International Journal of Pharmaceutical Science Invention
ISSN (Online): 2319 – 6718, ISSN (Print): 2319 – 670X
www.ijpsi.org Volume 6 Issue 4 ǁ April 2017 ǁ PP. 07-09

Clinical Case of Post-Vaccination Measles Followed By Severe Neutropenia

Dr. Rada Markova, M.D, PhD [1], Dr.Maria Gaydarova, M.D, PhD [1],
Dr. Denka Stoyanova [2], Assoc. Prof. Dr. Milka Markova, M.D, PhD [1]
[1]*MC "First pediatric consultative clinic" – Sofia*
[2]*Clinic of nephrology, University Children's Hospital , MC "First pediatric consultative clinic" – Sofia*
[2]*Hematology and Oncology Department – University Hospital "Tsaritza Ioana" - Sofia*
[1]*Clinical Laboratory - University Hospital for Pulmonary diseases "St. Sophia" , MC "First pediatric consultative clinic" – Sofia*

***Resume**: We present a 13 - month old girl, who develop a post vaccination measles infection after a MMR vaccine , followed by a severe neutropenia. The hematological changes last more than one year and resolved spontaneously. We report the clinical case as an extremely rare and unknown side effect of the vaccine.*
***Keywords:** measles , neutropenia , Priorix*

I. Introduction

Changes in white blood count during the infections can be associated with increase of leukocytes (leukocytosis) or their reduction (leukopenia). It is known that viral infections often lead to leukopenia (hepatitis virus, influenza, EBV, rubella and measles, etc.) and bacterial infections - to leukocytosis. In severe bacterial infections - sepsis and septicemia (meningo-, pneumococcal) also a leukopenia can occur. In cases of bacterial infections leukocytosis is associated with neutrophilia and vacuolization of the cytoplasm and also toxic granulations in neutrophils. Neutropenia is typical for viral infections. It is the result of direct cytotoxicity, inhibition of progenitors in the bone marrow or activation of interferon gamma. Neutropenia is defined as a decrease in absolute neutrophil count less than **1500 / mm ^{3}**. It is classified as : light (1000-1500 / mm ^{3}), moderate (500-1000 / mm ^{3}) and severe neutropenia (neutrophil count less than 500 / mm ^{3}).

The vaccine Priorix (GSK) is an alive attenuated combined vaccine containing measles, rubella and mumps viruses. The vaccine is given in two doses according to the immunization schedule of the Republic of Bulgaria on 13-15 months and 12 years of age (or 13-15 months, 4-6 years in Europe and North America). It must not be applied to person who is allergic to egg protein and Neomycin.

Description of the clinical case:

We present a 13 month – old girl (K.M.Z.), born from normal pregnancy and delivery , on term, regularly immunized , rarely sick. At the age of 13 months a MMR vaccine is applied (Priorix- GSK) regarding the immunization schedule by a general practitioner. A week later the child develop an intoxication syndrome, septic fever, fatigue, low tonus, red face, dry mouth, redness of the pharynx. The clinical assessment show manifestations of severe viral infection without any infectious focus, followed by a diarrhea syndrome - more than 5-10 loosen stools per day, without blood and mucous. The child is treated symptomatically.

On the seventh day of fever a generalized erythema appeared with macular rash and a tendency for confluence , covering the face, body and limbs, without itching and clinical characteristics of infectious exanthema. (18.07.2011.) – fig. 1 and 2. The rash and the fever disappear spontaneously.

