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IMMUNE THROMBOCYTOPENIA; FOLLOWING SEASONAL FLU VACCINE AND NON-STEROIDAL ANTI-INFLAMMATORY DRUG USE

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ABSTRACT… Immune thrombocytopenia (ITP) is an idiopathic disorder which could be triggered by various factors including; drugs, rheumatic diseases and malignancies. We aimed to present a 66 year old woman diagnosed with ITP whose history was relevant for influenza vaccine and non-steroidal anti-inflammatory drug (diclofenac) use. She responded well to standard ITP therapy. In conclusion, medications should be elaborately questioned in patients with thrombocytopenia, especially, when a diagnosis of ITP was considered.

Keywords: immune thrombocytopenia, influenza vaccine, non-steroidal anti-inflammatory drug, diclofenac

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INTRODUCTION

Immune thrombocytopenia (ITP); formerly, idiopathic thrombocytopenic purpura, is an autoimmune condition associated with accelerated platelet destruction caused by pathogenic auto-antibodies binded them which result in decreased lifespan of platelets.[1]

The disease is usually primary and idiopathic in adulthood, however, infections (hepatitis C and B), lymphoid neoplasms (lymphoma), medications and other autoimmune conditions (systemic lupus erythematosus) may be associated with immune thrombocytopenia.[2]

Thrombocytopenia after vaccination is a rare but well recognized entity.[3] Although underlying mechanism of immune thrombocytopenia is not clear, cases reported following use of measles, mumps and rubella (MMR) vaccine[4,5], diphtheria-tetanus-pertussis (DTP) vaccine[6], hepatitis B vaccine[7] and influenza and pneumococcal vaccines.[8]

We aimed to add to the current literature by presenting an ITP case which followed influenza vaccination.

CASE REPORT

A 66 year old woman was admitted to emergency room of our hospital because of nasal bleeding. She had such complaints for a week before admission. Her medical history was relevant for aspirin and non-steroidal anti-inflammatory drug use. Vital signs of the patient were as follows; blood pressure: 135/85 mmHg, body temperature: 36.5 celcius degree, heart rate: 80 beats per minute. Physical examination revealed widespread petechiaes on her legs and front arms, ecchymosis on right arm, on back, and on left inferior quadrant of abdominal skin. There was also a hemorrhagic bulla in her mouth.

An electrocardiography and a direct x ray film of the chest were normal. Hypertension (for 15 years) and surgery for osteoarthritis (3 months ago) were included in her medical history. She was using non-steroidal anti-inflammatory drugs (Diclofenac 75 mg, daily) for nearly twenty days for pain at her knee and was vaccinated with flu vaccine twenty days before hospital admission. She was used amlodipine 5mg and indapamide 1, 25 mg daily for last 15 years, doxazosin 2mg and acetylsalicylic acid 100 mg daily for last 10 years. She confessed cessation of non-steroidal anti-

inflammatory drugs and acetylsalicylic acid three days ago. Laboratory test results were as follows: white blood count 8100/mm^3, hemoglobin 13.3 g/dl hematocrit 39.3%, mean corpuscular volume 79 fL, platelet count 2.000/mm^3. Coagulation panel; prothrombin time, aPTT and INR were normal. A peripheral blood smear was consisted about 1 platelet in each field in x100 magnification. Blood smear was otherwise normal. The patient was hospitalized in our internal medicine department with a diagnosis of ITP. Prednisone 80 mg/daily prescribed along with lansoprazole 30 mg orally. A salt poor diet was recommended. Hemogram and peripheral blood smear of the case screened daily. Her platelet count reached to 12000/mm^3 on third and to 37000/mm^3 on the fourth day. At fifth day, platelet count was measured 50.000/mm^3 and peripheral blood smear was consisted about 100000/mm^3. Abdominal ultrasound revealed grade 2-3 hepatosteatosis. Serology of hepatitis virus (B and C) and HIV were negative. Serum vitamin B12 and folic acid levels were also in normal range. Direct Helicobacter pylori antigen test in gaita was also negative. Serum of the patient analyzed for anti-nuclear anticore and a negative result was obtained. As her symptoms resolved and platelet count reached to a safer level, patient discharged by prescribing oral prednisone 64 mg daily. She also referred to hematology department of another institution. She remained free of any symptoms in her follow-up.

