Journal Homepage: -www.journalijar.com
INTERNATIONAL JOURNAL OF ADVANCED RESEARCH (IJAR)
Article DOI:10.21474/IJAR01/6800
DOI URL: http://dx.doi.org/10.21474/IJAR01/6800

RESEARCH ARTICLE

CONGENITAL ADRENAL HYPERPLASIA: PRESENTING WITHHYPOCORTISOLISM; SEVEREHYPOCALCAEMIA; HYPOKALAEMIA AND HYPOGONADOTROPIC HYPOGONADISM.

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Manuscript Info

Manuscript History

Received: 21 January 2018
Final Accepted: 23 February 2018
Published: March 2018

Keywords:-
CAH-Congenital Adrenal Hyperplasia;DSD-Disorders of Sexual Differentiation;CT-Computerized Tomography;TTKG TransTubular Potassium Gradient ;17OHP-17 Hydroxy Progesterone;21OH-21 Hydroxylase;BMI -Body Mass Index; Hypokalaemia; PTH-Parathyroid Hormone.

Abstract

Congenital adrenal hyperplasia in milder forms is not very uncommonWe here report such a case of CAH who defaulted in taking glucocorticoid treatment after taking for nineteen years since the age of two years .For two years the patient did not take replacement steroid.He developed hypertension one year after discontinuation for which he was prescribed antihypertensive . The patient had been taking Indapamide for one year to control hypertension. His condition deteriorated for last two months and he lost weight, became anorectic ,started taking food sparingly. He presented to the hospital with severe weakness, pain ab-domen,nausea, vomiting,found to be hypokalaemic,hypocortisolaemic,hypocalcaemic and developed tetany 2-3 days after admission.

Introduction:-

Adrenal steroidogenesis is a dynamic process ,reliant on de novo synthesis from cholesterol,under stimulation of ACTH and other regulators.The synthesis of mineralocorticoids,glucocorticoids and adrenal androgens occur in separate adreno-cortical zones.Congenital adrenal hyperplasia encompasses a group of autosomal recessive enzymatic defects in cortisol synthesis.21-hydroxylase deficiency accounts for more than90% of cases ,and when milder or non classic forms are included ,21-OH deficiency is one of the most common genetic diseases[1, 2]. The phenotype of each CAH patient depends upon the defective enzyme and the severity of defect.Clinical manifestations derive from both failure to synthesize hormones distal to enzymatic block,often with diversion to other biologically active steroids.The most common form of CAH is 21-hydroxylase deficiency.

In classic 21-hydroxylase deficiency ,glucocorticoids are given in dosage suffi-cient to suppress androgen secretion and mineralocorticoids are given to nor-malise electrolytes and plasma renin activity.The management of CAH is com-plicated by iatrogenic Cushing's syndrome, inadequately treated hyperandrogenaemia or both.Close clinical monitoring of growth and development is essential to optimise treatment outcome[3]

Case Report:-

A twenty two year old male a known case of Congenital Adrenal Hyperplasia (Table 1) who defaulted in taking replacement steroid for two years presented with epigastric pain of moderate severity, nausea and vomiting and loose motion(4-6 times/day for 15 days).He was afebrile,mildly icteric with soft ab-domen.He also complained of weakness,and gave a history of loss of about 12 kg. weight in two months.His estimated weight was 64

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kg.,height-168 centime-ter,and BMI-22.67kg/m^2.General examination revealed his face,palms,tongue to be hyper pigmented(Figure 3) and(Figure 4). Examination of his vitals showed tachycardia (pulse-100/minute),respiratory rate-22/minute,blood pressure 168/84 mm of Hg. Initial laboratory investigations revealed hypokalaemia with potassium 1.46mEq/Land estimated TTKG was 9.2 .The patient had sodium of 142mEq / L.. Serum osmolality was 290mOsm/L and urine osmolality was 329mOsm/L.

His thyroid stimulating hormone was in the subclinical range(7.8miu/L), T4 was13.47 gm/dl, T3 was 142ng/dl. Random cortisol was29.59nmol/L .

ACTH estimation showed the level to be in the higher sideof normal i.e. 41.2pgm/ml. His gonadotrophins investigations showed FSH.

