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Maculopapular rash following tetanus toxoid injection

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Abstract

In post-vaccination era, tetanus is an increasingly rare diagnosis. Tetanus toxoid (TT) is a commonly utilized vaccine for active immunization against *Clostridium tetani* and is included in national EPI program of Pakistan. This case report highlights an allergic skin reaction, a maculopapular rash, induced by Intra-Muscular (IM) TT injection in a 15 year old male. A complete course of clinical review of vitals and laboratory investigations; complete blood count, electrolytes and ultrasonography were performed – all turned normal. He was diagnosed as a case of allergic reaction, maculopapular rash, and was treated with 500 mg azithromycin B.D plus 500 mg dexamethasone B.D per Orem for four days. After four days the rashes disappeared, and he was discharged from the hospital. Before IM administration of TT, a careful history taking, cutaneous hypersensitive testing should be done along with provision of emergency measures in case of adverse reactions.

Keywords

Tetanus toxoid; vaccination; maculopapular rash; dexamethasone; clostridium tetani; traffic accident.

Introduction

Tetanus Toxoid (TT), a commonly used vaccine, is routinely used against the gram-positive, spore forming anerobic bacillus, *Clostridium tetani* [1], which produces two exotoxins; tetanolysin and tetanospasmin. Tetanus vaccine is also included in Expanded Program on Immunization (EPI) (http://www.epi.gov.pk/immunisation-schedule/), by the Government of Pakistan [2], and is given intramuscularly either alone or in conjunction with vaccines for diphtheria and pertussis – also known as DPT (diphtheria-tetanus-pertussis) [3]. Literature evidence suggests that immune-protective antibody levels in most children and adults can be achieved after two doses, 4 weeks apart, of tetanus toxoid. Nonetheless, three doses may be required in children under 1 year of age [4]. However, particularly in older adults and infants, protective levels are short-lived, thus may require a booster dose at 6 to 12 months after essential series of vaccinations [5].

Following vaccination with tetanus toxoid, within 48 hours, minor local reactions, such as pain, erythema, swelling of less than 1 cm can occur – though the rate of reaction varies with the dose and type of toxoid used and also with the number of doses and method of injection [6]. More severe reactions are less common, such as more than 8 cm erythema and induration, often accompanied by swollen arm, a sore and systemic manifestations – fever and malaise being more frequent with high doses [7,8]. Until lately, purified Tetanus Toxoid (TT) has been replaced by plain TT owing to its propensity to stimulate higher and longer immune response [9]. Hypersensitivity reactions, such as TT induced anaphylaxis has been reported previously in a 6 year old girl from India. Two cases of allergic reaction by Tetanus Antitoxin desensitization injection were also reported in China [10]. Here in this report we describe TT induced maculopapular rash in a 15 year old male, to our knowledge, for the first time.

Case Presentation

A 15 year old male patient, resident of rural area of Punjab, Pakistan, presented to a Tehsil head-quarter hospital with soft tissue injuries in a road traffic accident. After examination, a pain killer tablet Dicloran 50 mg and injection of Tetanus Toxoid (IM) were prescribed. After 8 hours, the patient noticed rashes starting from the ankle (B/L) towards the thigh (Figure 1). The patient did not feel respiratory distress, chest tightness and dizziness. On examination, his Blood Pressure (BP) was found to be 120/80 mmHg, pulse rate 110/minute, respiratory rate 20/minute, Cardiovascular System (CVS) sounds; S1+S2+0 and intact Central Nervous System (CNS). No other symptoms were observed such as, itching, pain over lesions, pain on the injection site, vomiting, urine urgency, bleeding, nausea nor abdominal pain [10].

The following investigations were done to confirm the diagnosis;

Cutaneous examination; Maculopapular rash on B/L leg starts from foot and extended toward thigh (Figure 1). Complete Blood Count (CBC) Baselines values; CBC baseline values are summarized in Table 1. All the values lie in normal range except WBC, which had raised value due to normal inflammatory response of body, MCV is low maybe due to poor dietary intake of iron, MXD is low in percent due to increased risk of infection (Table 1).

As shown in Table 2, no changes in liver, gall bladder, pancreas, spleen or kidneys were observed neither in size nor in texture- though urinary bladder was mildly filled as per ultra-sonography report. Electrolyte balance report of the patient is summarized in Table 3. All the laboratory values of electrolytes were found within normal ranges (Table 3).

