Journal of Pediatric Endocrinology

Open Access

Austin Publishing Group

Case Report

An Early Association between X-Linked Adrenoleukodystrophy and Type 1 Diabetes Mellitus - A Case Report

Alnafisah M[1], Alanazi SM[2]* and Alshehri S[3]

[1]Department of Neurology, King Abdulaziz Medical City, Riyadh, Saudi Arabia

[2]Department of Pediatrics, Ministry of Health, Diabetes Center, Northern Borders Region, 14611, Saudi Arabia

[3]Department of Endocrinology, King Abdullah Specialist Children's Hospital, Riyadh, 14611, Saudi Arabia

***Corresponding author:** Sami M Alanazi, Department of Pediatrics, Ministry of Health Diabetes Center, Northern Borders Region, 14611, Saudi Arabia

Received: June 05, 2021; **Accepted:** June 30, 2021; **Published:** July 07, 2021

Abstract

X-linked Adrenoleukodystrophy (X-ALD) is a rare genetic disorder of peroxisomal metabolism and is one of the causes of primary adrenal insufficiency. X-ALD is also associated with various neurological manifestations, however the endocrine features may precede neurological symptoms. As it is rare to have two endocrinological conditions with X-ALD, here we present a unique case of a child with confirmed X-ALD and concurrent Type 1 Diabetes Mellitus (T1DM).

Keywords: Adrenoleukodystrophy; Diabetes mellitus Type 1; Autoimmune polyendocrinopathies; Adrenal insufficiency; Peroxisomal disorders

Introduction

This case describes a five-year-old Saudi boy who was diagnosed with Type 1 diabetes mellitus (T1DM) and primary adrenal insufficiency, which prompted the diagnosis and initiation of treatment for Autoimmune Polyglandular Syndrome Type 2 (APS-2); however, further genetic testing proved the diagnosis of X-Linked Adrenoleukodystrophy (X-ALD). To our knowledge, this is the first case reported in the Middle East of T1DM as an endocrine dysfunction associated with X-ALD.

Case Presentation

A 5-year-old Saudi boy known to have T1DM was referred to our pediatric endocrinology and diabetes department for further evaluation after developing multiple hyperpigmented lesions over the axilla and buccal areas. His parents denied any history of new medications, abnormal growth, failure to thrive, previous surgery, or radiation exposure. His past medical history was significant for T1DM diagnosed at the age of 2 years with no evidence of autoimmune markers. He was taking insulin replacement therapy at a dose of 1 unit per kilogram per day. There was no family history of congenital endocrine or metabolic disease. Upon physical examination, his weight and height were on the 10th percentile with no organomegaly. Comprehensive neurological examination did not reveal any abnormality. Skin examination showed scattered hyperpigmented areas over the palmar creases, abdomen, and buccal mucosa. Examination of the external genitalia was unremarkable.

Investigations

Initial laboratory investigations revealed a low morning cortisol level and a high adrenocorticotropic hormone (ACTH) level, consistent with primary adrenal insufficiency. Screening for thyroid and celiac diseases were unremarkable. Preliminary findings suggested a diagnosis of APS-2, and the patient was started on hydrocortisone and fludrocortisone meanwhile. Subsequently, the patient manifested neurological phenomena in the form of ataxia and repeated falls, which was not related to hypoglycemia or hypocortisolism. Basic workup for causes of ataxia revealed no abnormalities, so targeted genetic analysis for ataxia group gene mutations was performed. This revealed a mutation in the ABCD1 gene, confirming the diagnosis of X-ALD. On subsequent visits, analysis of Very-Long-Chain Fatty Acids (VLCFA) revealed a high level, suggesting peroxisomal disease.

Treatment and follow-up

The patient remained on insulin 1 unit per kg per day, hydrocortisone 10 mg twice daily, and fludrocortisone 0.1 mg once daily. His subsequent follow-up visits in the clinic included frequent monitoring of hemoglobin A1c, blood pressure, serum electrolytes, and ACTH level. He has not required hospital admission since diagnosis.

