



Henoch-Scholein Purpura Related to Fluoxetine Medication in a Child

Kun-Long Hung^{1,2}, Ying-Hsiang Chuo^{1†}, Chien-Han Chen¹, Yung-Hsien Huang¹

ABSTRACT

Background: Fluoxetine, one kind of selective serotonin reuptake inhibitors (SSRI), has rarely been reported to be related to vasculitis in adults.

Methods: Herein we present a boy who developed Henoch–Schönlein purpura (HSP) during treatment with fluoxetine.

Results: This 8-year-old boy suffered from depression about 3 months after he entered a new school. He visited a psychiatric clinic and fluoxetine was prescribed. The response was good and he went back to school smoothly. Sixth weeks later, he developed purpuric rash over bilateral lower extremities which extended to buttock and hands in two days. Mild painful swelling over left ankle was also noted when he was admitted. The investigations were normal including complete blood cell & platelet count, blood biochemistry, liver function tests, prothrombin time, partial thromboplastin time, serum immunoglobulin A and fibrinogen level. Yet D-dimer level was elevated to 8927 µg/dl (normal < 500), consistent with vasculitis. The diagnosis of HSP was made and fluoxetine ceased. Treatment was given with Prednisolone and Ranitidine, after which the purpura resolved in one week.

Conclusions: HSP related to fluoxetine medication has rarely been reported in the young adults. Our case may attribute to be the youngest one who receives fluoxetine therapy and give us an example of the potential adverse effect of fluoxetine to the children.

Keywords

Henoch-Scholein Purpura, Vasculitis

Introduction

Henoch–Schönlein purpura has been a common systemic vasculitis in children. It usually presents with a triad of purpura, arthritis/arthralgia, and abdominal pain or renal disease (tetrad) [1]. This disease is characterized by the deposition of immunoglobulin IgA immune complexes presented in the vessel walls of arterioles, capillaries and venules. HSP belongs to the group of nongranulomatous, predominantly

small vessel vasculitides, according to the new classification of childhood vasculitis [2].

HSP patients frequently have a preceding trigger of respiratory tract infection, with the common pathogens of streptococcus, staphylococcus, virus and mycoplasma [3,4]. Vaccination is another trigger factor [5]. The association between drug and HSP has also been implicated in several reports [6–8]. Herein we present a boy who developed HSP during treatment with fluoxetine.

¹Department of Pediatrics, Fu-Jen Catholic University Hospital, New Taipei, Taiwan

²School of Medicine, Fu-Jen Catholic University, New Taipei, Taiwan

[†]Author for correspondence: Ying-Hsiang Chuo, Department of Pediatrics, Fu-Jen Catholic University Hospital, New Taipei, Taiwan, Tel: +886-2-85128867, email: yinghsiangchuo@gmail.com



Figure 3: Purpuric skin changes in the patient with HSP.

Case Report

This 8-year-old boy suffered from depression about 3 months after he entered a new school. He visited a psychiatric clinic and fluoxetine was prescribed. The response was good and he went back to school smoothly. Six weeks later, he developed purpuric rash over bilateral lower extremities which extended to buttock and hands in two days (Figure 1). Most of the purpuras were slightly palpable without blanching when pressed. Mild painful swelling over left ankle was also noted when he was admitted. No abdominal pain was felt at all. The other physical findings were non-contributory. The investigations were normal including complete blood cell & platelet count, blood biochemistry, liver function tests, prothrombin time and partial thromboplastin time. Serum immunoglobulin A was 297 mg/dl (normal range: 70-400) and fibrinogen level 237mg/dl (normal range: 180-350). Serum antinuclear antibody was negative. The stool & urine analysis showed normal findings. Yet D-dimer level was elevated to 8927 $\mu\text{g}/\text{dl}$

(normal < 500), consistent with vasculitis. The diagnosis of HSP was made. According to the Adverse Drug Reaction (ADR) Probability Scale (Naranjo Scale) [9], the ADR probability score was 4 (possible association) and fluoxetine was stopped. Treatment was given with Prednisolone and Ranitidine, after which the purpura resolved in one week. The patient eventually outgrew depression and skin rash without further medication during the following months.

Discussion

The association between drugs and HSP has been reported in many studies, though the role of drug in the pathogenesis of HSP is uncertain. Among the drugs reported to be related to the development of HSP, there have been antibiotics [10], anti-emetics [11], analgesia [12], anticoagulants [13], anticonvulsants [14], TNF- α inhibitors [15] for autoimmune diseases, anti-hypertensive [16], anti-neoplastic [17] and anti-arrhythmic agents [18], as well as antidepressants [19].

Many antidepressants may induce a variety of skin reactions [19,20]. The common and less risk drug reactions contain drug-induced urticaria, maculopapular rash, photo-sensitivity and fixed drug reactions. Besides, there are severe skin complications associated with antidepressants, reported as erythema multiforme, Stevens-Johnson syndrome, toxic epidermal necrolysis and drug hypersensitivity vasculitis including HSP. There have been few reports [19,20], mostly from adult patients, describing on vasculitis related to selective serotonin reuptake inhibitors (SSRI). Fluoxetine, one kind of SSRI, has rarely been reported to be related to vasculitis in adolescents and young adults. In children,

there was only one ever reported on a 15 years old boy, as searched in the literature [21-23].