0.466miu/ml,LH 0.254miu/ml and serum testosterone was0:048ngm/ml.When pain abdomen was investigated His serum amylase was 173u/L,serum lipase2993u/L ,serum bilirubin1.6mg/dl and Lipid estimation was normal (Cholesterol-83,Triglyceride-79,VLDL-16 ,HDL-C-22,LDL-C-45 mg/dl)and CT abdomen revealed features suggestive of interstitial pancreatitis;CT Adrenals affirming the diagnosis of

CAH(Figure1).Abdomen was soft and pain abdomen subsided within 3-4 days after instituting hydrocortisone given to correct hypocortisolaemia increasing the level of serum cortisol to 1670nmol/L .Epigastric pain subsided within three days.

The patient was given 60 milliEq of potassium daily. .His serum Mg was1.27mEq/L,sodium on fourthday rose to151mEq/L.ABG analysis revealed PH 7.48,pco2-30.6,Hco3 22.7, 1.8,Na 151mEq/L .

On 4-5 th day of admission the patient developed tetany with carpopedal spasm(Figure 2). His serum calcium was found to be 6.9mg/dl,albumin 3.6gm/dl,phosphorous 2.6mg/dl,PTH-139pg/ml,vitamin D-9ng/dl .

Treatment and Outcome:-

The patient was treated with intravenous fluids ,antibiotics, and intravenous hydrocortisone hundred mg. 6 hourly. Sixty milliequivalent of potassium was infused daily since the day of his admission i.e. 16-07-2017. On the third day of admission the patient suddenly developed tetany.His serum calcium, phos-phorous and vitamin D revealed severe hypocalcaemia,hypophosphataemia and

Table 1:- Auxologic and Hormonal Parameters based upon which diagnosis of CAH was made.

Auxologic Measurements					
Height(cm)	105				
Weight(kg)	17.5				
Sexual Maturity Rate					
Penile size(cm)	6.5				
Testicular Volume(ml)	3.0				
Tanner Staging	A1		P 2		G5
Pigmentation(Genital& Axilla)	Present				
Hormonal Parameters	Rsult	Reference Range			
Serum Testosterone(ng/dl)	290	300	1000		
FSH(IU/L)	0.42	1.1	13.1		
LH(IU/L)	3.49	0.4		5.7	
T3(ng/dl)	142	90	190		
T4(microgm/dl)	13.47	4.5 12			
TSH(microIU/ml)	7.8	0.3		5.5	
PRA(ngm/hr/ml)	2.2	1.6		7.4	
17-OHP(ng/dl)	680	40	330		
DHEA(ngm/dl)	856	150		350	

Figure 1:- CAT scan showing bilateral adrenal hyperplasia

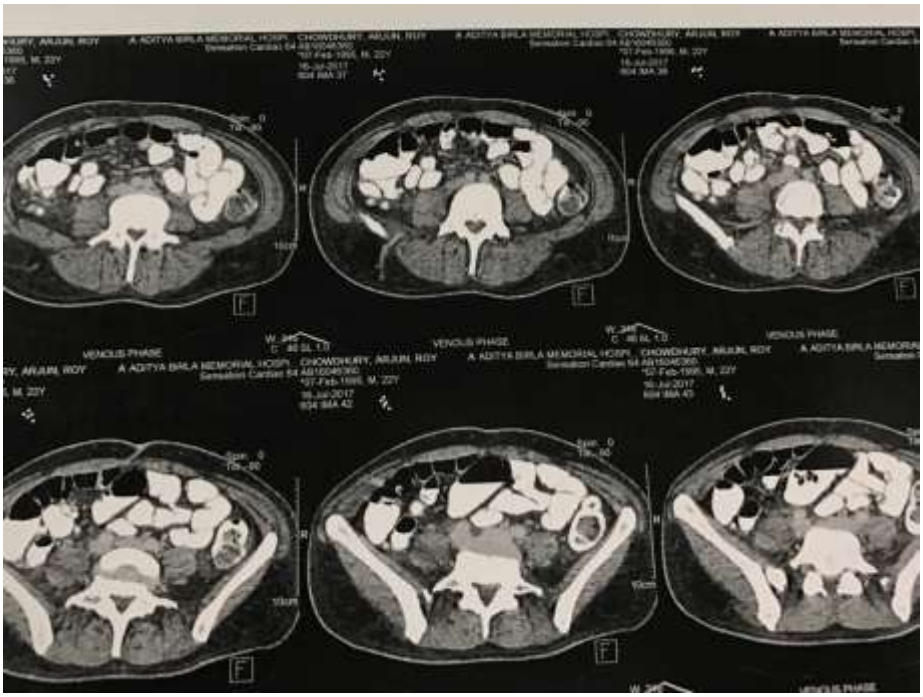


Table 2:- Haemato-Biochemical Parameters(July-2017)