Discussion

This case illustrates an unusual endocrine dysfunction in a five-year-old boy diagnosed with primary adrenal insufficiency with a background of T1DM and genetic testing confirmative of X-ALD. X-ALD is one of the genetic diseases causing adrenal insufficiency that follows an X-linked recessive inheritance pattern [1]. It is considered the most common inherited peroxisomal disorder [1-3] and is associated with VLCFA accumulating in specific tissues secondary to a mutation in the ABCD1 gene [1-4]. X-ALD has a wide variety of clinical presentations and varies in age of onset, with no specific phenotype-genotype association [1-5]; however, being an X-linked disease it manifests primarily in males [2]. The constellation of adrenal insufficiency, neurological symptoms, and gonadal dysfunction is ascribed to the tendency of VLCFA to accumulate in the myelin sheath, adrenal tissue, and Leydig cells [1,2,5,6]. In terms of endocrine manifestations of X-ALD, primary adrenal insufficiency is the most common presentation in affected males, with a peak onset between 3 and 10 years of age [2,5].

Citation: Alnafisah M, Alanazi SM and Alshehri S. An Early Association between X-Linked Adrenoleukodystrophy and Type 1 Diabetes Mellitus - A Case Report. J Pediatri Endocrinol. 2021; 6(1): 1043.

The co-occurrence of adrenal insufficiency in a child with T1DM in our case drove the suspicion of APS-2, which is the most prevalent type of glandular failure disease [7]. Nevertheless, preliminary investigations for ataxia were negative, so targeted genetic analysis for ataxia group gene mutations was performed, which interestingly established the X-ALD diagnosis.

Although the management of the conditions mentioned above (X-ALD and APS-2) includes hormone replacement, the difference in other therapeutic measures, morbidity, and mortality rates necessitates an accurate diagnosis. Upon reviewing the literature, no previous cases in the Middle East appear to have reported an association of T1DM as an endocrine manifestation of X-ALD.

One possible explanation for our case is a "double-hit" phenomenon in X-ALD, where a specific phenotype of the disease manifests when the two ABCD1 genes are mutated. An important note from our case is that implementing X-ALD within the newborn screening program may help in early diagnosis, preventing fatal complications from adrenal insufficiency, and facilitating early intervention.

Acknowledgement

Dr Samantha Miller for providing final proofreading and submission advice.

Author Contributions

S. Alanazi devised the idea for the manuscript. MA and S. Alanazi conducted the literature review. MA wrote the initial manuscript. S. Alanazi and S. Alsherhri performed the re-writing of the manuscript. All authors reviewed and approved the final manuscript.

Patient Consent

Written informed consent was obtained from the patient's parents for publication of this case report.

References

1. Hetman M, Jura M, Krakowska K, Barg E. X-linked adrenoleukodystrophy diagnosed in three brothers. Pediatr Endocrinol. Diabetes Metabol. 2019; 25: 95-98.

2. Burtman E, Regelmann MO. Endocrine Dysfunction in X-Linked Adrenoleukodystrophy. Endocrinol Metab Clin North Am. 2016; 45: 295-309.

3. Abdulhamid I, Saadeh S, Cakan N. A three-year-old boy with X-linked adrenoleukodystrophy and congenital pulmonary adenomatoid malformation: a case report. J Med Case Rep. 2009; 3: 9329.

4. Chen Y, Polara F, Pillai A. Rare variability in adrenoleukodystrophy: A case report. J Med Case Rep. 2018; 12: 182.

5. Eng L, Regelmann MO. Adrenoleukodystrophy in the era of newborn screening. Curr Opin Endocrinol Diabetes and Obes. 2020; 27: 47-55.

6. Suryawanshi A, Middleton T, Ganda K. An unusual presentation of X-linked adrenoleukodystrophy. Endocrinol. Diabetes & Metab Case Rep. 2015: 150098.

7. Michels AW, Gottlieb PA. Autoimmune polyglandular syndromes. Nat Rev Endocrinol. 2010; 6: 270-277.