DISCUSSION

We reported an ITP case followed vaccination for influenza which was compatible to data in literature. The diagnosis of ITP was precise in our patient although we could not show the autoantibodies to platelets. These pathologic autoantibodies could be shown in only 2/3 of the ITP cases.[2]

ITP may be manifest by mucocutaneous bleeding. When platelet count fallen below 20,000–30,000/mm^3, spontaneous hemorrhage (bruising, nosebleeds, gingival bleeding) should be encountered.[2] Platelet count decreased to as low as 2000/mm^3 in present case and spontaneous nosebleed and mucocutaneous hemorrhage were occurred.

Typically, hemogram tests only reveal isolated thrombocytopenia in patients with ITP, however, anemia may be present in cases with significant bleeding.[2] In concordance to current knowledge, there were no abnormalities in hemogram and peripheral blood smear other than thrombocytopenia in present ITP case.

Indications for bone marrow examination in ITP are unexplained cytopenias, elderly patients, and treatment resistance.[9] A bone marrow examination was not required in present case due to rapid response to standard ITP therapy. However, admission to a hematology department after discharge was recommended.

Although underlying cause of ITP was not clear, influenza vaccine could be the triggering factor for autoimmunity in present case. Kelton et al reported ITP, after vaccination for influenza.[8] Moreover, two cases of ITP reported from Canada which followed influenza vaccine.[3] We have to claim that influenza vaccine was not the only vaccine associated with ITP. Other certain types of vaccinations were reported to cause immune thrombocytopenia. [4,10-12] Besides ITP, influenza vaccine was found to be associated with other autoimmune conditions. It has been linked to other autoimmune pathologies; such as Giant cell arteritis, polymyalgia rheumatica, poly arteritis nodosa, Henoch-Schoenlein purpura and microscopic polyangiitis.[13-17] Therefore, it was possible that ITP be triggered by influenza vaccine in present case.

Our patient was also on medications which could result in thrombocytopenia such as NSAIDs which may induce ITP.[18,19] Ranieri et al reported immune thrombocytopenia in a patient one week after use of meloxicam.[20] Another report from Italy pointed out the association of NSAIDs and ITP.[21] In literature, authors described diclofenac induced immune thrombocytopenia in two cases.[22] In another study, a case of combined immune hemolytic anemia and immune thrombocytopenia induced by diclofenac treatment has been reported.[23]

Naproxen, a common prescribed non-steroidal anti-inflammatory drug was also found to be associated with immune thrombocytopenia.[24]

ITP was the diagnosis in present case. Although it is idiopathic in many cases, influenza vaccine and diclofenac use were two factors which could probably triggered ITP in our patient. She responded well to standard ITP therapy and long term remission achieved.

In conclusion, medications should be elaborately questioned in patients with thrombocytopenia, especially, when a diagnosis of ITP was considered. If possible, cessation or switching of suspected drugs should not be neglected.

