

Henoch-Schonlein Purpura following Anti Diphtheria, Tetanus, Acellular Pertussis and Inactivated Polio (DTaP-IPV) Vaccine: A Case Report

Sara De Nitto, Pasquale Stefanizzi, Katia Nicoletta Malcangi, Francesco Paolo Bianchi, Silvio Tafuri*

Department of Biomedical Science and Human Oncology, Aldo Moro University of Bari, Italy

***Corresponding author:** Silvio Tafuri, Department of Biomedical Science and Human Oncology, Aldo Moro University of Bari, Piazza Giulio Cesare 11, 70124 Bari, Italy. Tel: +39 0805478473; Fax: +39 0805478472; Email: silvio.tafuri@uniba.it

Citation: De Nitto S, Stefanizzi P, Malcangi KN, Bianchi FP, Tafuri S (2019) Henoch-Schonlein Purpura following Anti Diphtheria, Tetanus, Acellular Pertussis and Inactivated Polio (DTaP-IPV) Vaccine: A Case Report. Ann Case Report 12: 264. DOI: 10.29011/2574-7754/100264

Received Date: 22 October, 2019; **Accepted Date:** 10 December, 2019; **Published Date:** 15 October, 2019

Abstract

Background: HSP is the most common vasculitis in childhood. It is a systematic vasculitis disease, and mainly affects the small vessels of skin, joints, gastrointestinal tract, and kidneys. Its etiology and pathogenesis remain unknown despite the fact that a variety of factors, mainly infectious agents, drugs and vaccines have been suggested as triggers for the disease.

Case Presentation: A case of Henoch-Schönlein purpura occurred in a 6-year-old girl who 57 days before the onset of the disease received DTaP -IPV vaccine. The girl experienced, at the age of 15 months, an autoimmune hemolytic anemia 8 days after the administration of hexavalent vaccine.

Conclusions: Henoch-Schönlein purpura has been described after several vaccines, but never after DTaP-IPV vaccine; one case is not sufficient to postulate an association between vaccination and the disease but for the future, in case of other similar reports, Drug safety authorities have to evaluate the implementation of a specific surveillance program.

Keywords: Children; Henoch Schonlein Purpura; Vaccine

List of Abbreviations: DTaP-IPV: Diphtheria, Tetanus, Acellular Pertussis and Inactivated Polio; HSP: Henoch-Schönlein Purpura; FDPs: Fibrin Degradation Products; AST: Aspartate Aminotransferase; ALT: Alanine Aminotransferase; GGT: Gamma-Glutamyltranspeptidase; RF: Rheumatoid Factor; ASO: Streptolysin-O; MMR: Measles-Mumps-Rubella; WHO: World Health Organization

Introduction

Henoch-Schönlein Purpura (HSP) is the most common childhood vasculitis, that affects 10-20 children per 100,000 per year. More than 90% of patients affected by HSP are < 10 years of age, and the average age of insurgence is around 6 years [1, 2]. HSP is a leukocytoclastic vasculitis involving small vessels [3]. Clinical presentation includes cutaneous palpable purpura, joint pain, renal involvement, colicky abdominal pain and gastrointestinal bleeding [4]. The disease is usually self-limiting, except for serious gastrointestinal or renal involvement; long-term prognosis is generally good. The pathophysiology behind HSP

is not yet completely understood [5]. Because of the mechanism of pathogenesis of HSP is vasculitis, coagulation test results generally normal, except for Fibrin Degradation Products (FDPs), such as D-dimer, that are significantly increased in a very high proportion of HSP patients. These specific laboratory findings (normal coagulation assays with elevated FDPs and D-dimer) are helpful in diagnosing HSP [6]. HSP is currently diagnosed based on symptoms and signs and histopathological findings.

There are currently no specific biomarkers useful for diagnosis of HSP. Some biomarkers can show activity and could be related with the prognosis of the disease, but none have proven clinically useful [7, 8]. Although many antigens, such as foods, infective agents, drugs, and insect bites have been reported to be related to HSP, the causes of this disease remain unclear. HSP has also been reported after the administration of several vaccines. Some studies hypothesized that, after the administration of a vaccine, vaccine antigens and native antibodies could form immunocomplexes. An abnormal activation of the vaccine itself, involving triggering of autoreactive T cells or a deregulated cytokine network, have been postulated as possible mechanisms of insurgence of HSP. The final result is the deposition of immune complexes at the vessels,

thereby initiating a vasculitic process [9]. We described a case of HSP after DTaP-IPV vaccination.