He had fluoxetine medication for 1 week, due to depression from his father's death. He then developed generalized purpuric rash over lower legs associated with ankle and knee pain. The laboratory investigations showed almost normal except high level of D-dimer (3468 µg/dl) and mild proteinuria. The Naranjo scale was 6, which belonged to a probable causative association. Our case has the similar clinical picture, yet may attribute to be the youngest one who receives fluoxetine therapy. It could give us an example about the potential adverse effect of fluoxetine to the children.

References

- Trnka P. Henoch-Schönlein purpura in children. *J. Paediatr. Child. Health* 49(12), 995-1003 (2013).
- Ozen S, Ruperto N, Dillon MJ, et al. EULAR/PReS endorsed consensus criteria for the classification of childhood vasculitides. *Ann. Rheum. Dis* 65(7), 936-941 (2006).
- Weiss PF, Klink AJ, Luan X, et al. Temporal association of Streptococcus, Staphylococcus, and parainfluenza pediatric hospitalizations and hospitalized cases of Henoch-Schönlein purpura. *J. Rheumatol* 37(12), 2587-2594 (2010).
- Kano Y, Mitsuyama Y, Hirahara K, et al. Mycoplasma pneumoniae infection-induced erythema nodosum, anaphylactoid purpura, and acute urticaria in 3 people in a single family. *J. Am. Acad. Dermatol* 57(1), S33-S35 (2007).
- Watanabe T. Henoch-Schönlein purpura following influenza vaccinations during the pandemic of influenza A (H1N1). *Pediatr. Nephrol* 26(5), 795-798 (2011).
- Rolle AS, Zimmermann B, Poon SH. Etanercept-induced Henoch-Schönlein purpura in a patient with ankylosing spondylitis. *J. Clin. Rheumatol* 9(2), 90-93 (2013).
- Conti-Beltraminelli M, Pagani O, Ballerini G, et al. Henoch-Schönlein purpura (HSP) during treatment with anastrozole. *Ann. Oncol* 18(1), 131-134 (2006).
- Borrás-Blasco J, Enriquez R, Amoros F, et al. Henoch-Schönlein purpura associated with clarithromycin. Case report and review of literature. *Int. J. Clin. Pharmacol. Ther* 41(5):213-216 (2003).
- Naranjo CA, Busto U, Sellers EM, et al. A method for estimating the probability of adverse drug reactions. *Clin. Pharmacol. Ther* 30(2), 239-245 (1981).
- Wakefield IR, Hunter DA. Antibiotic associated Henoch-Schönlein purpura syndrome. *Br. J. Clin. Pract* 42(12), 525-526 (1988).
- Upputuri S, Prasad S. Metoclopramide-induced delayed non-thrombocytopenic purpuric rash. *Clin. Drug. Investig* 6(12), 745-747 (2006).
- Santoro D, Stella M, Castellino S. Henoch-Schönlein purpura associated with acetaminophen and codeine. *Clin. Nephrol* 66(2):131-134 (2006).
- Borrás-Blasco J, Girona E, Navarro-Ruiz A, et al. Acenocoumarol-induced Henoch-Schönlein purpura. *Ann. Pharmacother* 38(2), 261-264 (2004).
- Kaneko K, Igarashi J, Suzuki Y, Nijima S, Ishimoto K, Yabuta K. Carbamazepine-induced thrombocytopenia and leucopenia complicated by Henoch-Schönlein purpura symptoms. *Eur. J. Pediatr* 152(9), 769-770 (1993).
- Asahina A, Ohshima N, Nakayama H, et al. Henoch-Schönlein purpura in a patient with rheumatoid arthritis receiving etanercept. *Eur. J. Dermatol* 20(4), 521-522 (2010).
- Moots RJ, Keeling PJ, Morgan SH. Adult Schönlein-Henoch purpura after enalapril. *Lancet* 340(8814), 04-305 (1992).
- Aktas B, Topcuoglu P, Kurt OK, et al. Severe Henoch-Schönlein purpura induced by cytarabine. *Ann. Pharmacother* 43(4), 792-793 (2009).
- Kuo M, Winiarski N, Garella S. Nonthrombocytopenic purpura associated sequentially with nifedipine and diltiazem. *Ann. Pharmacother* 26(9), 1089-1090 (1992).
- Margolese HC, Chouinard G, Beauclair L, Rubino M. Cutaneous vasculitis induced by paroxetine. *Am. J. Psychiatry* 158(3), 497-497 (2001).
- Herstowska M, Komorowska O, Cubata WJ, et al. Severe skin complications in patients treated with antidepressants: a literature review. *Postepy. Dermatol. Alergol* 31(2), 92-97 (2014).
- Welsh JP, Cusack CA, Ko C. Urticarial vasculitis secondary to paroxetine. *J. Drugs. Dermatol* 5(10), 1012-1014 (2006).
- Cederberg J, Knight S, Svenson S, et al. Itch and skin rash from chocolate during fluoxetine and sertraline treatment: case report. *BMC Psychiatry* 4, 36 (2004).
- Süleyman A, Kurt FS, Soyata AZ, et al. Henoch-Schönlein purpura during treatment with fluoxetine. *J. Child. Adolescent. Psychopharmacol* 26(7), 651-651 (2016).