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Hypersensitivity Reaction to Parenteral Nutrition in an Intrauterine Growth-Restricted Newborn: A Case Report

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Hypersensitivity reaction to parenteral nutrition (PN) in infants is a rare condition, especially in the neonatal period. The authors report the case of a neonate with intrauterine growth restriction (IUGR) who presented symptoms of anaphylaxis while receiving standard PN. Given the very common practice of neonatal PN use, especially in newborns with

IUGR, clinicians should be alerted about possible acute reactions to this useful therapy. (*JPEN J Parenter Enteral Nutr.* XXXX;xx:xx-xx)

Keywords: critical care; intrauterine growth restriction; neonates; parenteral formulas/compounding; parenteral nutrition; pediatrics

Parenteral nutrition (PN) is an intravenous administration of nutrients and is widely used in the neonatal intensive care unit (NICU) when the gastrointestinal tract is impaired or if there is inadequate oral or enteral caloric intake. Allergic reaction to PN may be uncommon in neonates with intrauterine growth restriction (IUGR)¹⁻⁵ because this state has been described as related to overexpression of T helper 1 activity (Th1); allergy is rather related to overexpression of T helper 2 activity (Th2). We report the first case of a neonate with IUGR who presented a hypersensitivity reaction to PN.

Case Report

A term female newborn was admitted to the NICU because of respiratory distress. She was born from a 34-year-old woman with asthma and panic disorder who developed persistent hypertension at the 35th week of gestation. During the pregnancy, maternal treatment included terbutalin, paroxetine hydrochloride, labetalol, methyldopa, and

iron supplements. There was a family history of seasonal allergies for both parents. A fetal ultrasound performed at the 37th week of gestation showed IUGR with estimated weight at the fifth percentile and oligohydramnios. Delivery was induced at the 38th week of gestation, and at birth the newborn had Apgar scores of 5, 7, and 9 at 1, 5, and 10 minutes, respectively. Her weight was 2110 g (below the 3rd percentile), her length was 48 cm (10th percentile), and her head circumference measured 32 cm (below the 3rd percentile).

In the first 3 days of life, breastfeeding and enteral nutrition by nasogastric tube were complicated by frequent regurgitations and irritability, and therefore an intravenous infusion of 10% dextrose was started.

Abdominal X-rays and ultrasound were normal. On day 4, a PN solution containing exclusively amino acids (Travasol), glucose, electrolytes, lipid emulsion (soybean oil, egg yolk), vitamins (multi-12/K1, Sabex), and oligoelements (MV1-pédiatrique) was started. No other medication was given to our patient except erythromycin (0.5%) ophthalmic ointment and intramuscular vitamin K (1 mg) on admission in the NICU. After the first hour of infusion, the newborn began to cry and seemed uncomfortable, and her oxygen saturation decreased to 90%. She then abruptly developed tachypnea, wheezing, diaphoretic state, and generalized edema. Hives were noted on her face and trunk. She also had moderate tachycardia but normal blood pressure throughout the episode.

The PN solution was discontinued immediately, and the child received oxygen by bag and mask and 1 dose of intravenous antihistamine. Epinephrine was prepared but not given, as the patient began to improve and fully

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Table 1. Results of Skin Prick Tests at 7 Days and 3 and 22 Months of Life

	+7 Days (W/F)	+3 Months (W/F)	+22 Months (W/F)
Histamine 1 mg/mL	0/10	4/16	6/36
Negative control	0/3	0/8	0/14
Travasol 1/1	0/4.5	0/5	0/0
Intralipids 1/1	0/3.5	2/6	0/0
Multivitamins 1/1	0/8	0/0	0/0
Egg yolk (extract)		0/12	
Egg white (extract)		0/13	

W/F, wheal (mm)/flare (mm).

recovered after 90 minutes. After this episode, PN was withheld during the remaining 7 days stay in the NICU. The mother ate a normal diet, including a moderate amount of eggs, nuts, soy, peanuts, milk, and seafood during pregnancy and also while breastfeeding.

