

CASE REPORT**Anaphylactic shock due to hepatitis B immunoglobulin in a newborn**

ALI BULBUL, AHMET KARADAG, ESAD KÖKLÜ, UTKU PAMUK, &
SERDAR UMIT SARICI

Division of Neonatology, Department of Pediatrics, Gulhane Military Medical Academy, Ankara, Turkey

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Abstract

Hepatitis B immunoglobulin (HBIG) is administered for the passive immunisation of all infants born to HBsAg-positive mothers within 12 h of birth. Adverse effects of HBIG are very rare. In this study, we report a newborn (a female, 33 weeks' gestation and 2030 g birth weight) developing anaphylaxis after HBIG administration. The mother was a Hepatitis B virus (HBV) carrier. Hypotension and erythematous rash developed 7 min after HBIG administration. Reporting the first anaphylaxis case in newborns due to HBIG in literature, we suggest the condition be taken into account, and requisite precautions should be taken against this probable complication in the newborn.

Keywords: *Hepatitis B immunoglobulin, anaphylaxis, newborn, adverse effect*

Introduction

All infants born to HBsAg-positive women should receive both active and passive immunisation within 12 h of birth [1]. Adverse effects of Hepatitis B immunoglobulin (HBIG) administration are (reported in childhood age): local pain, predominantly back pain, myalgia, tenderness, headache, flushing and thrombocytopenia [2]. To date, anaphylaxis or any other life-threatening adverse effects due to HBIG administration in either neonatal period or childhood have, to our knowledge, not been reported. Only one adult case of angioedema and severe urticaria due to HBIG administration has been reported [3]. In this study, we report a newborn developing anaphylaxis after HBIG administration.

Case report

A female, preterm infant was born by section caesarean of twin pregnancy achieved after *in vitro* fertilisation at 33 weeks' gestation with a birth weight of 2030 g. She had premature rupture of membranes and acute foetal distress. The mother was 34 years old, and cervical ligation had been performed for

cervical insufficiency at the 25th gestational week. No allergic specification was present in her family history. The mother was a Hepatitis B virus (HBV) carrier. No specific drug was mentioned to have been used in prenatal period. At birth the female infant was with tachypnea and had retractions, with an Apgar score of 6 at 1st, and 8 at 5th min. She was hospitalised with a diagnosis of respiratory distress syndrome, and surfactant was given at the 30th min of life. The baby was vaccinated with 10 µg HBV vaccine (Engerix B[®], Glaxo SmithKline, Belgium, Lot Number: AHBVB468AB). At sixth hour, 100 IU of HBIG (HyperHEP BTM S/D Research Triangle Park, NC, USA, Lot Number: 26N9P71) was administered intramuscularly. Erythematous rash developed 7 min after HBIG administration beginning from the scalp and face and invading all over the body in about 5 min (Figure 1). The ventilatory settings were increased in order to stabilise the patient. Moderate metabolic acidosis (venous pH: 7.21, pCO₂: 58 mmHg, pO₂: 32 mmHg, HCO₃: 16 mmol/L and base excess: (8 mmol/L) was detected. Intravenous dexamethasone (0.3 mg/kg) and diphenhydramine (2 mg/kg) were administered immediately after the blood pressure was detected as hypotensive (43/28 mmHg,



Figure 1. Erythematous rash beginning from the scalp and face developed after HBIG administration.

mean blood pressure: 31 mmHg, prior to the administration to HBIG blood pressure was 61/39 mmHg, mean 44 mmHg). The rash began to fade in 15 min, and her blood pressure and blood gases were normalised after 30 min. The generalised rash faded away entirely at the end of the second hour. She was extubated and discharged on the postnatal 10th day passing gradually to full enteral feeding on the third day. She remains well at eighth month of age without any allergy complaints.

Discussion

Anaphylaxis is a potentially fatal hypersensitivity reaction resulting in cutaneous, respiratory, cardiovascular, or gastrointestinal signs and symptoms [4]. These findings are seen in a maximum of 4 h after exposure, requiring treatment, in order to be accepted as anaphylaxis in childhood [1]. It is reported that vaccines used in infants containing the vaccine antigen (tetanus toxoid), animal protein (gelatin), antibiotics (neomycin) and latex used in vial stoppers and syringe plungers have the potential to cause vaccine-associated anaphylaxis [4]. It was not likely an anaphylaxis due to vaccine in our patient since the reactions occurred 6 h after exposure.

Newborns are less likely to develop anaphylaxis via either IgE-mediated immunity or non-immune mechanisms, since their immune system is weaker than older infants and children. However, proven reports of patients and animal studies with anaphy-

laxis are available in limited number in the literature [5]. Rare cases of newborns with anaphylaxis or anaphylactoid shock due to ceftriaxone, thiopentone, atracurium, cow's milk protein, old-dissolved immunoglobulin and BCG vaccination have also been reported [6–10]. To date, the possible mechanism of anaphylaxis formation in the newborn is still obscure.

Anaphylaxis is usually triggered by an agent such as an insect sting, food, or medication, through a mechanism involving IgE and the high-affinity IgE receptor on mast cells or basophils. Less commonly, it is triggered via other immunologic mechanisms, or non-immunologic mechanisms. In some individuals described as having idiopathic anaphylaxis, FcεRI receptors may be aggregated via autoimmune mechanisms. Non-immunologic factors including radiocontrast media, and medications such as opioids and vancomycin, which activate mast cells, were not yet fully understood [11].

Adverse reactions against immunoglobulin can be local or systemic. Local reactions by the route of intramuscular injections are relatively common, and severe systemic reactions are less frequent, as well [12]. Systemic reactions can be rapid or late. Rapid reactions occur during or within minutes of starting the injection, and are anaphylactic in type (flashing flank pain, rigour, dyspnea or signs of shock). Late reactions may occur within hours or days, are usually less severe, and may consist of urticaria, arthralgia, pyrexia or diarrhea [12].

The causes of adverse reactions to HBIG were not yet thoroughly understood. The possible potential immunologic mechanisms in anaphylaxis include involvement of immune aggregates, IgG, IgM, platelets, and T cells; shift in eicosanoid metabolism towards leukotriene formation; and activation of the complement or coagulation systems [11].

The HBIG preparation includes a glycine stabiliser and sodium carbonate. HBIG contains no preservative. No anaphylaxis due to glycine and sodium carbonate has been reported, and thus, HBIG vaccination plus HBs antigen from the mother aggregating and activating indirectly the complement system should have given rise to the anaphylaxis in our patient.

Reporting the first anaphylaxis case in newborns due to HBIG in literature, we suggest the condition be taken into account, and requisite precautions should be taken against this probable complication in the newborn.

Declaration of interest: The authors have indicated they have no conflict of interest and financial relationships relevant to this article to disclose.

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