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ADULT CONGENITAL ADRENAL HYPERPLASIA

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CONGENITAL adrenal hyperplasia is a rare disease of adults. Probably the oldest recorded case in the literature is of a 57-year-old woman (Logan and McMillan, 1964) who presented as an abdominal emergency. Most of the published reports and standard references are concerned with the biochemical data and there is little suggestion of a characteristic clinical picture. The following case is presented to illustrate the clinical and biochemical features in the oldest subject yet reported.

Case Report

A 58-year-old male electrician was admitted to the Southern General Hospital, Glasgow on 10.8.64 with a history of abdominal pain and swelling of three days' duration. The pain was colicky and epigastric in site. It had settled on antacid therapy before admission. There was a rather vague history of indigestion of this type occurring (as on this occasion) after drinking alcohol.

He stated that he had always had dark skin and that there was no racial basis to this. He had no history of industrial exposure to pigmenting agents.

His previous medical history was of little consequence but he had been admitted to the Southern General Hospital in September, 1954 with a fracture of the zygoma, sustained in a car accident. He was not unconscious on that occasion and there is no history of shock and no comment on pigmentation in the admission summary. Recovery was uneventful without specific therapy.

His family history is summarised in Figure 1. There is a history of cutaneous pigmentation in the father of the patient and two maternal uncles (Figure 1). No blood relatives of the patient were known to be surviving in 1964. He himself had been married for 27 years and though he had wanted and attempted to have children, there were none. He had not consulted anyone about this problem and did not know of any reason for this infertility.

On Examination. The following abnormal features were noted. He was a grey-haired, small man (height 151 cm.—4 ft. 11½ inches) whose span (155 cm.—5 ft. 1 inch) was greater than his height. He had diffuse melanotic pigmentation. His testicles were small and atrophic but he had normal distribution of body hair.

There were bilateral basal crepitations audible on auscultation of the chest but no other abnormal chest findings.

Examination of the abdomen revealed free fluid in the peritoneal cavity (positive shifting dullness test). The liver edge was palpable one inch below the costal margin but was of normal consistency. All other clinical findings were normal and these include a blood pressure of 110/70 mm. Hg. on admission and of 140/80 some months later, before the start of steroid therapy.

Investigations. Normal results: ECG; abdominal plain X-rays; liver function tests; SGOT, SGPT; Bromsulphthalein excretion test; faecal occult bloods; absence of porphyrobilinogen or Bence-Jone's protein in urine; buccal smear—male sex; sputum culture sterile; no fluid was obtained on abdominal paracentesis on 26.8.64.

Abnormal results: Hb 10.8 g./100 ml.; WBC 13,000/cu. mm. with a neutrophilia; ESR 129 mm./hr.; serum iron 20 μg./100 ml.; TIBC 270 μg./100 ml. Electrophoresis of serum protein showed increase in α2 globulins. Barium meal was suggestive but not diagnostic of a duodenal ulcer. Maximum urine specific gravity obtained was 1.014; urine urea 1.3 g./100 ml. There was persistent mild proteinuria (boiling test) and urine microscopy revealed occasional WBC's and granular casts. The urine was sterile on culture. Blood urea ranged from 127-88 mg./100 ml. over the next four months while blood

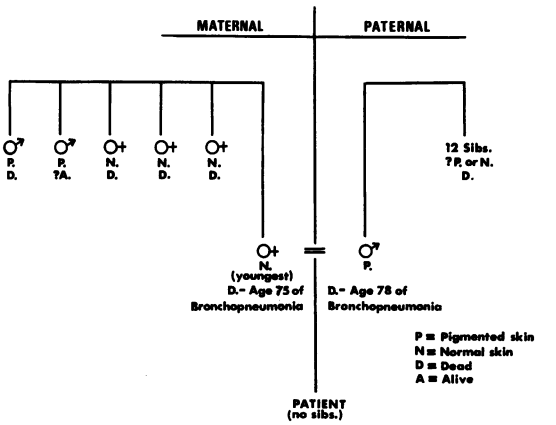

FIG. 1.—Patient's family tree.

TABLE 1

(SEPTEMBER 1964)

Day	Procedure	17-Ketos. mg./day	17-OH-Cort. mg./day		Pregnanetriol mg./day
			(Kornel)	Borohydride	
1	NIL	41.8	5.9	92.1	5.2
2	NIL	40.0	6.6	83.6	3.7
3	75 units ACTH by 8 hr. infusion	50.4	8.3	109.2	30.4
4	Betamethasone 0.5 mg. q.i.d.	—	—	—	—
5	„ „	17.0	6.6	50.8	8.6
6	„ „	10.3	5.5	27.6	6.6

TABLE 2

Time	Date	Procedure	Plasma Cortisol μg./100 ml.
9 a.m.	5.9.64	8 hr. infusion of 75 units of ACTH	16.0
1 p.m.	5.9.64		18.0
5 p.m.	5.9.64		21.0
9 a.m.	7.9.64	Betamethasone 0.5 mg. q.i.d.	3.0

TABLE 3

RESPONSE TO THERAPY

Date	Procedure	17-Ketos. mg./day	(Kornel) 17-OH-Cort. mg./day	Plasma Cortisol μg./100 ml.	Urinary Gonadotrophin (mouse units/day)
5.9.64	NIL	41.8	5.9	16.0	<5
11.2.65	12.5 mg. Cortisone Acetate b.d. for 3 mths.	26	6.6	—	—
19.7.65	12.5 mg. Cortisone Acetate t.i.d. for 5 mths.	11.9	9.6	13.5	>5 <10

electrolytes were normal. Chest X-ray on 12.8.64 was reported as showing patchy bilateral inflammation which had resolved slightly by 28.10.64. Adrenal function test results as obtained on September, 1964 are shown in Tables 1 and 2. Table 3 contains the comparable results obtained of 5.9.64, 11.2.65 and 19.7.65.