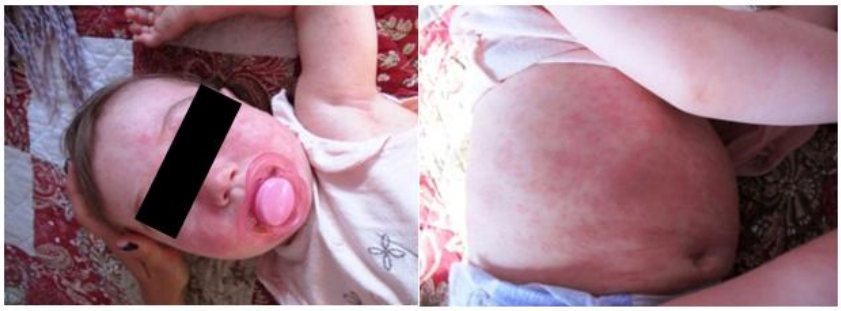

Fig. 1 and 2 - Changes in body and face during the rash

After 5 days, the second febrile episode occurs with other skin lesions - vesicles and bullae with characteristic of staphylococcal pyoderma. The performed CBC (complete blood count) on 22.07.2011.showed inflammatory activity with a high CRP , light anaemic syndrome, combined with severe neutropenia with an absolute neutrophil l count of **70 / mm3**. (tab. 1) The broad -spectrum antibiotic is started - Cefuroxime (Zinnat) at a dose of 30 mg / kg / day for 10 day course and a topical treatment of the skin lesions with antibiotic and antiseptic – fig. 3 and 4.

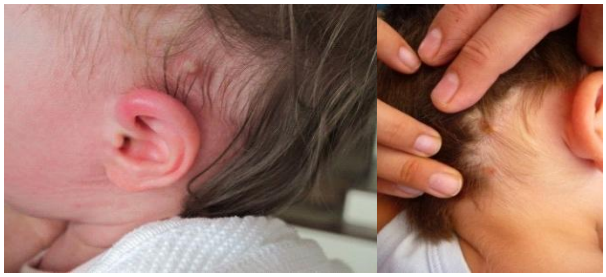

Fig. 3 and 4 – Staphylococcal skin infection – lesions on the head

On 24.07.2011 the child perform a broad laboratory and serological investigation in order to assess the clinical and laboratory phenomena. Serological samples prove a post-vaccination measles infection with high titer of antibodies against measles. Persistent agranulocytosis is assumed to be a result of the measles infection. On 28.07.2011 a haematology consultation is made and after a thorough peripheral morphology and clinical examination, the child has a confirmed diagnosis: **Severe neutropenia as a result of post-vaccination measles infection**. Parents refuse myelogram and subsequent administration of granulocyte colony stimulating factor (G - CSF). On 6.08.2011 a new CBC is made when the absolute number of neutrophils increased up to 780 / mm3. From 17.07.2012 neutrophils remain below 500 / mm3 which lead to a repeated myelogram proposal, which was rejected. The child during this period has twice bacterial infections, which need an antibiotic treatment: tracheobronchitis and tonsillitis.

After 1 year and 2 month monitoring - clinical and laboratory, the control CBC and differential leukocyte counts show spontaneous normalization of all parameters and the absolute neutrophil count from 28.10.2012 is normal. All subsequent vaccines are cancelled for the child. The severe adverse effect of the vaccine is reported and documented to Bulgarian Health Authorities.

Parameter	**22.07.2011**	**25.07.2011**	**10.08.2011**	**16.07.2011**	**28.10.2012**
Hb	109g/l	117g/l	106g/l	115g/l	120g/l
Er (RBC)	3.96	4.11	3.99	3.97	4.07
Hct	0.33	0.33	0.31	0.32	0.35
Leu (WBC)	7.0	9.69	10.8	7.0	12.7
Thr (PLT)	518	814	348	231	307
St	2%	2%	2%	0%	1%
Sg	1%	1%	6%	7%	47%
Eo	1%	1%	4%	4%	1%
Ba	-	-	1%	1%	-
Mo	40%	13%	12%	16%	9%
Ly	49%	83%	74%	70%	41%
Pl	7%	0%	1%	2%	1%
ESR	28 mm	45mm	12mm	6 mm	8mm
CRP	13.74 mg/l	4.84 mg/l			
LDH		756U/l	LDH		
Varicella		0.36 IU/ml (neg)	Varicella		
EBV		<10 IU/ml (neg)	EBV		
Measels		positive	Measels		

Tab. 1 – Laboratory changes during the observation period

Priorix vaccine is used since 1970 in more than 90 countries around the world as a combined vaccine.
Possible side effects and their frequency include :

