it is also possible that the *Clostridium difficile* associated diarrhea and cytomegalovirus colitis contributed significantly to our patient's eventual demise in addition to his uncommon rheumatic manifestation of his underlying HIV.

Conclusion

In summary, rheumatic manifestations of HIV such as HSP although rare, might be under-reported and recognised. They can have serious and even fatal consequences as in our patient. Clinicians managing HIV even in the modern era of highly active anti-retroviral treatment need to be aware of rheumatologic manifestations of the disease especially as more patients reconstitute their immune systems through effective therapy. This will help to ensure good outcomes for our patients.

REFERENCES

1. Jithpratuck W, Elshenawy Y, Saleh H, Youngberg G, Chi DS, Krishnaswamy G. The clinical implications of adult-onset henoch-schonelin purpura. Clin Mol Allergy 2011;9:9.
2. Hung SP, Yang YH, Lin YT, Wang LC, Lee JH, Chiang BL. Clinical manifestations and outcomes of Henoch-Schonlein purpura: comparison between adults and children. Pediatr Neonatol 2009;50:162-8.
3. Zhang X, Li H, Li T, Zhang F, Han Y. Distinctive rheumatic manifestation in 98 patients with human immunodeficiency virus infection in China. J Rheumatol 2007;34:1760-4.
4. Bunupuradah T, Puthanakit T, Pancharoen C, Butterworth O, Phanuphak P, Ananworanich J. Henoch-Scholein purpura and thrombocytopenia after planned antiretroviral treatment interruption in a Thai girl with HIV infection. Int J Infect Dis 2009;13:e31-3.
5. Weiss PF, Feinstein JA, Luan X, Burnham JM, Feudtner C. Effects of corticosteroid on Henoch-Schönlein purpura: a systematic review. Pediatrics 2007;120:1079-87.
6. Weiss PF, Klink AJ, Localio R, Hall M, Hexem K, Burnham JM, et al. Corticosteroids may improve clinical outcomes during hospitalization for Henoch-Schönlein purpura. Pediatrics 2010;126:674-81.
7. Mahr A, Chaigne-Delalande S, De Menthon M. Therapeutic plasma exchange in systemic vasculitis: an update on indications and results. Curr Opin Rheumatol 2012;24:261-6.

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