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A Case of Addisons Disease Presenting as Acute Abdomen (Common Presentation of an Uncommon Disease)

KEYWORDS: Addisons disease, diagnosis.

Dr. P.Srinivasulu	Dr. K.Gouthami Sree	Dr.Prathap Bingi
Professor of Endocrinology, Government General Hospital Kurnool Medical College, Kurnool.	Assistant Professor of Dermatology, Government General Hospital Kurnool Medical College, Kurnool.	Junior Resident in General Medicine, Government General Hospital Kurnool Medical College, Kurnool.

ABSTRACT *Thomas Addison was first to describe adrenocortical failure in 1855. Despite advances in the treatment of this condition, the diagnosis is still often delayed and sometimes missed with potentially fatal consequences. Here we report a case of Addisons disease whose diagnosis was delayed for a period of around a year. Finally the patient came to us and he is diagnosed and is under treatment for the same, which improved his symptoms drastically. Hereby we report this case to highlight on the importance of early diagnosis and high index of suspicion among the treating physicians.*

Case report:

A 16 year old male patient presented to us with complaints of recurrent vomiting, pain abdomen, loss of weight for the past 8-9 months. Present history started 8 months back with weight loss. Patient did not seek any medical intervention for this symptom initially. Later he developed vomiting and jaundice for which he consulted a gastroenterologist and was found to have gall stones and was offered conservative treatment. After 2 months patient again developed vomiting, fever and abdominal pain and has taken medical consultation again. Conservative therapy was offered and patient got relief of his symptoms. After a gap of 3 months patient went to Gastroenterologist for jaundice, vomiting and abdominal pain and was again offered conservative treatment. 1 week after discharge from there patient developed intractable vomiting, fever , abdominal pain and chest discomfort and was taken to local hospital in Kurnool and got admitted there and was evaluated for about a week. They offered a medical therapy and was symptom free for 1 week. Again he presented with fever, chills and vomiting and got admitted in a local hospital and was treated symptomatically . He was referred to surgery department in view of gallstones in USG abdomen. Surgeon deferred cholecystectomy in view of asthenic built and pallor and advised follow up after 15 days. In mean time he came to us and in view of the asthenic built(figure 1), pigmentation over face, tongue and hands (figure 2) and postural hypotension we suspected adrenal insufficiency and blood samples for cortisol levels and cosyntropin test were taken and treatment was started. Patient improved well with the treatment and was under follow up.

Figure 1 & 2:

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• **List of all the investigations performed in this patient before our visit:**

Date	Investigation	Result
30 Dec 2013	LFTs	Bilirubin- 1.4mg/dl Indirect- 1.1mg/dl SGOT- 24U/L SGPT- 26 U/L
	Peripheral smear	Normal study
	US abdomen	Cholelithiasis
05 Feb 2014	UGI endoscopy	Normal
	US abdomen	Cholelithiasis
May 2014 (in Asian Institute)	Osmotic fragility test	Initial hemolysis- 0.55% Complete hemolysis- 0.40%(Normal)
	Reticulocyte count	0.4%
	HBsAg, Anti HCV, retroviral	Negative
	Vit B12 levels	479pg/ml
	G6PD levels	420mIU/10⁹ RBCs
	ESR	5mm/hr
	FBS	80mg/dl
	Gene analysis for Gilbert syndrome	Negative

Date	Investigation	Result
June 2014	US abdomen	**Gall stones**
In medical unit GGH Kurnool	Thyroid profile	Normal
	Peripheral smear	Microcytic hypochromic **anemia** of moderate degree Hemoglobin- 7.2gm%
	Sr. Amylase Sr. Lipase	Normal
	CECT abdomen	Acute calculous **cholecystitis** with impacted stone **(Mirrizzi's syndrome)**
	Urine analysis	Normal

Investigations performed after visting us:

After admission in Endocrinology	Investigation	Result
In	Serum cortisol 8A.M	<0.2 mcg/dL
	Co Syntropin stimulation test Serum cortisol 1hour later	<0.2mcg/dL
	Thyroid profile	T3- 0.71ng/dL T4- 5.60mcg/dL TSH- 4.80mIU/ml
	Chest X-Ray P/A view	No evidence of tuberculosis lesions
	Mantoux test	Negative
	Sputum for AFB	Negative
	Ultrasound abdomen	Cholelithiasis
	CT abdomen	Evidence of atropy of both adrenal glands
	Serum electrolytes	Na- 132mmol/L K - 4.4mmol/L Cl – 105mmol/L(after treatment)
	Serum creatinine	0.8 mg/dL

CECT ABDOMEN showed no visualized lateral limb of right adrenal gland, thin medial limb of right adrenal and a small left adrenal gland.

Discussion:

Addison's disease is a rare disease with an estimated prevalence [4]-11 per 100000 population of which 2/100000 is due to primary cause i.e., adrenal gland defect . One in 100000 cases will have autoimmune pathology. Out of these 40% are due to isolated autoimmune adrenalitis and the rest are due to association with autoimmune polyglandular syndromes. In developing countries tuberculous adrenalitis is most common cause. Autoimmune disease is moct common in developed countries.