Parameters					Results	Reference Range		
Haemoglobin					12	13	-17	
TLC(10	3	/mm	3	)				
					9.5	4-10		
DLC								
							-75	
Neutrophils(%)					71.2	40		
Lymphocytes(%)					21.9	20	-40	
Monocytes(%)					6.3	2 -10		
Eosinophils(%)					0.3	1	-6	
Basophils(%)					0.3	0	-2	

Table 3:- Hormonal Parameters(July-2017)

Parameters	Results	Reference Range	
Serum cortisol(nmol/L)	29.59	171	-536
ACTH(pg/ml)	41.4	9 -50	
Aldosterone(ng/dl)	1.77	1.17	-23.6
PRA(ng/ml/hr)	0.04	1.6	-7.4
PTH(pg/ml)	139.8	15	-65
25(Hydroxy)VitaminD(nmol/L)	23.7	75 -250	
1; 25(Hydroxy)$_2$Vit D(pg/ml)	35.5	19.6	-54.3
T3(nmol/L)	1.66	1.2	-3.1
T4(nmol/L)	151.2	66-181	
TSH(microiu/ml)	3.40	0.5	-4.5

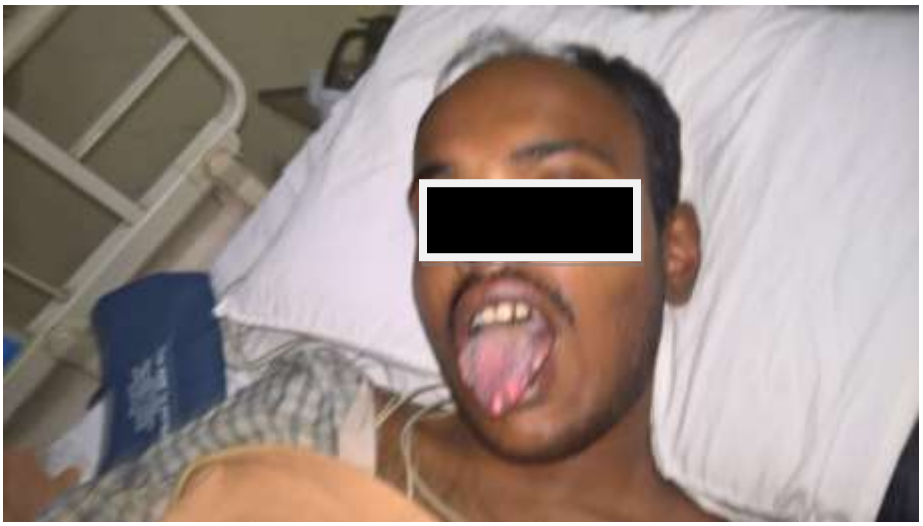
Table 4:- Enzymes and Electrolytes(July-2017)

Parameters	Results	Reference Range			
Serum bilirubin(mg/dl)	1.6	0.2		-1.3	
ALT(U/L)	44	17		-59	
AST(U/L)	64	21		-72	
Urea(mg/dl)	10.7	19.26-42.8			
Serum creatine(mg/dl)	0.92	0.66-1.2			
Serum Amylase(U/L)	173	30	-	110	
Serum Lipase(U/L)	2993	23	-	300	
Calcium(mg/dl)	6.4	8.4	-	10.2	
Phosphorous(mg/dl)	1.8	2.5		-4.5	
Sodium(mEq/L)	147.2	135		-145	
Potassium(mg/dl)	1.49	3.3		-5.5	
Mg(mEq/L)	2.8		2	.5	-4.5

Figure 2:- Carpopedal Spasm

Figure 3:- Pigmented Hand in Addison's

Figure 4:- Pigmented Tongue in Addison's



vitmin D deficiency .Injection calcium gluconate was infused in dextrose solution with the rate of 93 mg/hour and from next day onwards five ampoules/day given till tetany resolved and corrected calcium reached around 8 mg/dl.He was given six lacs units of injection vitamin D.On improvement of all parameters and stabilization of patient's condition he was discharged on 1250 mg of calcium tablet ,syrup potassium two teaspoonful after food three times daily for 15 days,Tablet hydrocortisone 30 mg/day in three divided doses. Table (3) and Table (4).