REFERENCES

1. Woods VJ, Oh EH, Mason D, McMillan R. **Autoantibodies against the platelet glycoprotein IIb/IIIa complex in patients with chronic ITP. Bloo**d. 1984;63(2):368-375.
2. Minichiello. PFFaT. **Disorders of Hemostasis, Thrombosis, and Antithrombotic Therapy.** In: Maxine A. Papadakis SJM, Michael W. Rabow., ed. 2015 CURRENT Medical Diagnosis & Treatment 54th ed: Lange, McGraw Hill Publication; 2015:536-561.
3. Jadavji T, Scheifele D, Halperin S, Canada CPSH. **Thrombocytopenia after immunization of Canadian children, 1992 to 2001.** Pediatr Infect Dis J. Feb 2003;22(2):119-122.
4. Nieminen U, Peltola H, Syrjala MT, Makipernaa A, Kekomaki R. **Acute Thrombocytopenic Purpura Following Measles, Mumps and Rubella Vaccination - a Report on 23 Patients.** Acta Paediatr. Mar 1993;82(3):267-270.
5. Miller E, Waight P, Farrington P, Andrews N, Stowe J, Taylor B. **Idiopathic thrombocytopenic purpura and MMR vaccine.** Arch Dis Child. Mar 2001;84(3):227-229.
6. Arya LS, Ghai OP, Saraya AK. **Thrombocytopenic Purpura Following Dpt Vaccination.** Pediatr Hemat Oncol. Oct-Dec 1993;10(4):381-383.
7. Neau D, Bonnet F, Michaud M, et al. **Immune thrombocytopenic purpura after recombinant hepatitis B vaccine: Retrospective study of seven cases.** Scand J Infect Dis. 1998;30(2):115-118.
8. Kelton JG. **Vaccination-Associated Relapse of Immune Thrombocytopenia.** Jama-J Am Med Assoc. 1981;245(4):369-371.
9. Mak Y, Yu P, Chan C, Chu Y. **The management of isolated thrombocytopenia in Chinese adults: does bone marrow examination have a role at presentation?** Clinical & Laboratory Haematology. 2000;22(6):355-358.
10. Peltola H, Heinonen OP, Valle M, et al. **The elimination of indigenous measles, mumps, and rubella from Finland by a 12-year, two-dose vaccination program.** The New England journal of medicine. Nov 24 1994;331(21):1397-1402.
11. Meyboom RH, Fucik H, Edwards IR. **Thrombocytopenia reported in association with hepatitis B and A vaccines.** Lancet. Jun 24 1995;345(8965):1638.
12. Schattner A. **Consequence or coincidence? The occurrence, pathogenesis and significance of autoimmune manifestations after viral vaccines.** Vaccine. Jun 10 2005;23(30):3876-3886.
13. Wharton CF, Pietroni R. **Letter: Polyarteritis after influenza vaccination.** British medical journal. May 11 1974;2(5914):331-332.
14. Blumberg S, Bienfang D, Kantrowitz FG. **A Possible Association between Influenza Vaccination and Small-Vessel Vasculitis.** Arch Intern Med. 1980;140(6):847-848.
15. Kelsall JT, Chalmers A, Sherlock CH, Tron VA, Kelsall AC. **Microscopic polyangiitis after influenza vaccination.** J Rheumatol. Jun 1997;24(6):1198-1202.
16. Perez C, Loza E, Tinture T. **Giant cell arteritis after influenza vaccination.** Arch Intern Med. Sep 25 2000;160(17):2677-+.
17. Brown MA, Bertouch JV. **Rheumatic Complications of Influenza Vaccination.** Aust Nz J Med. Oct 1994;24(5):572-573.
18. Moulis G, Sommet A, Sailler L, Lapeyre-Mestre M, Montastruc JL, Regional FA. **Drug-induced immune thrombocytopenia: A descriptive survey in the French PharmacoVigilance database.** Platelets. 2012;23(6):490-494.
19. Cantarini L, Tinazzi I, Biasi D, Fioravanti A, Galeazzi M. **Sulfasalazine-induced immune thrombocytopenia.** Postgrad Med J. Jun 2007;83(980).
20. Ranieri MM, Bradley EF, Simon AB. **Meloxicam-Induced Thrombocytopenia.** Pharmacotherapy. Feb 2014;34(2):E14-E17.
21. Bertuola F, Morando C, Menniti-Ippolito F, et al.

Association between Drug and Vaccine Use and Acute Immune Thrombocytopenia in Childhood A Case-Control Study in Italy. Drug Safety. 2010;33(1):65-72.

22. Epstein M, Vickars L, Stein H. **Diclofenac Induced Immune Thrombocytopenia.** J Rheumatol. Oct 1990;17(10):1403-1404.

23. Kramer MR, Levene C, Hershko C. **Severe reversible autoimmune haemolytic anaemia and thrombocytopenia associated with diclofenac therapy.** Scandinavian journal of haematology. Jan 1986;36(1):118-120.

24. Bougie D, Aster R. **Immune thrombocytopenia resulting from sensitivity to metabolites of naproxen and acetaminophen.** Blood. Jun 15 2001;97(12):3846-3850.

PREVIOUS RELATED STUDY

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Muhammad Siddique, Sayyed Naveed Masood, Rubeena Nazli Shaffi, Asad Ullah Jaafri, Fayyaz Hussain. THROMBOCYTOPENIA IN CRITICALLY ILL SURGICAL PATIENTS; A STUDY EVALUATING ATTRIBUTABLE PATIENT'S MORTALITY AND TRANSFUSION REQUIREMENT (Original) Prof Med Jour 13(1) 138-144 Jan, Feb, Mar, 2006.

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AUTHORSHIP AND CONTRIBUTION DECLARATION

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1	Gulali Aktas	Wrote the manuscript	
2	Rabia Altinordu	Collected medical data	
3	Zuhal Mercan	Literature review	
4	Haluk Savli	Critical review of the paper	