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(CASE REPORT)

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Delay in diagnosis of testicular feminization in a child with auto-immune polyendocrine syndrome type-1 (APS-1): Who is responsible?

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Abstract

Complete Androgen Insensitivity Syndrome (CAIS) is a rare X-linked recessive disorder. Patients have 46 XY karyotype, and the external genitalia is of a normal female.

In this manuscript, we describe a nine year old child diagnosed at three years of age with Autoimmune Polyendocrine Syndrome type-1 (APS-1). The external genitalia was of normal female with no hernia. Parents initially declined any endocrine disorder in the family. Genetic study, which was recently available to us, revealed an X-linked recessive (AR) gene associated with androgen insensitivity in a 46 XY individual. Screening the family indicated that the maternal aunt is also having androgen insensitivity. Parents then admitted that they knew that they have a child with testicular feminization. The management of this disorder and the importance of education are highlighted.

Keywords: Autoimmune Polyendocrine Syndrome type-1 (APS-1); Complete Androgen Insensitivity Syndrome (CAIS); 46XY female phenotype; Genetic study; Management; Education

1. Introduction

Androgen Insensitivity Syndrome (AIS), formerly known as testicular femininization is an X-linked recessive disorder lead to failure of musculation of the external genitalia in males. It can be either complete or partial depend on the amount of receptor function. Patients have 46XY karyotype and external genitalia is of female (1-7). It has been estimated that the incidence of CAIS is one in 20,400 to 100,000. In Saudi Arabia based on clinical experience and limited published clinical data which indicated that it is not that uncommon (8).

Autoimmune Polyendocrine Syndrome type-1 (APS-1) known as Auto-Immune Polyendocrinopathy Candidiasis-Ectodermal Dystrophy (APECED) is a rare and complex recessively inherited disorder that result from various mutations in the auto-immune regulatory gene (AIRE). It characterised by the triad of hypoparathyroidism, Addison disease and chronic Mucocutaneous candidiasis. Other Auto-immune diseases may present (9-14). The incidence is variable which estimated to be one per 10,000 to 120,000 individuals world wide. The majority of cases are reported from Finland, Sardinia and Iran (15,16).

We report on a nine year old child who presented at age of three with hypoparathyroidism, alopecia, nail dystrophy and recurrent fungal infection which was diagnosed with Auto-immune Polyendocrinopathy Syndrome type-1. Parents

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were consanguineous with strong family history of Systemic Lupus Erythematosus. The patient was later found to have testicular feminization syndrome.

2. Case summary

A nine year old child who was diagnosed to have hypoparathyroidism at one year of age. Later the child developed alopecia, nail dystrophy and recurrent fungal infection and therefor diagnosed as Auto-immune Polyendocrine Syndrome. No clinical or biochemical evidence of hypo adrenal function. External genitalia was normal female and no hernia. Family history revealed highly educated parents who are second degree relatives with a strong history of Auto-immune disorders (Auto-immune haemolytic anaemia and systemic lupus erythematosus. They denied any further endocrine disorders. Genetic study, which was recently available to us, revealed an X-linked recessive gene associated with androgen insensitivity in a 46XY individual. Screening the family indicated that maternal aunt to have androgen insensitivity. Parents, then, admitted that they have one member of the family with androgen resistance. Ultrasound (US) pelvis revealed no uterus while Magnetic Resonance Imaging (MRI) of pelvis showed a well-formed lower end of vagina with no evidence of cervix or uterus. Bilateral oval shaped soft tissue most likely testis

3. Discussion

We present a unique case of a nine year old child with complete androgen insensitivity syndrome with auto-immune polyendocrinopathy. Androgen insensitivity syndrome is the most single entity that lead to 46XY under virilization. It's a rare X-linked recessive disorder with variable presentation (1-8). Genetic tests suggested the diagnosis (17). On the other hand Auto-Immune Polyendocrine Syndrome type-1 is a rare and complex recessive inherited disorder of immune cell dysfunction with multiple auto-immunities. It's characterized by the triad of hypoparathyroidism, Addison disease and chronic Mucocutaneous candidiasis. This is a result of variable mutations in auto-immune regulatory gene. The diagnosis of APS-1 is made by the diagnosis of at least 2 of 3 major components (9,12,14).

This case reported here raise the question whether the combination of AI and APS is an association or incidental, the most likely. Further genetic studies are required to identify the role of androgens on AR gene variant. The diagnosis of androgen insensitivity syndrome should be based on clinical suspicion supported by hormonal, molecular and radiological investigations. The management of AIS is challenging and complex that require an expanded multidisciplinary team of specialists which constitute of paediatrician, endocrinologist, genetics, gynaecologist, surgeon, urologist, plastic surgeon, psychiatrist and psychologist to minimize the long term consequences (18-20). Psychological counselling should be recommended for the patient and their parents. Psychiatric disorder is often associated with AIS (20-21). Family counselling include decisions on sex assignment, timing of gonadectomy, fertility and psychological outcomes. Educate parents and family about the nature of the disorder. All questions must be answered clearly (22-24).

Finally, this case has demonstrated the importance of declaring the family history correctly and clearly. Giving wrong information or hiding certain aspects of history should be avoided. This might lead to delay in diagnosis, and, hence, poor management.

4. Conclusion

This case which was reported in here indicated the importance and value of the family history in the management. Parents could contribute to rapid diagnosis through providing accurate and honest family history. This is an essential step toward an appropriate management.

Compliance with ethical standards

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Disclosure of conflict of interest

The authors have no conflicts of interest to declare.

Statement of informed consent

Informed consent was obtained from all individual participants included in the study.

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