



**CASE REPORT**

**Isovaleric Acidemia in a 5 Years of Boy: A Case Report**

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**Abstract**

Isovaleric acidemia (IVA) is an autosomal recessive disease of leucine metabolism due to deficiency of isovaleryl-CoA dehydrogenase (IVD). In this case report a five years old boy was admitted to National Institute of Neurosciences and Hospital, Dhaka Bangladesh with the history of fever, cough, vomiting, diarrhea, stupor and extreme sleepiness for 3 days. Second degree consanguinity was documented between the parents. Neurological examination revealed exaggerated reflexes and ankle clonus was present bilaterally. EEG and MRI of brain had normal results. Urine organic acid analysis by gas chromatography-mass spectrometry showed slight increment in concentration of 3 hydroxyisovaleric acid and an elevated concentration of isovalerylglycine. Tandem mass spectrometry of acylcarnitines in dried blood spots showed elevated C5-carnitine isovalerylcarnitine (10.3umol/l). Based on history, clinical examination and laboratory results, a diagnosis of isovaleric academia was ascertained. Patient was treated accordingly with rehydration fluid, correction of metabolic acidosis, antibiotic and supportive care. [*Journal of Current and Advance Medical Research 2019;6(1):64-66*]

**Keywords:** Isovaleric academia; autosomal recessive disease; leucine metabolism

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**Cite this article as:** Haque N, Saha N, Alam MB, Mohammad QD, Hoque SA, Islam A, Chowdhury YS. Isovaleric Acidemia in a 5 Years of Boy: A Case Report. J Curr Adv Med Res 2019;6(1):64-66

**Conflict of Interest:** There was no conflict of interest to any of the authors.

**Contributions to authors:** Nazmul Haque has searched and has collected the literature; Nazmul Haque & Bithi Debnath have managed the patient. Narayan Saha, Ariful Islam & Yamin Sahriar Chowdhury have prepared; Quazi Deen Mohammad, Md Badrul Alam & SK Azimul Haque have revised the manuscript.

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**Introduction**

Isovaleric acidemia (IVA) is an autosomal recessive disease of leucine metabolism due to deficiency of isovaleryl-CoA dehydrogenase (IVD). Acute and

chronic intermittent forms have been described. In both forms, an acute episode of metabolic decompensation may occur during a catabolic state such as an infection. Clinical manifestations in the acute form include vomiting and severe acidosis in

the first few days of life, followed by progression to lethargy, convulsions, coma and death if proper therapy is not initiated<sup>1</sup>.

The characteristic odor of “sweaty feet” may be present<sup>1</sup>. In the milder chronic intermittent form, the first clinical manifestation may not appear until the child is few months or a few years old. In both forms, an acute episode of metabolic decompensation may occur during a catabolic state such as an infection<sup>1</sup>. Episodes can be triggered by upper respiratory infections or by excessive consumption of high protein foods.

### Case Presentation

A five years old boy was admitted to National Institute of Neurosciences and Hospital, Dhaka Bangladesh with the history of fever, cough, vomiting, diarrhea, stupor and extreme sleepiness for 3 days. Past history of similar illness occurred many times for which he needed hospitalization with 3 times needs PICU support. In between episodes he was symptom free. Birth history was uneventful but during neonatal period he exhibited unusual lethargy and a history of partial seizure at the 2 months of age. He also had delay in developmental milestone. Second degree consanguinity was documented between the parents. At initial assessment the patient was lethargic, hypothermic and dehydrated with marked kussmaul breathing and had sweaty feet odor in the body. Neurological examination revealed exaggerated reflexes and ankle clonus was present bilaterally. Blood gas analysis revealed metabolic acidosis (pH 7.23; PCO<sub>2</sub> 15 mmHg, HCO<sub>3</sub> 8 mmol/L) with a high anion gap (17.8 mmol/L) and an increased base excess (-14.9 mmol/L). EEG and MRI of brain had normal results. Results of biochemical analysis were within normal limits except mildly increased levels of fasting serum ammonia (109 umol/l). Ketonuria was also present. Urine organic acid analysis by gas chromatography-mass spectrometry showed slight increment in concentration of 3 hydroxy-isovaleric acid and an elevated concentration of isovaleryl-glycine. Tandem mass spectrometry of acylcarnitines in dried blood spots showed elevated C5-carnitine isovaleryl-carnitine (10.3umol/l, normal range being <1.70). Based on history, clinical examination and laboratory results, a diagnosis of isovaleric academia was ascertained. Patient was treated accordingly with rehydration fluid, correction of metabolic acidosis, antibiotic and supportive care. Levocarnitine and sodium benzoate were also added.