Case Report

On 23 September 2012, a 6-year-old girl was admitted to emergency room of a hospital in Southern Italy. On admission, examination revealed purpura lesions on the lower extremities and buttocks, abdominal pain, knee joint pain and stiffness. Respiratory rate was 15/min; body temperature 37°C; heart rate 100/min. Pathological anamnesis indicated that, on 26 July 2012 (57 days before hospital admission), Anti-Diphtheria, Tetanus and Acellular Pertussis Vaccine (DTaP) and Inactivated Polio Vaccine (IPV) were administered to the patient. Few days after the administration of the anti-DTaP-IPV vaccine, the patient reported pallor, episodes of vomiting with blood striations, cramp-like abdominal pains, lack of appetite; the symptoms lasted for more than a month. Blood tests and abdominal ultrasound performed few days after the onset of symptoms did not show abnormalities. Remote anamnesis showed also that, on March 2007, at the age of 15 months, 8 days after the administration of 3rd dose of hexavalent (DTaP-IPV-Hib-HBV) vaccine, the girl manifested an autoimmune hemolytic anemia for which she was admitted to a hospital.

During hospitalization the child performed blood transfusions and oral steroid was started and sign and symptoms regressed, then the girl was discharged. At the admission on September 2012, blood chemistry tests showed a white cell count of 16.700 x ml, a platelet count of 437,000/mm³. Biochemical studies revealed serum creatinine of 0.78 mg/dl, blood urea nitrogen of 26 mg/dl, protein 7.47 g/dl, serum albumin of 4.56 g/dl, Aspartate Aminotransferase (AST) 19 IU/L, Alanine Aminotransferase (ALT) 8 IU/L and Gamma-Glutamyltranspeptidase (GGT) 7 g/dl. Erythrocyte sedimentation rate and C-reactive protein level were 26 mm/h and <0.33 mg/dl (<0.5 mg /dl) respectively. Blood coagulation tests showed D-Dimer 623 ng/ml. C3, C4, ANA, AMA, ASMA, APCA, other immunoglobulin levels, Rheumatoid Factor (RF) and Anti Streptolysin-O (ASO) were all negative. Hemocult test and calprotectin were positive. The EBV serology tests showed anti VCA IgG and anti EBNA IgG negative, anti VCA IgM uncertain.

During hospitalization, repeated urinalysis were performed that showed microscopic haematuria, proteinuria, red blood cells, white blood cells, leukocyte esterase 1+, hemoglobin 2+. Serodiagnosis of typhoid fever (S.Typhi AgO, S.Typhi AgH, Paratyphi B) and serodiagnosis of Brucella Melitensis and Mycoplasma Pneumoniae were negative. Abdominal ultrasonography and abdominal x-ray did not show abnormal results. On the third day of hospitalization, intravenous steroid therapy with methylprednisolone started and was carried out for ten days; after ten days, oral steroid therapy was started. She was

discharged about a month after; the diagnosis was “Schonlein-Henoch Purpura complicated by gastrointestinal (hematemesis and recurrent abdominal pain), renal (proteinuria) and articular (knees, elbow and wrist) manifestations”. A pharmacological therapy was recommended, that provided cortisone, calcifediol and pantoprazole and it was taken for about two years because the patient presented other two episodes of Schonlein-Henoch Purpura in November 2012 and in January 2013. The patient’s medical history revealed that in May 2011, she was admitted to the Pediatric Unit for a bilateral reactive arthritis.

Results and Discussion

Our report describes a case of Schonlein-Henoch Purpura in a patient who received Anti-Diphtheria, Tetanus and Acellular Pertussis Vaccine (DTaP) and Inactivated Polio Vaccine (IPV), two months before the onset of symptoms. HSP following vaccine administration has been described in case reports and in a small number of observational studies conducted during vaccination campaigns. Cases have been reported following several vaccines, including polysaccharide and conjugate meningococcal C vaccines, and in this case researchers supposed that vasculitis results from an immunological response to meningococcal antigen, but a causal relationship has not been established [10]. HSP has also been associated with the influenza vaccine, Measles-Mumps-Rubella (MMR) vaccine, meningococcal B and meningococcal ACYW135 vaccine [11-15]. A case-control study published in 2016, described 4 cases of HSP occurred after Diphtheria, Tetanus, Acellular Pertussis (DTaP) vaccine but the general quality of analysis was badly affected by the lack of causality assessment [16].

There is not consensus about the interval between vaccine administration and the development of HSP, but in a short report published in 2015 that describes some cases of HSP associated with meningococcal B vaccine, it was observed a clustering of cases occurred within the first 18 weeks after vaccination [14]. Researchers discussed two possible intervals: onset within a few days of vaccination (which are more consistent with hypersensitivity reactions) or within weeks or months (which are more consistent with delayed immune reactions). In conclusion, latency periods can range from days to years for post vaccination autoimmunity [9]. In our case, HSP has reported 8 weeks after the administration of DTaP-IPV vaccine and we can consider this time interval consistent with an immune reaction. Furthermore, 5 years earlier, our patient had already presented an autoimmune hemolytic anemia episode after the administration of 3rd dose of hexavalent vaccination. Autoimmune hemolytic anemia is a disease characterized by the destruction of red blood cells (hemolysis) by autoantibodies directed against the antigens (proteins) present on their surface. Also in this case, the relation with the vaccine has been postulated, but never ascertained [17].