He was considered a case of allergic reaction as evidenced by the development of a maculopapular rash (Figure 1) and related reports (Table 1-3). Vitals (including blood pressure, pulse rate, blood sugar level and temperature) were monitored hourly. CBC baseline findings, cutaneous examination were done on a daily basis. The condition of the patient was stable. Treatment was continued for four days with azithromycin 500 mg per Orem to combat skin infection and dexamethasone 500 mg per Orem for allergic reaction and to reduce swelling.

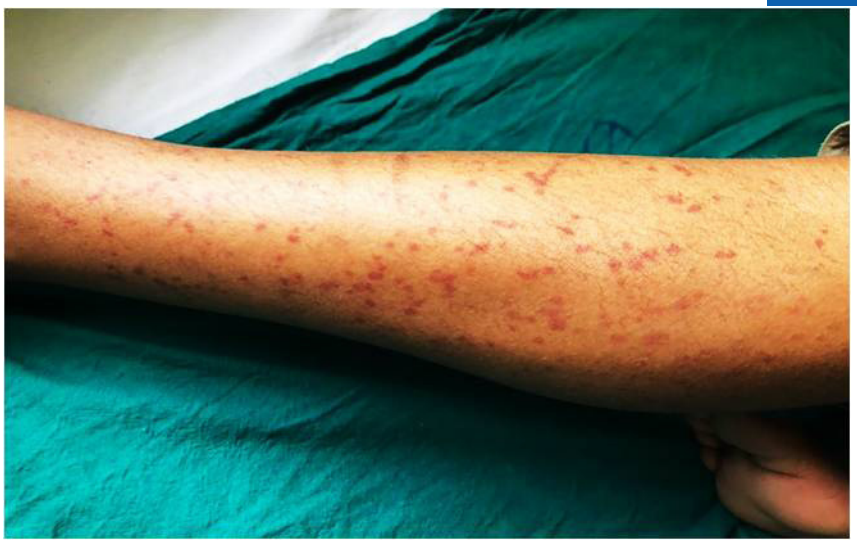

Figure 1: Maculopapular rash on left crus.

Table 1: Complete blood count (CBC) baseline values.

Complete blood count (CBC)baseline values		
Components	**Patient values**	**Normal range**
WBC (/uL)	23.8 x 10^3	4.0 x10^3 – 11 x10^3
RBC (/uL)	4.88 x 10^6	4.69 - 6.13
HGB (g/dl)	13.0	11.5 – 16.0
HCT (%)	41.7	36.0 – 46.0
MCV (fL)	78.3	80 - 96
MPV (Fl)	9.4	9.4 – 12.3
MCH (pg)	26.1	30.0 – 35.0
MCHC (g/dL)	33.3	30.0 – 35.0
PLT (/uL)	213 x 10^3	150.0 – 400.0
LYM (%)	42.3	20.0 – 50.0
MXD (%)	8.8	11.5-14.5
P-LCR (%)	21.3	15 – 35.0
LYM# (/uL)	2.8 x 10^3	1 x 10^3 – 4.8 x 10^3
MXY# (/uL)	0.6 x 10^3	4 x 10^3 – 10 x 10^3
NEUT# (/uL)	3.3 x 10^3	1.5x 10^3 – 8 x 10^3
RDW (fL)	42.9	39.0 – 46.0
PDW (Fl)	11.6	8.6 – 15.5

Abbreviations: WBC: White blood cells; RBC: red blood cells; HGB: Hemoglobin; HCT: Hematocrit; MCV: Mean corpuscular volume; MPV: Mean platelet volume; MCH; Mean corpuscular hemoglobin; MCHC: Mean corpuscular hemoglobin concentration; PLT: Platelets; LYM: lymphocytes; MXD: Mixed cell count; P-LCR: Platelet large cell ratio; LYM#: lymphocytes: MXY#: Mononuclear cells; NEUT#: Neutrophils: RDW: Red cell distribution width; PDW: Platelet distribution width.

Table 2: Ultra-sonography report of the abdomen and pelvis.

