DOI: 10.7860/JCDR/2024/66728.19221

Case Report

Paediatrics Section

# Allergic Reaction to Aminophylline in a Case of Lower Respiratory Tract Infection with Measles: A Rare Case Report

ANUJA SATISH HANDARGULE[1], AMAR TAKSANDE[2], REVAT MESHRAM[3], POONAM UKE[4]




## ABSTRACT

Measles is an acute respiratory infectious disease caused by the measles virus. It leads to respiratory involvement with manifestations such as pneumonia, laryngobronchitis, pneumonitis, etc. It can also cause secondary bacterial and fungal infections. Aminophylline is a methylxanthine bronchodilator composed of theophylline and ethylenediamine. Airway blockage is reversed by bronchial smooth muscle relaxation, increased myosin light chain kinase activity, and decreased intracellular calcium concentration. It relaxes the smooth muscle of the bronchial airways and pulmonary blood vessels, reducing airway responsiveness to histamine, methacholine, adenosine, and allergens. Allergic skin reactions secondary to aminophylline administration have been rarely seen. Aminophylline can be given orally as well as intravenously. A seven-month-old male infant presented with a lower respiratory tract infection and a maculopapular rash involving the face and trunk. A history of contact with measles was present. Intravenous aminophylline was administered for persistent wheezing. The infant developed a generalised erythematous papular rash with a more widespread distribution than before within one hour of administration. The child was treated with antihistamines for the same. After a detailed physical examination, looking at the pattern of the rash and excluding other causes like environmental factors and drug history, the diagnosis of an allergic reaction to aminophylline was made. Early identification of allergic reactions is paramount, as prompt cessation of the offending agent and initiation of appropriate medical interventions can significantly mitigate the severity of the reaction and prevent potential life-threatening complications.

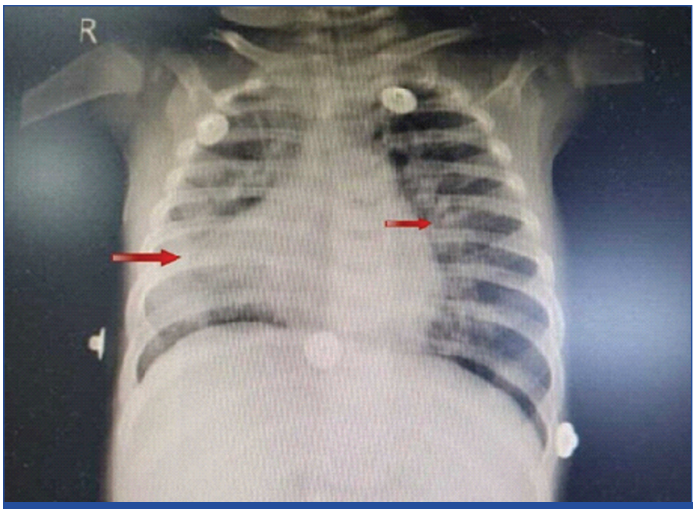

**Keywords:** Bronchodilator, Drug allergy, Methylxanthine, Pneumonitis

## CASE REPORT

A seven-month-old male infant was brought to the Department of Paediatrics, AVBRH Hospital in Wardha, Maharashtra, India, with complaints of fever, cough for two days, and difficulty breathing for one day. The baby was Muslim by religion, first by birth order, and born out of a non consanguineous marriage. As narrated by the mother, the infant was apparently asymptomatic two days back when he developed high-grade fever, relieved with medication with no diurnal variation. The infant also developed a non productive cough with no diurnal variation. The mother noticed a maculopapular rash over the face, gradually spreading to the trunk area for one day. The patient received symptomatic treatment at home for one day for fever and cough. The antenatal history was not significant.