The patient was reviewed after one month. There was normalization of potassium ,calcium and phosphorous(calcium 9.3mg/dl,phosphorous-4mg/dl ,potassium-4.8mg/dl),although hyperpigmentation had not improved.

Discussion:-

Our patient presented with pain epigastric region of moderate severity which was diagnosed as acute interstitial pancreatitis.It was confirmed by CAT scan of pancreas which revealed mild interstitial inflammation of pancreas .Serum Amylase level was173U/L, and Serum Lipase was 2993U/L.. Drug induced pancreatitis as a causative factor was suspected.As the patient was taking Indapamide to control hypertension which causes renal loss of potassium as occurred in this case as well as diuretic induced pancreatitis could have been a possible agent.Ksiadzyna et al [4] observed that drug induced pancreatitis belongs to rather seldom reported adverse drug reactions,probably because of difficulty in proving the relationship between an inflammation of pancreas and the pharmacotherapy with a certain drug.Lipid profile was normal.He opined that pharmacological agents are among aetiologic factors to be considered in all patients presenting with signs and symptoms consistent with acute pancreatitis.A high index of suspicion and thorough drug history is crucial for making the final diagnosis.Lankisch et al [5] among their 1613 patients treated for acute pancreatitis found 22 of them having drug induced pancreatitis and diueretic was among them.

Our patient had severe hypokalaemia with serum potassium being 1.6mmol/L .It was because of poor food intake,diarrhoea,and diuretic intake .Hypokalaemia defined as plasma potassium < 3.5mEq/L is a common electrolyte abnormality in clinical practice. Because etiologies of hypokalaemia are numerous, the diagnosis of drug induced hypokalaemia may be overlooked. Evaluation and management of a hypokalaemic patient should include careful review of medication history to determine if a drug is capable of causing or aggravating this electrolyte is present[6].Sung et al [7] warn that early recognition of drug induced hypokalaemia with prompt management is still the key to avoid life threatening complications.Bose et al [8] describe a case of 45 year old woman who presented with cardiac arrest. They opined that the low serum potassium was most likely caused by combination of a very deficient diet and use of thiazide diuretic.They further advise that patient on diuretic treatment with suspected malnutrition or chronic gastrointestinal losses require regular monitoring of electrolytes.

The patient was severely hypocalcaemic with serum calcium 4.0 mg/dl which was corrected for albumen.Serum magnesium was normal. Hypocalcaemia as-sociated with hypokalaemia resulted in carpopedal spasm.Hypocalcaemia is en-countered in all areas of clinical practice, in primary care,where vitamin D defi-ciency is often the case,and in unselected secondary care ,where hypocalcaemia has a prevalence of 18% ,rising to 85% in intensive care environment. Hypocalcaemia is potentially life threatening and carries a risk for serious errors in management.Acute hypocalcaemia can result in severe symptoms that require immediate admission to hospital and correction with intravenous calcium[9].

On hormonal testing the patient was noted to be having low gonadotropins as well as low serum testosterone suggestive of hypogonadotropic hypogonadism.It was due to malnutrition associated with weight loss of 12kg body weight in a span of two months and of functional etiology. Functional forms of hypogonadotropic hypogonadism is characterized by a transient defect in GnRH secretion, because of significant weight loss,exercise or stress . Hypothalamic Hypogonadism is typically characterized by low circulating sexual steroids associated low or inappropriately normal gonadotropin levels.The precise and early diagnosis of hypogonadotropic hypogonadism can prevent negative physical and psychological sequelae ,preserve normal peak bone mass,and restore fertility [10].In our case secondary hypogonadism was due to weight loss .

Conclusion:-

This patient presented with severe enzyme and electrolyte abnormality associated with hypocortisolism .The patient fortunately did not land in addisonian crisis. This emphasizes the critical importance of multispeciality team approach while dealing with Congenital Adrenal Hyperplasia patients that requires life long therapy and supervision.

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