### Discussion

Isovaleric acidemia is a clinically variable disorder in the subcategory of organic acidemia that can manifest with early metabolic crises often leading to coma, or it can result in a later chronic condition. Patient may be developmentally normal, but mild to severe mental retardation has been reported<sup>2</sup>. Most organic acidemia present in the newborn period as an acute episode of fulminant metabolic acidosis which may lead to coma and death if not treated adequately. Beyond the neonatal period, patients often present with developmental delay, with or without a history of recurrent acidotic episodes during catabolic stress. Typical laboratory findings during metabolic crises are metabolic acidosis, hyperammonemia, ketonuria, hypo or hyperglycemia, anemia, thrombocytopenia, neutropenia, or pancytopenia. Untreated episodes of metabolic crises may lead to death or severe neurological sequelae<sup>1</sup>. Metabolic decompensations can be triggered by infections, surgical intervention, dehydration or excessive protein intake<sup>1,3</sup>.

A study by Grunert et al<sup>4</sup> demonstrated that gastroenteritis is the most common trigger, while protein excess or surgery did not play a major role as a precipitating factors. The first attack of metabolic crisis in our patient occurred at the age of 17 days and was triggered by gastroenteritis. Two forms of isovaleric acidemia are recognized: the acute neonatal form, leading to massive metabolic acidosis from the first days of life and rapid death<sup>5</sup> and a chronic form with periodic attacks of severe ketoacidosis occur with asymptomatic intervening periods<sup>6</sup>. This patient had periodic attacks of severe ketoacidosis with asymptomatic intervening periods.

Sidbury et al<sup>7</sup> observed that 4 children of a second cousin marriage died in the first 2 weeks of life with the symptoms convulsions, lethargy, dehydration and an unusual urinary odor like that of sweaty feet which occurred after the first 3 days. This case born to second degree consanguineous marriage, presents with recurrent illness like lethargy, dehydration and one episodes of convulsion and had unusual odor of the body during acute illness. The unusual odor was the result of butyric and hexanoic acids. They suggested that it is an inborn error of short-chain fatty acid metabolism and more specifically, that a defect in green acyl dehydrogenase may be involved. In a second family a brother and sister with unrelated parents had a similar ailment. These cases are considered to have been instances of isovaleric academia (IVA)<sup>7</sup>.

The diagnosis of IVA is usually based on the detection of typical metabolites of isovaleryl CoA in the urine organic acid analyses and of elevated C5- carnitine (isovaleryl-carnitine) levels in blood and in molecular analysis<sup>1</sup>. This case has fulfilled first two criteria but without molecular diagnosis because facility for such test is not available in our country and much costlier if performed from abroad.

The treatment of acute metabolic decompensation in IVA cases comprises a high caloric infusion therapy, correction of metabolic acidosis and supplementation with L-carnitine and L-glycine to enhance the detoxification of isovaleric acid<sup>8</sup>. L-glycine is not available in Bangladesh; hence this cannot be used in this case.

### Conclusion

This present case report illustrates that organic acidemias should be kept in mind in the differential diagnosis when patient present with periodic vomiting, lethargy, coma, ketoacidosis and born to consanguineous marriage, though patient may be

normal in between episodes.

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