The patient's blood workup on the day of reaction revealed a normal complete blood count, including a normal level of eosinophils, total immunoglobulin E (IgE), and C-reactive protein. The skin prick tests (SPT) done at 7 days of life did not show any reaction to histamine, amino acids, intralipid, and multivitamins (Table 1). The radio-allergo sorbent tests (RAST) for white and yellow egg, soy, and latex were also negative.

The child was breastfed exclusively during the following days, without any further complications, and discharged when she was 11 days old.

At the first follow-up visit at 3 months of age, her growth was within normal range. We repeated the SPT with egg, amino acids, lipid, multivitamins, and histamine (Table 1). At 22 months of age, her growth was still normal, she ate a regular diet without any problem, and repeated SPTs were unchanged.

Discussion

We report the case of a newborn with IUGR who developed sudden onset of irritability, urticaria, generalized edema, tachycardia, and respiratory distress 1 hour after her first exposure to PN at 4 days old. These symptoms disappeared 90 minutes after discontinuation of PN and following a dose of antihistamine.

The constellation of symptoms and the sudden onset after the beginning of PN infusion, in the absence of clinical or laboratory signs of sepsis, strongly suggest a hypersensitivity⁶⁻⁸ reaction.

The multicomponent nature of PN makes identification of the allergen implicated difficult. Most components of PN have already been shown to cause hypersensitivity

reaction.^{9,10} Dermal allergy tests revealed sensitivity to trasvasol, magnesium sulfate, and multivitamins.¹¹ Inactive components such as polysorbates, used as emulsifiers in multivitamins, also have been associated with hypersensitivity.⁹ Lipid emulsions have been associated with delayed allergic reaction.^{12,13} Moreover, allergens of soybean oil or egg yolk, included in lipid emulsions, may also be allergenic.^{14,15}

Latex-induced hypersensitivity reaction is one possible etiology in our case, and as many products used in the NICU contain latex, the child was likely exposed during the previous 3 days of hospitalization. However, latex-induced anaphylaxis more frequently occurs in children with repeated exposure from multiples surgeries early in life or mucosal exposure such as during urinary catheterization.¹⁶⁻¹⁸

Mechanisms of specific immunity, involving T or B lymphocyte and antigen-presenting cells, are gradually developed during intrauterine life.⁵ Allergen sensitization may occur in utero via the fetal gut and circulation or during the first attempts of feeding after birth.

The negativity of RAST or SPT for components of PN or latex suggests that this neonate developed non-IgE-mediated hypersensitivity reaction.^{7,8}

PN-induced hypersensitivity reactions in the literature often report negative or inconclusive results for skin prick testing using PN components.^{10,19} In several cases, confirmation of PN as the inciting agent was confirmed only by stepwise single-component rechallenge.^{9,10,18} For ethical reasons, no challenges were attempted in our case, and the triggering component remains unknown.

Some reports suggest that the risk of allergy is related to postnatal overexpression of Th2 activity,^{2,5} whereas IUGR neonates may have overexpression of Th-1 activity that could potentially reduce that risk. However, Hesselmar et al⁴ could not find this protective effect of IUGR on the development of allergy in infants.

As cases of allergy to PN reported in the literature^{9-11,19-21} frequently involve patients with immunodysregulation, it has been suggested that this condition could be a risk factor for hypersensitivity reaction to PN.²² The association of zinc deficiency and thymus atrophy reported in an IUGR neonate²³ could have induced an immunodysregulation state and anaphylaxis to PN in our case.

Conclusion

This case shows that hypersensitivity reaction to PN may occur in newborns with IUGR. The mechanism of the immune response leading to this reaction is as yet unknown. In this case, there was possible genetic predisposition to the development of atopic responses, as both parents had atopy. Whether this predisposition increases reaction risk

remains to be determined. Given the common use of PN, we would like to alert clinicians to the possibility of such a potentially life-threatening reaction in neonates.

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