- Very common: ≥10%: fever, local redness at the injection site
- Common: ≥1% and <10%: fever, , upper respiratory tract infection, rash, swelling at the injection site
- Rare: ≥0.1% and less than <1%: otitis media, lymphadenopathy, anorexia, insomnia, conjunctivitis, bronchitis, diarrhea, vomiting, increased parotid glands, meningitis, arthritis
- Very rare: ≥0.01% and <0.1%: seizures, allergic shock, thrombocytopenia
- Extremely rare: <0.01%

In the medical data there are discussions regarding the association between MMR vaccine and possible autism or inflammatory bowel disease, which is not accepted recently . We make a thorough search through the system Medline / Wolter Kluwer and since 1960 there was no evidence for a such hematological side effect, that we reported , which is also confirmed by the Medical department of the company - manufacturer GSK. Hematologic abnormalities connected with the vaccine were identified in the 1980s. Italian team De Martino, Orienti and Lami, proved that live measles virus in vitro reduced chemotaxis of granocytes in healthy children. Same conclusion seven days after the vaccine administration made R. Toraldo et all in 1992 in their publication in Acta Pediatrica.

The reported clinical case is a very rare and undescribed side effect of MMR vaccine with subsequent measles infection and prolonged hematological disorders in white blood cells and granulocyte count. Spontaneous normalization of blood parameters demonstrate a favorable clinical outcome and the need for monitoring and mainly" wait and see" behavior in such patients.

References

[1]. Farruggia P, Dufour C. Diagnosis and management of primary autoimmune neutropenia in children: insights for clinicians. *Ther Adv Hematol*. 2015 Feb. 6 (1):15-24

[2]. Lalezari P, Khorshidi M, Petrosova M. Autoimmune neutropenia of infancy. *J Pediatr*. 1986 Nov. 109(5):764-9

[3]. Kobayashi M, Ueda K, Kojima S, Nishihira H, Ishiguro A, Shimbo T. Serum granulocyte colony-stimulating factor levels in patients with chronic neutropenia of childhood: modulation of G-CSF levels by myeloid precursor cell mass. *Br J Haematol*. 1999 May. 105(2):486-90

[4]. Lyall EG, Lucas GF, Eden OB. Autoimmune neutropenia of infancy. *J Clin Pathol*. 1992 May. 45(5):431-4

[5]. Shete M, Thompson JW, Naidu SI, Stocks RM, Wang WC. Olaryngologic manifestations in children with chronic neutropenia. *Int J Pediatr Otorhinolaryngol*. 2012 Mar. 76(3):392-5

[6]. Fioredda F, Calvillo M, Burlando O, et al. Infectious complications in children with severe congenital, autoimmune or idiopathic neutropenia: a retrospective study from the Italian Neutropenia Registry. *Pediatr Infect Dis J*. 2013 Apr. 32 (4):410-2

[7]. Lindqvist H, Carlsson G, Moell J, Winiarski J, Sundin M. Neutropenia in childhood: a 5-year experience at a tertiary center. *Eur J Pediatr*. 2015 Jun. 174 (6):801-7

[8]. Vlacha V, Feketea G. The clinical significance of non-malignant neutropenia in hospitalized children. *Ann Hematol*. 2007 Dec. 86(12):865-70

[9]. Audrain M, Martin J, Fromont P, Prie N, Thomas C, Muller EJ. Autoimmune neutropenia in children: analysis of 116 cases. *Pediatr Allergy Immunol*. 2011 Aug. 22(5):494-6

[10]. De Martino M, Redi Orienti M, Adami Lami C, Vierucci A. - In-vitro block of granulocyte chemotaxis with attenuated measles virus. Ann Sclavo. 1980 Sep-Oct;22(5):837-45

[11]. R Toraldo, C Tolone, P Catalanotti, R Ianniello, M D'Avanzo, G Canino, F Galdiero and F Iafusco. Effect, of measles-mumps-rubella vaccination on polymorphonuclear neutrophil functions in children – Acta Padiatrica Nov 1992 (887–890)