The infant, one day later, developed increased work of breathing, for which the child was taken to a local hospital. There, the child was started on injection meropenem, injection vancomycin, and syrup oseltamivir, and then referred to our institute for further management. A history of contact with measles was present in the family 12 days ago. The history suggested multiple admissions for lower respiratory tract infections. Almost every 15 days, the child was admitted for 2-3 days with a history suggestive of lower respiratory tract infection.

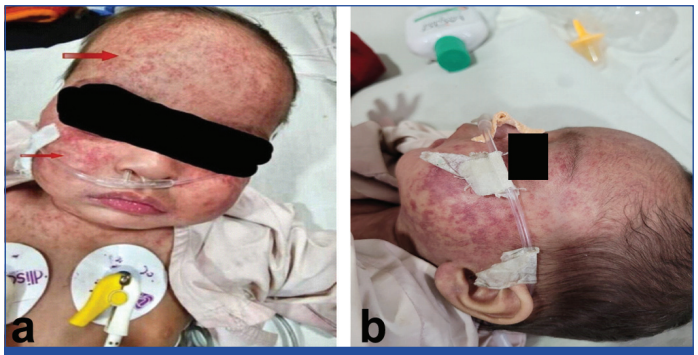
On admission, the infant was tachypnoeic with a respiratory rate of 56/min and maintaining oxygen saturation on $O_2$ of 98% by nasal prongs at 2L/min. On auscultation, bilateral wheeze was present. A chest X-ray was performed, which suggested bilateral infiltrates as shown in [Table/Fig-1]. The complete blood count showed haemoglobin 10.8 g/dL, White Blood Cell (WBC) count 9400/mL, and platelets 3.66 lacs/mL. A provisional diagnosis of viral pneumonia was made. Reverse Transcriptase Polymerase Chain Reaction (RT-PCR) was sent for measles, which later turned out to be positive.




**[Table/Fig-1]:** Chest X-ray of the child showed bilateral pulmonary infiltration.

The infant was put on $O_2$ by nasal prongs at 2L/min and started on injection meropenem at 40 mg/kg/dose 8 hourly, injection vancomycin at 15 mg/kg/dose 6 hourly, vitamin A, syrup oseltamivir at 20 mg per oral BD, and nebulisation with bronchodilators like levosalbutamol and budesonide. As there was no improvement in wheezing, the infant was started on an injection of magnesium sulfate at 20 mg/kg/dose over 20 minutes once daily. Despite this, there was no improvement, and there was an increase in respiratory distress. The infant was given an intravenous loading dose of injection aminophylline at 6 mg/kg diluted in 10 mL of normal saline over 20 minutes. Before starting the maintenance

dose, the infant developed a sudden erythematous papular rash over the face with a more widespread distribution than previous lesions as shown in [Table/Fig-2a,b]. The infant received an injection of avil 0.1 mg/kg and a stat dose of dexamethasone 10 mg/kg. The redness considerably decreased in two days. However, the infant was intubated two days later due to severe respiratory distress. An arterial blood gas was performed, showing pH 7.4, $pO_2$ 60, $pCO_2$ 20, and bicarbonate 17. A blood culture was conducted, which suggested *Candida albicans* on day 7 of admission. The infant passed away five days later.




**[Table/Fig-2]:** a,b) The picture depicts an allergic reaction after administration of aminophylline. This picture was taken one hour after giving aminophylline. Written consent for publishing image was taken.

Clinically and based on investigations, ruling out other causes, a diagnosis of severe sepsis and bronchopneumonia was made. However, an autopsy could not be performed as the parents were not willing.

## DISCUSSION

Bronchial asthma is very common in the Indian paediatric population, with the median prevalence being 4.75% [1]. Aminophylline is a methylxanthine bronchodilator composed of theophylline and ethylenediamine. Aminophylline is an essential drug for the treatment of bronchial asthma, commonly allergic asthma. It is also widely used to treat severe bronchitis that doesn't respond to the usual bronchodilators like beta 2 agonists and corticosteroids. Aminophylline can be administered orally as well as intravenously. In the paediatric population, aminophylline is given intravenously as a loading dose of 6 mg/kg followed by a maintenance dose according to the age group. In a child from six months to one year, it is given at 0.6-0.7 mg/kg/hr. Monitoring serum levels of aminophylline is essential, especially in infants and young children [2].

