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CONGENITAL HYPOPITUITARISM VARIABLE PRESENTATION FOR THE SAME DIAGNOSIS

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ABSTRACT

Background: Congenital hypopituitarism is a rare clinical syndrome of deficiency in pituitary hormones. It is a life threatening.
Design and selling: A retrospective hospital- based study was conducted at King Khalid University Hospital (KKUH), Riyadh, Saudi Arabia during the period January 1989 and December 2014
Methods: Medical records of patient who were diagnosed to have congenital hypopituitarism were retrospectively reviwed. Data included age, sex, clinical presentation and results of the relevant laboratory and radiological investigations.
Results: Eight patients were diagnosed to have congenital hypopituitarism. Hypoglycemia was the commonest presentation in five (62.5%) patients. Three (37.5%) patients presented with micropenis and bilateral undescended testicle with neonatal cholestasis was the clinical presentation in one.
Conclusion: Congenital hypopituitarism is a rare disorders. It had variable presentations. Hypoglycemia, micropenis in boys and neonatal cholestasis were among the commonest.

INTRODUCTION

Hypopituitarism is a clinical syndrome of deficiency in pituitary hormones production. Panhypopituitarism refers to involvement of more than one pituitary hormone while involvement of one hormone refers to partial hypopituitarism. It is an uncommon disorder of the hypophyseal system but could be life threatening, however, it is treatable. It could be congenital or acquired secondary to birth trauma or asphyxia, or as a part of several midline defect syndromes. The most common disorders is septo-optic dysplasia. This disorder includes absence of the septum pellucidum found in 50% of cases, and underdevelopment of the optic nerves associated with variable degrees of reduced vision. Other midline associations include the presence of fused deciduousupper central maxillary incisors, cleft lip and/or palate, choanal atresia and encephalocele. Genetic mutations involving the anatomic development of the pituitary gland. One of the earliest transcription factors gene involved in the embryogenesis of the pituitary gland is RpX (Rathke's pouch homeobox), also called Hesx1, PROP – 1 and PIT-1 (Geffner, 2002, Mehta and Dattani, 2008, Brodsky *et al*, 2004).

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The diagnosis might be difficult.Certain association of severe neonatal hypoglycemia with micropenis, isolated growth hormone (GH) deficiency, isolated cortisol deficiency, cardiomyopathy and neonatal hepatitis, could indicate the diagnosis. (Sheehan *et al*, 1992, Lovinger *et al*, 1975, Salisbury *et al*, 1984, Al Hussaini *et al*, 2012, Jain *et al*, 2011, Alatzoglou and Dattani, 2010). In this communication, we try to discuss the variable clinical presentations of the disorders and highlight the importance of understanding such clinical fact inthe course of diagnosis.

MATERIALS AND METHODS

This is a retrospective hospital-based study conducted at King Khalid University Hospital (KKUH), Pediatric Endocrine service, Riyadh, Saudi Arabia, during the period between January 1989 and December 2014. The medical records of patients with congenital hypopituitarism were reviewed. The diagnosis was based on clinical, hormonal and radiological studies. Data reviewed include, age, sex, clinical presentation and the relevant biochemical and radiological investigation.

RESULTS

During the period under review, January 1989 and December 2014, a total of eight patients were diagnosed with congenital

hypopituitarism. Their mean age was 6 months (range between 2 weeks to 14 months). Table 1, summarized the demographic and clinical features. Hypoglycemia was the commonest presentation found in five (62.5%) patients and micropenisand bilateral undescended testicle in three (37.5%). They shared in common anterior pituitary gland aplasia or hypoplasia or being small in magnetic resonance imaging (MRI), Figure 1.

Table 1. Demographic and clinical data of 8 patients with congenital hypopituitarism

Patient	Age	Sex	Diagnosis	BW	Clinical Presentation	Magnetic Resonance Imaging
1	6 weeks	F	Panhypopit with TSH, GH, ACTH deficiencies	3.2 kg	Cholestatic jaundice	Ectopic PP Hypoplastic AP
2	8 months	M	Panhypopit with TSH, GH, ACTH deficiencies	3.5 kg	Micropenis, Bilateral undescended testicle, wide fontanele	Ectopic PP Hypoplastic AP
3	3 months	M	Panhypopit with TSH, GH, ACTH deficiencies	2.7 kg	Micropenis, Bilateral undescended testicle, hypoglycemia septic shock	Ectopic PP Hypoplastic AP
4	2 weeks	M	Panhypopit with holoprosencephaly cleft lip	2.5 kg	ACTH, GH deficiencies	Ectopic PP Hypoplastic AP
5	12 months	M	Partial hypopit with isolated GH deficiency	3.0 kg	failure to thrive	Small AP, Normal PP
6	3 months	M	Partial hypopit with isolated ACTH deficiency	2.6 kg	Prematurity hypoglycemia	Small AP, Normal PP
7	12 months	F	Partial hypopit with isolated ACTH deficiency	2.5 kg	hypoglycemia	Small AP, Normal PP
8	14 months	F	Partial hypopit with isolated GH deficiency	3.1 kg	Septo-optic dysplasia with impaired vision	Ectopic PP Hypoplastic AP

Panhypopit = panhypopituitarism, F = female, M = male, BW =birth weight, GH = growth hormone, ACTH = adrenocorticotrophic hormone, TSH = thyroid stimulating hormone, AP = anterior pituitary, PP = posterior pituitary.

