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RESEARCH ARTICLE

ADRENAL INSUFFICIENCY IN CHILDREN : TWENTY-FIVE YEARS' EXPERIENCE AT A MAJOR TEACHING HOSPITAL, RIYADH, SAUDI ARABIA

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ABSTRACT

Background

Adrenal insufficiency, the clinical manifestation of deficient, production or action of glucocorticoids with or without deficiency in mineralocorticoids and androgen. It is a life-threatening disorder.

Design and Setting

A retrospective, hospital-based study was conducted at King Khalid University Hospital (KKUH), Riyadh, Saudi Arabia during the period January 1989 and December 2014.

Material and Methods

The medical records of children with the diagnosis of adrenal insufficiency were retrospectively reviewed. Data included age, sex, clinical presentation, and results of relevant laboratory and radiological investigations.

Results

During the period under review, (January 1989 and December 2014), a total of 148 patients with adrenal insufficiency were seen. Primary adrenal insufficiency was the commonest occurrence found in 84.5% of patients with the predominance of congenital adrenal hyperplasia (CAH). A diversity of other causes were also seen.

Conclusion

A wide spectrum of aetiological causes were noted. Congenital adrenal hyperplasia was the commonest. In Saudi Arabia, where consanguineous mating is high, these findings were not unusual.

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INTRODUCTION

Adrenal insufficiency is a disorder first described by Thomas Addison in 1855 which is characterized by deficient production or action of glucocorticoids with or without deficiency in mineralocorticoids and adrenal androgens. It is a life-threatening disorder that can result from primary adrenal failure or secondary adrenal disease due to impairment of hypothalamic-pituitary axis (Figure 1). The clinical symptom of adrenal insufficiency includes weakness, fatigue, anorexia, abdominal pain, weight loss, orthostatic hypotension, salt craving and characteristic hyperpigmentation of the skin occurring with primary adrenocortical failure.

Prompt diagnosis and management are essential. The clinical manifestations of primary adrenal insufficiency results from deficiency of all adrenocortical hormones, but they can also include signs of other concurrent autoimmune conditions. In

secondary or tertiary adrenal insufficiency, the clinical picture results from glucocorticoid deficiency only, but manifestations of the primary pathological disorder can be present. The diagnostic investigations, although well established, can be challenging, especially in patients with secondary or tertiary adrenal insufficiency.¹⁻⁴

This article is an attempt to report on adrenal insufficiency in children, over twenty-five years, at a major teaching hospital, central province (Riyadh), Saudi Arabia.

MATERIALS AND METHODS

During the period under review (January 1989 and December 2014), all patients who were diagnosed with adrenal insufficiency either primary, secondary or tertiary were retrospectively reviewed. Data included age, sex, clinical

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presentation and results of radiological and relevant laboratory investigations.

Adrenal insufficiency can be primary, resulting from the direct insult to the adrenal cortex or an enzyme deficiency, or secondary, from adrenocorticotropic hormone (ACTH) or corticotrophin-releasing hormone (CRH) hyposecretion as a result of pituitary or hypothalamic dysfunctions. Therefore, the appropriate history and physical examination is the key for management. Inappropriately low cortisol secretion, determining whether the cortisol deficiency, primary or secondary, depending on adrenocorticotropic hormone (ACTH) level which can suggest the source of the disorder. Further, laboratory specific tests and radiological images, were also reviewed, if indicated.

RESULTS

During the period under review, January 1989 and December 2014, a total of 148 patients were evaluated for adrenal insufficiency by the author at King Khalid University Hospital (KKUH), Riyadh, Saudi Arabia. The majority, 84.5% were due to primary causes, while the rest either secondary or tertiary (Table 1).

Table 1 Causes of adrenal insufficiency in 148 patients

Diagnosis	No.	%
Primary adrenal insufficiency	125	84.5%
Secondary / tertiary adrenal insufficiency	23	15.5%

Table 2 Causes of primary adrenal insufficiency in 125 patients

Diagnosis	No.	%
Genetic disorders		
• congenital adrenal hyperplasia	103	82.4%
• 21-r-hydroxylase deficiency	84	-
• 11-S-hydroxylase deficiency	15	-
• 3-S-hydroxysteroid dehydrogenase deficiency	4	-
• Congenital adrenal hypoplasia	4	3.2%
•		
• Bilateral adrenal haemorrhage	2	1.6%
• Autoimmune	14	11.2%
• isolated	7	-
• APS-1	6	-
• Adreno-leukodystrophy	1	-
• Triple A syndrome (Allgrove syndrome)	2	1.6%

Table 3 Causes of secondary / tertiary adrenal insufficiency in 23 patients.

Diagnosis	No.	%
Hypothalamic / pituitary tumours	6	26.1%
Congenital hypopituitarism	3	13.0%
Isolated ACTH deficiency	2	8.7%
Streptococcal meningitis	2	8.7%
Histocytosis - X	2	8.7%
Septo-optic hypoplasia	2	8.7%
Cushing syndrome	1	4.3%
Drug-induced glucocorticoid therapy	5	21.7%

Table 2 shows, shows the etiology of the primary adrenal insufficiency, where congenital adrenal hyperplasia was the commonest finding 82.4%. Other aetiologies include congenital adrenal hypoplasia, bilateral adrenal haemorrhagic,

autoimmune adrenal disorders either isolated or part of syndromes of autoimmune polyendocrinopathy and triple A syndrome. Table 3, shows the etiological causes of secondary or tertiary adrenal insufficiency. Pituitary or hypothalamic tumours (Figure 3), and drug-induced glucocorticoids suppression among the commonest.