Many cases of allergic reactions after the administration of aminophylline orally are seen [3]. These allergic reactions caused by aminophylline are manifested as skin eczema, urticaria, or asthma and may be associated with erythema multiforme drug eruption [4]. aminophylline can cause death in toxic doses due to the inhibition of the medulla oblongata. Common side-effects of aminophylline include nausea, abdominal discomfort, and affected appetite. Skin and allergic reactions to ethylenediamine, given systemically in the form of aminophylline, need to be better recognised. It is possible that aminophylline as a compound, rather than only aminophylline, is responsible for allergic reactions [4]. aminophylline dissociates in the body, and ethylenediamine is a potent allergen. It can be theorised that this ethylenediamine is responsible for the allergic reaction. Some trials have shown cell-mediated hypersensitivity to ethylenediamine [5].

Measles is an acute febrile illness, potentially fatal, and highly contagious, transmitted through the respiratory mode. The prodromal phase is characterised by fever, rhinorrhoea, conjunctival congestion, and a dry hacking cough. Koplik spots, considered pathognomonic of measles, appear on the 2nd or 3rd day of the illness. The rash usually appears on the fourth day with a rise in fever as faint reddish macules behind the ears, along the hairline, and on the posterior aspects of the cheeks. The rash rapidly becomes maculopapular and spreads to the face, neck, chest, arms, trunk, thighs, and legs over the next 2-3 days.

Complications of measles include pneumonia (3-9% depending on age), otitis media, laryngotracheobronchitis, diarrhoea, and acute encephalitis [6]. Some cases of measles pneumonitis have been reported [7]. Hecht's giant cell pneumonia, also referred to as primary measles pneumonia, is observed in approximately 3-4% of individuals who contract measles, particularly those with weakened immune systems. Secondary pneumonia primarily stems from bacterial infections, although viral infections, particularly adenovirus, can also be a contributing factor. This secondary pneumonia typically manifests at a later stage and is marked by a sudden worsening of symptoms and clinical indicators, typically appearing around 5 to 10 days after the onset of the measles rash [8]. There is an increased case death rate in children under five years and immunodeficiency, and there are often secondary respiratory and neurologic complications [9]. Corticosteroids and vitamin A have proven effective in treating measles pneumonia [10].

In the above-discussed case, aminophylline was administered to a patient with a fever, rash, and lower respiratory tract infection. As the rash became more reddish and papular, it was difficult to differentiate between an allergic reaction and a measles rash. The child was treated with antihistamines, and the severity of the inflammation subsided. Out of 147 reported reactions to aminophylline, 45 of them were related to dermatological or allergic reactions, with two instances involving exfoliative dermatitis. In contrast, among 61 reported reactions to theophylline, only seven mentioned skin or allergic responses, and none of these specifically noted dermatitis or a particular type of rash [4].

## CONCLUSION(S)

Early detection and treatment of allergic reactions to drugs prevent severe anaphylaxis and shock in paediatric patients. There was a worsening of the already existing rash. An allergic reaction should be suspected whenever there is a urticarial reaction or worsening of the previous lesion. Healthcare professionals should maintain a high index of suspicion for allergic reactions to aminophylline, especially in patients with a history of drug allergies or asthma. Furthermore, this case report emphasises the importance of comprehensive patient history-taking, vigilant monitoring during drug administration, and immediate action in the face of suspected allergic reactions. Clinicians should be well-versed in the signs and symptoms of aminophylline hypersensitivity and be prepared to implement evidence-based management strategies. Authors bring forward this rare case for reporting allergic reactions and advise cautious dosing in children. A test dose should be administered, and subsequent dosing should be done. Though non fatal reactions are seen, it significantly increases morbidity.