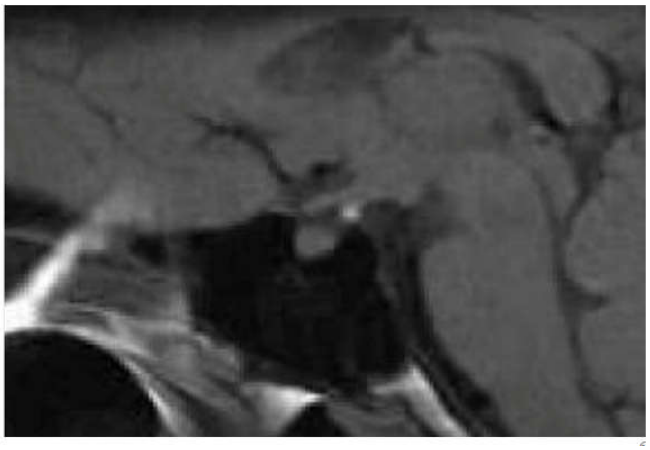

Figure 1. Axial T1 – Weighted Magnetic resonance imaging (MRI) showing congenital ectopic of the posterior pituitary gland with anterior pituitary gland Hypoplasia

DISCUSSION

Hypopituitarism is a clinical syndrome characterized by deficiency of pituitary hormones from disorders of the pituitary hormone production. This may result from disorders of the pituitary gland, hypothalamus or surroundings structures. It could be partial, involving the deficiency of one hormone or complete "Pan" involving the deficiency of more than one hormone. The condition may be life threatening. Onset can be at any time of life. Early diagnosis and treatment promote the best possible outcome. The congenital form of disease is rare compared with the high incidence of hypopituitarism induced by pituitary tumors, transphenoidal surgery or radiotherapy. The incidence of congenital hypopituitarism is estimated to be between 1:3000 and 4000 births. Congenital hypopituitarism is commonly diagnosed either in infancy with neonatal hypoglycemia, micropenis and prolonged neonatal jaundice or mid-childhood because of short structure. Clinical, biological and radiological work up is very important. The clinical manifestations are variable depending on the type and severity of the deficiency. The most important presenting feature of congenital hypopituitarism is hypoglycemia. (Geffner, 2002, Sheehan *et al*, 1992, Lovinger *et al*, 1975, Bell *et al.,* 2004) This occurs secondary to the presence of growth hormone (GH) deficiency with or without associated adreno-corticotrophic hormone (ACTH) deficiency, as both GH and cortisol are important counterregulatory hormones (anti-insulin) that protect against hypoglycemia. Hypoglycemia may often be recurred and severe, however the hypoglycemia usually resolves with replacement of GH and/or cortisol. Therefore, any term infant who develops hypoglycemia with no underlying risk factor, such as prematurity, intrauterine growth retardation infants of diabetic mother, etc., the diagnosis of hypopituitarism must be considered. Additionally, severe cortisol deficiency may result in presentation with hyponatremia (Geffner, 2002). Some children with congenital hypopituitarism manifest with cholestatic jaundice and raised liver enzyme. Cortisol deficiency play a major role in the pathogenesis (Al Hussaini *et al*, 2012, Jain *et al*, 2011, Alatzoglou and Dattani, 2010, Bell *et al*, 2004, Gong *et al*, 2006). Another unique feature of congenital hypopituitarism is the presence, at birth, of a microcephallus (micropenis) in some affected male infants. This may results from isolated GH deficiency or from combined GH and gonadotrophin deficiency. The latter leading to testosterone deficiency in the second and third trimesters and postnatally. The micropenis may enlarge solely in response to the treatment with GH, suggesting that GH has a critical role in penile growth at least in fetal and early postnatal life (Geffner, 2002, Salisbury *et al*, 1984).

Birth asphyxia or trauma, midline defects or malformation, such as cleft lip, cardiomyopathy, certain syndrome such as Beckwith – Wiedmann syndrome and chronic bilateral slipped capital femoral epiphysis (Geffner, 2002, Mehta and Dattani, 2008, Brodsky *et al*, 2004,Jain *et al*, 2011,Baiocchi, 2014, Bowden and Klingele, 2009,Akin *et al*,2014) are known to be associated with congenital hypopituitarism. The presence of extra pituitary birth defects in a short child is a sensitive marker to diagnose congenital hypopituitarism. Subtle abnormalities of the the visual pathway should be investigated for hypothalamus-pituitary target hormones (Dutta *et al*, 2014). In conclusion, congenital hypopituitarism is a rare

disorders. It had variable presentations such as hypoglycemia, microphallus in boys and neonatal cholestasis were among the commonest.

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