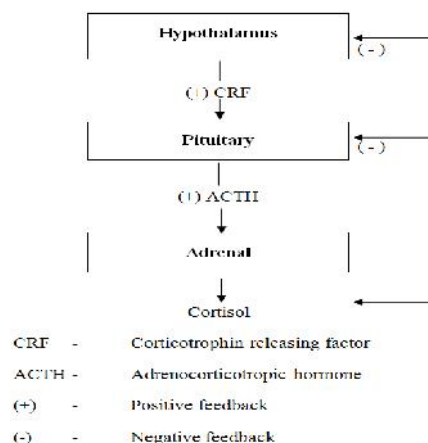


Figure 1 Regulation of the adrenal cortex

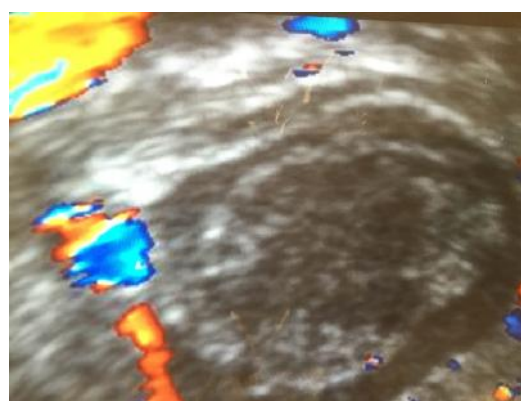


Figure 2 An ultrasound of the adrenal gland showing adrenal hemorrhage



Figure 3 Sagittal unenhanced magnetic resonance imaging (MRI) revealing a huge mass craniopharyngioma

DISCUSSION

Adrenal insufficiency is a disorder first described by Thomas Addison in 1855 in which a deficient production of glucocorticoids. It is a life-threatening condition that can result

from primary adrenal or secondary due to impairment of the hypothalamic-pituitary adrenal axis. Recent epidemiological studies indicate a rising incidence of the disease. The clinical symptoms of adrenal insufficiency include weakness, fatigue, anorexia, abdominal pain, weight loss, orthostatic hypotension, salt craving and characteristic hyperpigmentation of the skin occurring with primary adrenocortical failure.¹⁻¹⁰

The etiology of primary adrenal insufficiency has changed over time. Prior to 1920, the most common cause of primary adrenal insufficiency was tuberculosis, while since 1950, the majority of cases (80%) in the western world, have been described due to "autoimmune" disorders which can be isolated (40%) or in the context of an autoimmune polyglandular syndromes (60%).^{1,4,11-14} In Saudi Arabia, this is not the case where the rate of consanguineous mating is high (60%), as well as multiple siblings inherited disorders such as congenital adrenal hyperplasia (CAH) constituted the majority, 82.4%.¹⁵⁻¹⁷ CAH, is one of the common endocrine disorders, encountered by the practitioner in this part of the world. It is caused by reduced or complete absence of the enzymatic activities of steroid biosynthesis pathway.⁹

In contrast to other reports worldwide, autoimmune disorders are the second most common in our series, found either isolated Addison's disease, or as part of autoimmune polyendocrine syndromes. Antibodies that react against steroid 21-hydroxylase are detected in approximately 90% of patients with autoimmune disorders.¹⁻⁴ Patients with autoimmune polyendocrinopathy syndrome type 1 (APS-1) may present with chronic mucocutaneous conditions, adrenal insufficiency, hypoparathyroidism.¹⁴ Bilateral adrenal infarction caused by haemorrhagic or adrenal vein thrombosis may also lead to adrenal insufficiency. The diagnosis is usually made in critically ill patients.¹⁸ A computed tomography (CT) scan or an ultrasound of the abdomen show bilateral adrenal enlargement (Figure 2). Many infectious agents may affect the adrenal gland and result in adrenal insufficiency including tuberculosis, bacteria, fungal infections, HIV associated infections and cytomegalovirus as in our series, two patients with streptococcal pneumonia meningitis.¹⁹

Secondary adrenal insufficiency may be caused by any disease process that affects the anterior pituitary and interfere with ACTH secretions. The ACTH deficiency may be isolated or occur in association with other pituitary hormone deficiencies.^{6,20} The tertiary adrenal insufficiency can be caused by any process that involves the hypothalamus. Chronic administrations of synthetic glucocorticoids suppress the hypothalamic-pituitary-adrenal (HPA). It is the second most common in our series.²¹

The clinical manifestations of adrenal insufficiency depend upon the extent of loss of adrenal function. The onset is often gradual and may go undetected until an illness or other stress precipitates an adrenal crisis. The clinical manifestations, includes general malaise, fatigue, weakness, anorexia, weight loss, nausea, vomiting, abdominal pain or diarrhea, which may alternate with constipation, hypotension, electrolyte abnormalities, hyperpigmentation, however, this does not occur in secondary or tertiary. Hypoglycaemia is more common in

secondary adrenal insufficiency. Clinical manifestations of a pituitary or hypothalamic tumour, such as symptoms and signs of deficiency of other anterior pituitary hormone, headache or visual field defects, may also be presented.^{1-4,6,10}

The treatment depends on the Aetiology and should include family education. Patients should understand the need for life-long replacement therapy, the need to increase the dose of glucocorticoids during minor or major stress.²²⁻²⁴

In conclusion, wide spectrums of aetiological causes were noted. Congenital adrenal hyperplasia (CAH) was the commonest. In Saudi Arabia, were consanguineous mating is high with multiple siblings involvement should be always considered.

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