DTaP-IPV and hexavalent are very similar vaccine, then we can consider this episode as a positive re-challenge which has an important role in evaluation of consistent causal association to immunization according to the last updated algorithm of World Health Organization (WHO) causality assessment [18]. Although the relationship between the vaccination and the development of HSP may be coincidental, past reports of temporally associated vaccinations and vasculitis without other identifiable etiologies or historical factors set a precedent for association.

Our report describes one of the five cases of HSP after administration of DTaP-IPV vaccine and five cases are not sufficient to postulate an association between vaccination and the disease; for the future, in case of other similar reports, Drug safety authorities have to evaluate the implementation of a specific surveillance program.

Acknowledgements

Not applicable.

Conflict of Interest

The authors declare that they have no conflict of interest.

References

1. Chen O, Zhu XB, Ren P, Wang YB, Sun RP, et al. (2013) Henoch Schonlein purpura in children: clinical analysis of 120 cases. *Afr Health Sci* 13: 94-99.
2. He X, Yu C, Zhao P, Ding Y, Liang X, et al. (2013) The genetics of Henoch-Schonlein purpura: a systematic review and meta-analysis. *Rheumatol Int* 33: 1387-1395.
3. Yang YH, Tsai IJ, Chang CJ, Chuang YH, Hsu HY, et al. (2015) The interaction between circulating complement proteins and cutaneous microvascular endothelial cells in the development of childhood Henoch-Schonlein purpura. *PLoS One* 10: e0120411.
4. Sohagia AB, Gunturu SG, Tong TR, Hertan HI (2010) Henoch schonlein purpura - a case report and review of the literature. *Gastroenterol Res Pract* 2010: 597648.
5. Yang YH, Chuang YH, Wang LC, Huang HY, Gershwin ME, et al. (2008) The immunobiology of Henoch-Schonlein purpura, *Autoimmun Rev* 7: 179-184.
6. Yilmaz D, Kavakli K, Ozkayin N (2005) The elevated markers of hypercoagulability in children with Henoch-Schonlein purpura. *Pediatr Hematol Oncol* 22: 41-48.
7. Hočevár A, Rotar Z, Jurčić V, Pižem J, Čučnik S, et al. (2016) IgA vasculitis in adults: the performance of the EULAR/PRINTO/PRES classification criteria in adults. *Arthritis Res Ther* 18: 58.
8. Yang Y-H, Yu H-H, Chiang B-L (2014) The diagnosis and classification of Henoch-Schönlein purpura: an updated review. *Autoimmunity Reviews* 13: 355-358.
9. Agmon-Levin N, Paz Z, Israeli E, Shoenfeld Y (2009) Vaccine and autoimmunity. *Nat Rev Rheumatol* 5: 648-652.
10. Courtney PA, Patterson RJ, Lee RJE (2001) Henoch-Schonlein purpura follow-ing meningitis C vaccination. *Rheumatology* 40: 345-346.
11. Liu JY, Wu QS, Liu M, Wang L, Gao YH, et al. (2016) Henoch-Schönlein purpura nephritis following influenza vaccination: a case report and review of the literature. *Southeast Asian J Trop Med Public Health* 47: 945-950.
12. Watanabe T (2011) Henoch-Schönlein purpura following influenza vaccinations during the pandemic of influenza A (H1N1). *Pediatr Nephrol* 26: 795-798.
13. Da Dalt L, Zerbinati C, Strafella MS, Renna S, Riceputi L, et al. (2016) Menniti-Ippolito F; Italian Multicenter Study Group for Drug and Vaccine Safety in Children. Henoch-Schönlein purpura and drug and vaccine use in childhood: a case-control study. *Ital J Pediatr* 42: 60.
14. Sexton K, McNicholas A, Galloway Y, Radke S, Kieft C, et al. (2009) Henoch-Schönlein purpura and meningococcal B vaccination. *Arch Dis Child* 94: 224-226.
15. Lambert EM, Liebling A, Glusac E, Antaya RJ (2003) Henoch-Schonlein purpura following a meningococcal vaccine. *Pediatrics* 112: e491-e495.
16. Da Dalt L, Zerbinati C, Strafella MS, Renna S, Riceputi L, et al. (2016) Menniti-Ippolito F and Italian Multicenter Study Group for Drug and Vaccine Safety in Children. Henoch-Schönlein purpura and drug and vaccine use in childhood: a case-control study. *Ital J Pediatr* 42: 60.
17. Montagnani S, Tuccori M, Lombardo G, Testi A, Mantarro S, et al. (2011) Autoimmune hemolytic anemia following MF59-adjuvanted influenza vaccine administration: a report of two cases. *Ann Pharmacother* 45: e8.
18. World Health Organization. Causality assessment of an adverse event following immunization (AEFI). User manual for the revised WHO AEFI causality assessment classification (Second edition).