

- 2006; 35: 233-6.
- AMANN-VESTI BR, KOPPENSTEINER R, RAINONI L, PFAMATTER T, SCHNEIDER E: Immediate and long-term outcome of upper extremity balloon angioplasty in giant cell arteritis. *J Endovasc Ther* 2003; 10: 371-5.
 - BOTH M, ARIES PM, MULLER-HULSBECK S *et al.*: Balloon angioplasty of arteries of the upper extremities in patients with extracranial giant-cell arteritis. *Ann Rheum Dis* 2006; 65: 1124-30.
 - BOTH M, JAHNKE T, REINHOLD-KELLER E *et al.*: Percutaneous management of occlusive arterial disease associated with vasculitis: a single center experience. *Cardiovasc Intervent Radiol* 2003; 26: 19-26.
 - HOFFMAN GS, CID MC, HELLMANN DB *et al.*: A multicenter, randomized, double-blind, placebo-controlled trial of adjuvant methotrexate treatment for giant cell arteritis. *Arthritis Rheum* 2002; 46: 1309-18.
 - DASGUPTA M, HASSAN N; BRITISH SOCIETY FOR RHEUMATOLOGY GUIDELINES GROUP: Giant cell arteritis: recent advances and guidelines for management. *Clin Exp Rheumatol* 2007; 25 (Suppl. 44): S62-5.

Henoch-Schönlein purpura associated with pidotimod therapy

Sirs,

Henoch-Schönlein purpura (HSP) is a small-sized vasculitis affecting mainly children and young adults. The mean age of patients is six years; 90% of patients are under ten years of age (1, 2).

A wide variety of drugs, pathogens and other environmental exposures have been associated with HSP. Although the precise etiology of the disease is unknown, it is clear that antigenic stimuli causing elevation of circulating Immunoglobulin A (IgA) have a pivotal role in the pathogenesis of HSP (3). The clinical manifestations of HSP are a consequence of widespread vasculitis resulting from IgA deposition in vessel walls and the renal mesangium (3, 4). HSP is characterized by palpable, non-thrombocytopenic purpura, arthritis and/or arthralgia, abdominal pain, gastrointestinal haemorrhage and/or nephritis (2).

We report the first case of HSP associated with treatment with pidotimod.

A nine-year-old female came under our observation in January 2007 for a non-pruritic palpable purpuric rash with lower limb predominance, diffuse abdominal pain and arthritis involving knees and ankles; the arthritis was painful and inhibited walking. Laboratory analysis showed a white blood cell count of $8.45 \times 10^3/\text{mm}^3$ and a platelet

count of $357 \times 10^3/\text{mm}^3$. Serum IgA were slightly increased. C-reactive protein, erythrocyte sedimentation rate, kidney function and urine sediment were normal. Antistreptolysin was not increased. Antinuclear antibodies, cryoglobulins and antineutrophilic cytoplasmic antibodies (perinuclear and cytoplasmic patterns) were negative.

The patient had started treatment with pidotimod 400 mg per day eight days before her visit due to recurring tonsil infections and adenoid-tonsillar hypertrophy. She had had her last infection three months earlier, and she was living with her parents who were in good health.

Pidotimod ((R)-3-[(S)-(5-oxo-2-pyrrolidinyl) carbonyl]-thiazolidine-4-carboxylic acid, PGT/1A, CAS 121808-62-6) is a synthetic biological response modifier which acts by stimulating cell-mediated immunity (5) and which has been shown to enhance several immune parameters in humans, both *in vitro* and *in vivo* (6, 7). Pidotimod is active on T-lymphocytes in early maturation stage (8) and is able to enhance peripheral blood mononuclear cell proliferation through an increased interleukin-2 production (IL-2) (7). IL-2 has been shown to induce interleukin-5 (IL-5) production by T-lymphocytes, in a dose-dependent manner, and IL-5 induces IgA production from B-lymphocytes and is also recognized by its activity as an IgA-enhancing factor (9).

She was diagnosed with drug related HSP and discontinuation of the drug led to a complete resolution of the disease; abdominal pain was resolved in four days, purpuric rash disappeared within ten days and arthritis improved over the following two weeks. The occurrence of HSP was probably related to pidotimod therapy.

There was a close temporal relationship between drug ingestion and onset of symptoms and when its intake was interrupted the patient's clinical picture improved.

For this reason, and on the basis of the Naranjo algorithm (10), adverse drug reaction could be considered possible and we believe that our patient may represent the first clear evidence of a relationship between HSP and pidotimod treatment.

Although this is the first report of HSP associated with pidotimod, clinicians should be aware of a possible association between HSP and the intake of pidotimod; it is also possible that the intake of cell mediated immunity stimulating drugs may trigger the development of cell mediated immunity diseases in genetically predisposed patients.

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References

- CALVINO MC, LLORCA J, GARCIA-PORRUA C, FERNANDEZ-INGLESIA S JL, RODRIGUEZ-LEDO P, GONZALEZ-GAY MA: Henoch-Schönlein purpura in children from northwestern Spain: a 20-year epidemiologic and clinical study. *Medicine* 2001; 80: 279-90.
- TRAPANI S, MICHELI A, GRISOLIA F *et al.*: Henoch-Schönlein purpura in childhood: epidemiological and clinical analysis of 150 cases over a 5-year period and review of literature. *Semin Arthritis Rheum* 2005; 35: 143-53.
- SAULSBURY FT: Henoch-Schönlein purpura. *Curr Opin Rheumatol* 2001; 13: 35-40.
- SAULSBURY FT: Clinical update: Henoch-Schönlein purpura. *Lancet* 2007; 369: 976-8.
- COPPI G, MANZARDO S: Experimental immunological screening tests on Pidotimod. *Arzneimittelforschung* 1994; 44:1411-6.
- PUGLIESE A, GIRARDELLO R, MARINELLI L, FORNO B, PATTARINO PL, BIGLINO A: Evaluation of Pidotimod effects on some immune parameters. *J Chemother* 1991; 3: 144.
- AUTERI A, PASQUI AL, GOTTI G *et al.*: The effect of a new biological response modifier (Pidotimod) on surgery-associated immunodeficiency. *Int J Immunotherapy* 1993; IX: 95.
- BENETTI GP, FUGAZZA L, STRAMBA BADIALE M *et al.*: *Ex vivo* evaluation of pidotimod activity on cell-mediated immunity. *Arzneimittelforschung* 1994; 44: 1476-9.
- KURAOKA M, HASHIGUCHI M, HACHIMURA S, KAMINOGAWA S: CD4-c-kitCD3εIL-2Rα⁺ Peyer's patch cells are a novel cell subset which secrete IL-5 in response to IL-2: implications for their role in IgA production. *Eur J Immunol* 2004; 34: 1920-9.
- NARANJO CA, BUSTO U, SELLERS EM *et al.*: A method for estimating the probability of adverse drug reactions. *Clin Pharmacol Ther* 1981; 30: 239-45.