Autoimmune polyendocrine syndrome type 1 (APS type 1) which is due to a mutation in the autoimmune suppressor gene (AIRE) located on chromosome 21q22.3, or in adults in isolation or as genetically more complex autoimmune polyendocrine syndrome type 2 (APS type 2). About 80% of patients with APS type 1 develop Addison's disease and other characteristic disease associations include mucocutaneous candidiasis and hypoparathyroidism. About 18% develop type 1 diabetes mellitus.1

In contrast, APS type 2 is polygenic syndrome associated polymorphism of HLA system.2 In particular, genotypes HLA–DR3/DQ2 and DR4/DQ8 haplotypes seems to confer increased risk. Associated conditions classically include thyroid disease and type 1 diabetes but many other autoimmune diseases such as pernicious anemia, vitiligo, alopecia, celiac disease3 and gonadal insufficiency has been described. Vigilance and early testing for adrenocortical failure should be undertaken in these groups even without classic symptoms.

The clinical features and treatment of the condition are well established.4-7 However, the diagnosis is still often

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delayed or missed with potentially serious consequences.8 It is not uncommon for these patients to be misdiagnosed with other conditions such as chronic fatigue, thyroid disease (often co-existent), depression9 and rheumatological conditions.

Introduced in 1960s the 'cosyntropinn stimulation test' remains the gold standard test for the biochemical diagnosis of Addison's disease.10 This test involves the parenteral administration of a large dose of synthetic ACTH (Cosyntropin) in order to maximally stimulate the adrenal cortex. The response is assessed by measurement of serum cortisol levels.11. Other biochemical tests can also be useful in identifying primary adrenal failure. Classical endocrine feedback regulates the secretion of adrenal cortical hormones and, analogous to the rise in TSH seen in primary hypothyroidism, ACTH levels start to rise in early primary adrenal failure. Reliable ACTH assays are now widely available and should be utilized to help confirm the diagnosis. ACTH levels in this context are usually hugely elevated and partial homology between ACTH and melanocyte stimulating hormone (MSH) results in the classical pigmentation seen in primary adrenal failure.12

Production of the adrenal androgens DHEAS and Androstenedione are also stimulated by ACTH. Aldosterone production from the zona glomerulosa of the adrenal cortex is under the control of renin angiotensin system. Lack of aldosterone leads to salt wasting and elevated renin levels. In fact raised renin levels are one of the earliest changes seen in this condition. Renin and aldosterone measurements are now more robust and available and should therefore also be considered as an adjunct to diagnosis. Modest elevation of Serum TSH level is common in untreated glucocorticoid deficiency.13 This is thought to be due to a direct effect of glucocorticoid deficiency and reverses with replacement therapy . Persistent elevation of TSH after adequate replacement therapy or markedly raised TSH level at presentation in association with positive thyroid autoantibodies, however, suggests concomitant autoimmune thyroid disease.

Autoimmune adrenal failure occurs due to T-cell mediated adrenal cortical destruction but reliable assays for measurement of autoimmune T cells are not widely available. Instead clinicians rely on autoantibodies as surrogate markers to detect disease activity. Adrenocortical antibodies (ACA) measured using indirect immunofluorescence techniques on cryostatic sections of adrenal gland tissue can be found between 60% and 80% patients with Addison's disease at diagnosis. Recognition of the enzyme steroid 21 hydroxylase as the major adrenocortical autoantigen has resulted in development of sensitive assays and antibodies against 21 hydroxylase (21OHAb) can be found in high proportion (80–90%) of patients with Addison's disease at diagnosis. Results from a study in 222 patients with primary adrenal failure suggested that presence of both ACA and 21OHAb was unequivocally associated with autoimmune aetiology. Therefore assessment of the patient with possible primary adrenal failure should include measurement of electrolytes, ACTH, cortisol, renin, aldosterone androstenedione and DHEAS in addition to anti-adrenal cortex antibody. In cases where adrenal antibodies are negative alternative causes for adrenal failure (such as infection or infiltration) should be sought and cross sectional imaging (CT or MRI scan) of the adrenals should be performed.

Once the diagnosis is suspected, the patient should be started on hydrocortisone replacement therapy without further delay, ideally after obtaining a blood sample for above tests but treatment should not be delayed pending biochemical confirmation. The cosyntropin stimulation test remains an important part of the confirmation of primary adrenal failure but this could be done at a later date after withdrawing hydrocortisone for 24 h.

The dose of the hydrocortisone is dictated by patient's clinical condition. Patients who are acutely unwell should be treated with large doses (50–100 mg/6 h) of intravenous hydrocortisone. At such high dosage hydrocortisone will have sufficient mineralocorticoid activity to warrant monotherapy. Patients who are not acutely unwell should be started on oral hydrocortisone (suitable dose would be 15–10 mg on waking and 5–10 mg late afternoon/early evening) together with 50-100 mcg of oral Fludrocortisone and referred to secondary care for the confirmation of the diagnosis.

Summary:

Addison's disease can present with non-specific clinical features to a variety of medical practitioners. We present this case which illustrate the varied clinical presentation of Addisons disease and to highlight on the need for high index of suspicion to make a diagnosis of this rare entity. Once the diagnosis is confirmed patients should be started on hydrocortisone and fludrocortisone replacement and should be on optimal long-term management.

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