Organs	Patient Values	Normal Range
Liver	10.8 cm, normal in size and texture.	<15 cm length (mid clavicular)
Gall bladder	Normal in size	<4 mm wall thickness when distended and <8 mm wall thickness post voids
Pancreas	Normal in size and state	Head ≤ 3 cm Body ≤ 2.5 cm Tail ≤ 2.5 cm
Spleen and Portal duct	Not enlarged	<13 cm length <7 cm wide
Right and Left kidney	Normal in size and position	9-12 cm length (asymmetric if size difference >1.5 cm, Cortical thickness >1 cm
Urinary Bladder	Mild filled and normal in size	<4 mm wall thickness when distended and <8 mm wall thickness post voids.

Table 3: Electrolyte balance report

Electrolytes	Patient values	Normal ranges
Calcium (*mg/dL****)***	8.1	8.5-10.5
Phosphorus (*mg/dL****)***	3.6	2.5-4.5
Sodium (*mmol/L****)***	139	135-145
Potassium (*mmol/L****)***	3.8	3.5-5.0
Magnesium (*mg/dL****)***	2.2	1.6-2.5

Discussion

In this case study, the patient after TT injection presented with the complaint of Adverse Drug Reaction (ADR) without any history of hypersensitivity towards drugs. After careful search for the potential drug-drug interactions, drug-vaccine (dicloran and tetanus toxoid) and vaccine-vaccine interactions (patient did not have any history of vaccination during the past 7 -15 days) [11], all these apparent elements were ruled out as among the possibilities of reported ADR. The other more pertinent and tangible aspects could be the components of the TT vaccine that included toxoid, adsorbent and preservative. Thus, TT vaccine consists of Toxoid, a modified form of pathogenic microorganism, absorbed onto aluminum hydroxide/phosphate gel as adjunct with addition of thimerosal 0.01% as preservative. i.e. 0.05mg/dose. Each 0.5ml dose yields at least 40IU. Anti-tetanus component of the vaccine has been associated with local and systemic reactions – local in duration to anaphylactic shock [12,13]. In general, as reported previously, in most of the cases, the ADRs to TT vaccine are mild to moderate and are restricted to injection site [14]. Several ADRs have been attributed to TT vaccination that ranges from mild local edema and urticaria to angioedema and severe anaphylaxis.

The occurrence of anaphylaxis has been related to the administration of TT vaccination [15] and it is presumed that any of the vaccine components, i-e., antigen, adsorbent and preservative can cause this reaction [16]. In this context, two case studies have been reported on TT vaccine related ADRs, which suggest that potential causes of ADRs could be the additive components of vaccine, i.e., thimerosal preservative and aluminum hydroxide. These two components are potent enough to produce immediate or delayed urti-

caria, edema, angioedema or erythema. Besides, the degradation products of thimerosal have been associated to eye hypersensitivity and the accumulation of these products increases in the presence of light and at room temperature [17]. We observed that the patient did not develop these symptoms, rather an allergic reaction was noticeable on the flexor and extensor aspects of his leg. The rashes appeared reddish in color and hot on touch – typically a maculopapular rash.

Since TT vaccine is widely used in the hospitals and included in EPI program run by the government of Pakistan, the attending physician should therefore be prepared for a possible ADR related to its use with apt provisions to take emergency measures. Withdrawing the drug is not an option in this case. Nevertheless, physicians must take past history of any known allergies to TT and DPT. It is highly suggestive to take routine cutaneous hypersensitivity testing before IM administration. Seemingly, we are left in unsatisfactory state of mind regarding future administration of TT, especially in those developing a rash. Therefore, it is advisable that those receiving TT intramuscular injection should be observed at least for an hour by a physician to ensure that any ADR occurred is treated immediately. Without any doubt, the continued use of thiomersal in vaccine preparations is questionable.

Conclusion

In conclusion, the attending physicians must consider all those factors, which can lead to the noxious or unintended response of the drug, e.g., patient hypersensitive status, expiration date of vaccine, storage conditions and patient's history before initiating TT administration. Tetanus and diphtheria toxoid vaccines should never be frozen. Medical personnel must be prepared for any untoward reaction with necessary paraphernalia, such as drugs; antihistamine for itching, analgesics for the pain, dexamethasone for swelling, and equipment for symptomatic management.

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