## REFERENCES

[1] Pal R, Dahal S, Pal S. Prevalence of bronchial asthma in Indian children. Indian J Community Med. 2009;34(4):310-16. Doi: 10.4103/0970-0218.58389. PMID: 20165624; PMCID: PMC2822191.
[2] Tripathi KD. Essentials of Medical Pharmacology. 8th ed. New Delhi: Jaypee Brothers Medical Publishers; 2018. Pp-1080.
[3] Jiao F, Gao N, Zhang S, Yang Y. A clinical analysis and study of 110 paediatric cases with aminophylline poisoning. Glob Drugs Therap. 2018;3(3):01-03 Doi: 10.15761/GDT.1000148.
[4] Thompson PJ, Gibb WR, Cole P, Citron KM. Generalized allergic reactions to Aminophylline. Thorax. 1984;39(8):600-03.
[5] Elias JA, Levinson AI. Hypersensitivity reactions to ethylenediamine in aminophylline. Am Rev Respir Dis 1981;123(5):550-552.
[6] Paul VK, Bagga A. Ghai essential pediatrics. New Delhi: CBS Publishers & Distributors Pvt Ltd; 2013;783.
[7] Radoycich GE, Zuppan CW, Weeks DA, Krous HF, Langston C. Patterns of measles pneumonitis. Pediatr Pathol. 1992;12(6):773-86. Doi: 10.3109/15513819209024234. PMID: 1448387.

[8] Schoini P, Karampitsakos T, Avdikou M, Athanasopoulou A , Tsoukalas G, Tzouveleki A. Measles pneumonitis. Adv Respir Med. 2019;87(1)63-67. Doi: 10.5603/ARM.a2019.0010.
[9] Kongthavonsakul K, Washington CH, Oberdorfer P. A 6-year-old boy with fever, rash and severe pneumonia. BMJ Case Rep. 2012;2012:bcr1220115411. Doi: 10.1136/bcr.12.2011.5411. PMID: 22605878; PMCID: PMC3369465.
[10] Rupp ME, Schwartz ML, Bechard DE. Measles pneumonia: Treatment of a near-fatal case with corticosteroids and vitamin A. Chest. 1993;103(5):1625-26. Doi: 10.1378/chest.103.5.1625. PMID: 8486065.

**PARTICULARS OF CONTRIBUTORS:**
1. Junior Resident, Department of Paediatrics, Datta Meghe Institute of Higher Education and Research, Wardha, Maharashtra, India.
2. Professor, Department of Paediatrics, Datta Meghe Institute of Higher Education and Research, Wardha, Maharashtra, India.
3. Associate Professor, Department of Paediatrics, Datta Meghe Institute of Higher Education and Research, Wardha, Maharashtra, India.
4. Associate Professor, Department of Paediatrics, Datta Meghe Institute of Higher Education and Research, Wardha, Maharashtra, India.

**NAME, ADDRESS, E-MAIL ID OF THE CORRESPONDING AUTHOR:**
Dr. Anuja Satish Handargule,
Junior Resident, Department of Paediatrics, Datta Meghe Institute of Higher Education and Research, Wardha, Maharashtra, India.
E-mail: anujahandargule@gmail.com

**PLAGIARISM CHECKING METHODS:** [Jain H et al.]
- Plagiarism X-checker: Jul 29, 2023
- Manual Googling: Oct 26, 2023
- iThenticate Software: Feb 08, 2024 (9%)

**ETYMOLOGY:** Author Origin

**EMENDATIONS:** 7

**AUTHOR DECLARATION:**
- Financial or Other Competing Interests: None
- Was informed consent obtained from the subjects involved in the study? Yes
- For any images presented appropriate consent has been obtained from the subjects. Yes

Date of Submission: **Jul 28, 2023**
Date of Peer Review: **Oct 17, 2023**
Date of Acceptance: **Feb 10, 2024**
Date of Publishing: **Apr 01, 2024**