

**Possible adverse drug reaction to parenteral amino acids in an infant:
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commercial use, distribution,
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medium, provided the original
work is properly cited.**ABSTRACT**

A case report of a possible adverse drug reaction to 10% parenteral amino acid formulation in a 5½ month male patient diagnosed with bronchopulmonary pneumonia with acute respiratory distress syndrome in septic shock, is presented. There was a temporal relationship between the administration of the parenteral amino acid formulation and the onset of the exanthem. This was further evidenced by the regression of the exanthem following the discontinuation of the formulation. The causality assessment of this adverse drug reaction has been done, and the likely causes of this hypersensitivity reaction have been analyzed.

Keywords: Amino acid, Hypersensitivity, Adverse drug reaction, Exanthem**INTRODUCTION**

A case report of a possible adverse drug reaction to 10% parenteral amino acid formulation in a 5½ month male patient diagnosed with bronchopulmonary pneumonia with acute respiratory distress syndrome (ARDS) in septic shock is presented. There was a temporal relationship between the administration of the parenteral amino acid formulation and the onset of the exanthem. This was further evidenced by the regression of the exanthem following the discontinuation of the formulation. The causality assessment of this adverse drug reaction has been done, and the likely causes of this hypersensitivity reaction have been analyzed.

CASE REPORT

A 5½ month male patient was admitted on 03 December, 2013 with a history of fever and cough for 4 days. Clinical

examination revealed wheeze and bilateral crepitations. The vitals recorded on admission were pulse - 146 bpm, blood pressure (BP) - 88/50 mm of Hg, respiratory rate (RR) - 50, temperature - 100°C, SpO₂ - 98% on room air. The blood reports were as mentioned: hemoglobin (Hb) - 11.20 g%, total erythrocyte count (TLC) - 18,210/mm³ (N-40, L-53, E-2, M-5, B-0), platelet count - 658,290 mm³, prothrombin time - 18.9, activated partial thromboplastin time - 30.4, international normalized ratio - 0.7, serum creatinine - 0.7, Na⁺ - 138.7, K⁺ - 5.2. He was started on injection amoxicillin clavulanic acid 150 mg batrachochytrium dendrobatidis (BD) intravenous (IV) along with a salbutamol nebulization.

On 04 December, 2013, on the basis of X-ray findings and the various blood parameters, a diagnosis of bronchopulmonary pneumonia with ARDS with septic shock was made. The patient was started on injection amikacin 50 mg BD IV.

On 05 December, 2013 child worsened with increasing respiratory distress. He was ventilated with peak inspiratory pressure - 16/positive end-expiratory pressure - 5 FiO₂ - 100%. Inotropes were administered and antibiotic was escalated to injection vancomycin in a dose of 70 mg in 15 ml NS over 30 mins QID IV along with cap oseltamavir 75 mg (1 cap divided in 10 ml sterile water - 2 ml BD). Gradually the ventilator settings were decreased, and the child was shifted to oral feeds on 9/12/13 after being extubated. The blood reports on 09 December, 2013 were: Hb - 8.78 g%, TLC - 15,510 (N-57, L-38, E-4, M-1, B-0)/mm³, platelet count - 318,000 mm³, C-reactive protein - 27.3, Na - 146, K - 3.8. On 10 December, 2013 injection amoxicillin clavulanic acid was stopped and injection meropenem 120 mg was added in 3 divided dose, to the treatment plan, in view of worsening ARDS.

On 12/12/13, following the daily dose of vancomycin at 10 am, injection 10% parenteral aminoacid formulation was started at 12:15 pm at a dose of 1.5 g/kg at a rate of 4 ml/hr (Table 1). At around 2:30 pm, the baby developed a blanching erythematous rash, which was generalized in nature,

Table 1: Composition of the 10% parenteral aminoacid formulation.

Composition (each 100 ml)	
L-Leucine	130 g
L-Isoleucine	0.80 g
L-Lysine acetate	1.20 g
Δ-L-Lysine	0.851 g
L-Methionine	0.312 g
L-Phenylalanine	0.375 g
L-Threonine	0.440 g
L-Tryptophan	0.201 g
L-Valine	0.900 g
L-Arginine	0.750 g
L-Histidine	0.476 g
Glycine	0.415 g
Taurine	0.040 g
L-Serine	0.767 g
L-Alanine	0.930 g
L-Proline	0.971 g
N-acetyl-L-tyrosine	0.5176 g
Δ-L-Tyrosine	0.420 g
N-acetyl-L-cysteine	0.070 g
L-malic acid	0.262 g
Δ-L-Cysteine	0.052 g
Total amino acid	100 g/L
Total nitrogen content	14.9 g/L
pH value	5.5-6.0
Titration acidity	27-40 mmol NaOH/L
Theoretical osmolarity	885 mosm/L

involving the face trunk and, limbs. The vitals as recorded were: pulse 140 bpm, BP - 88/60 mm of Hg, RR - 44, temperature 102.4°C, SpO₂ - 100%. Injection aminoven was stopped immediately, and injection pheniramine malate and injection hydrocortisone was administered and dermatology opinion was sought. The baby was shifted to oral feeds (Figures 1 and 2).

The dermatologist confirmed it as a drug induced exanthem and advised symptomatic treatment with calamine lotion. Following the discontinuation of parenteral aminoacids, the patient's rash reduced by 17 December, 2013 (Figures 3 and 4).

Causality assessment

The causality assessment of the above reaction using Noranjo scale was found to be 4 (possible) which were similar to the assessment by the WHO probability scale. It was assessed as a moderate (level 3) reaction according to the Hartwigs scale for determining the severity of adverse drug reaction. Since it was a definitely preventable reaction on the modified Shumock Thornton scale for determining the probability of an adverse drug reaction, it is important to report such incidences for further evaluation.



Figure 1: Picture of the erythematous rash on the chest and abdomen on 12 December, 2013.



Figure 2: Picture of the erythematous rash on the right arm on 12 December, 2013.



Figure 3: Picture of the resolving rash on 15 December, 2013.



Figure 4: Picture of the resolving rash on 17 December, 2013.

DISCUSSION

Parenteral aminoacids are prescribed for providing essential aminoacids as a part of a parenteral nutrition regimen.¹ It is administered with concurrent monitoring of serum electrolytes, fluid balance and renal function tests. In this particular case, the sequential occurrence of the rash within 2 hrs of the administration of parenteral amino acids, followed by its regression on discontinuation, supports the possibility of it being due to the amino acids. This hypothesis can be substantiated with the previous reports of possible hypersensitivity reactions to parenteral nutrition.^{2,3} In a previous report by Crespi Monjo et al., a probable case of hypersensitivity reaction to total parenteral nutrition (TPN) has been reported, where the onset of TPN infusion coincides with the time of the onset of a disseminated pruritic cutaneous eruption that repeats after a second exposure to nutrition.⁴

Though, it is not possible to determine which component of the formulation caused the hypersensitivity reaction, it can be suggested that that n-acetyl cysteine, which is an important constituent of this formulation can be responsible for the cutaneous manifestations.⁴ Adverse reactions, often leading to treatment delay, are frequently associated with both IV

and oral acetylcysteine and are a common source of concern among treating physicians.⁵ As evidenced by previous reports, it has been previously proven to cause allergy.⁶ The literature review suggests that there are few previous case reports of similar erythematous rash and urticarial rash following administration of IV amino acids, which have been attributed to the bisulfite excipient in the formulation.⁷ In another case report IV amino acid formulation that contained an added MVI had caused a similar type of rash.⁸

Such a cutaneous reaction, in this patient, may also be attributed to the vancomycin infusion, which is known to cause a wide spectrum of skin reactions, including red man syndrome. Findings associated with vancomycin can range from minimal skin and mucosal involvement to extensive dermal exfoliation, nephritis, lymphadenopathy, hepatitis, and multiple serologic abnormalities.⁹ However, previous literature suggests the occurrence of such episodes is more predominant in patients of colitis or existing renal disease,¹⁰ which was not present in our case.

There exists a temporal relationship between administration of 10% parenteral aminoacid formulation and the occurrence of the exanthem, which cannot be overlooked. A rechallenge was not possible in our case, but the resolution of the erythematous rash and fever, following discontinuation gives us further evidence of the association to the drug.

CONCLUSION

According to our causality assessment with various validated scales, the relationship between the drug and the onset of the apparent exanthem is possible and likely to be attributed to n-acetylcysteine and sulfur containing aminoacids. Prescribers of parenteral aminoacids should be aware of the possibility of such a reaction. Since, there are only a few reports of this reaction to parenteral aminoacids, this case report may prove to be a valuable resource to provide a basis for further research in the field of parenteral nutrition.

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