The 17-ketosteroids were estimated by the method of Moxham and Nabarro (1956) as were the total 17-ketosteroids. Porter-Silber chromogens were determined by Kornel's (1959) procedure. Pregnanetriol was measured according to Fotherby and Love (1960). Plasma cortisol was estimated by a modification of the method of Mattingly (1962).

In the control urines the finding of markedly elevated 17-ketosteroids with low-normal Porter-Silber chromogens (Kornel) is consistent with a diagnosis of an adrenogenital syndrome involving defective hydroxylation at C-21. This could be bilateral hyperplasia or else a tumour, and the suppression of the 17-ketosteroids by betamethasone confirms that it is due to the former condition. The wide discrepancy between the 17-hydroxy-corticosteroid figures as measured by the two techniques is understandable, since only the borohydride procedure estimates 21-deoxy-compounds of the type found in such a condition.

The pregnanetriol figures, whilst elevated, are not so high in the control urines as might be expected; but the response to ACTH is again characteristic of congenital adrenal hyperplasia.

So, too, the normal plasma cortisol level, in response to the increased circulating corticotrophin (evidenced by skin pigmentation) and the almost complete failure to respond to exogeneous ACTH is consistent with a diagnosis of congenital adrenal hyperplasia.

Urinary gonadotrophin assay was performed by Loraine's (1949) technique. In September, 1964 the assay revealed less than 5 mouse units excreted in 24 hours—a subnormal response. Repeat assay in July, 1965 revealed greater than 5 but less than 10 mouse units excreted in the urine in 24 hours—a normal result. This again is consistent with pituitary gonadotrophin suppression by the abnormal androgens of the adrenogenital syndrome. The July result reflects probable suppression of adrenal androgen production by exogenous cortisone.

The diagnosis of congenital adrenal hyperplasia due to a 21-hydroxylase deficiency was made. The other diagnoses were of duodenal ulcer and subsequent iron deficiency anaemia. The causes of the chronic renal failure and ascites were not discovered.

Management

The patient had a short course of penicillin and streptomycin for his chest infection and this produced some improvement in X-ray appearances. His weight fell 4 lbs., his shifting dullness disappeared and abdominal paracentesis was negative after bendrofluazide and potassium therapy. He was given a course of ferrous sulphate for his mild hypochromic anaemia. Cortisone therapy was started on 2.12.64 at a dosage of 12.5 mg. cortisone acetate b.d. As a result of the urinary ketosteroid results of 11.2.65 (Table 3) the dosage was increased to 12.5 mg. t.i.d.

Discussion

As already stated, this is probably the oldest recorded case of congenital adrenal hyperplasia. This is of special interest because of his pigmentation which was characteristic of hypoadrenalism. The presence of adrenal insufficiency is further supported by the failure of his plasma cortisol to rise normally in response to the ACTH infusion. Pigmentation is an unusual presentation of adult congenital adrenal hyperplasia cases since they tend to be predominantly females, discovered following investigation of hirsutism, masculinisation or sexual precocity (Wyk, 1962; Thorn, 1963; Bongiovanni and Eberlein, 1955). There is occasional mention of pigmentation in congenital adrenal hyperplasia in children in standard references (Thorn, 1963; Lisser and Escamilla, 1957).

The patient was started on steroid therapy to control his hypoadrenalism and to reduce the known risks of developing adrenal carcinoma in untreated congenital adrenal hyperplasia (Hamwi, Serbin and Kruger, 1957). As yet there has been no regression in his pigmentation but his urinary ketosteroids have fallen to a normal level (Table 3).

The patient's involuntary infertility is also of considerable interest. Perlhoff and Hadd (1957) reported the case of a 36-year-old unmarried male who presented with impotence and general tiredness. He had the adrenogenital syndrome. The testicles, though apparently grossly normal, were revealed by biopsy to have reduced maturation of spermatozoa. This was confirmed by a low sperm count and a reduction in motility of his sperm. Gabrilove (1958) reported a case of a 28-year-old male with the adrenogenital syndrome. He also had a maturation arrest of his spermatozoa on testicular biopsy and a reduced sperm count. In both cases the authors reported an increase in sperm count and motility on steroid therapy. In the present case, the rise in urinary gonadotrophin secretion, occurring after adequate steroid therapy, probably reflects release of the pituitary gonadotrophin secretion from the inhibiting influence of adrenal androgen. It is possible that a number of potentially curable cases of involuntary infertility are not being treated because of failure to recognise cases of adrenal hyperplasia. As Gabrilove's (1958) case had no abnormalities in his secondary sexual characters and no pigmentation, routine examination of the urinary 17-ketosteroids appears indicated in all instances of male infertility.

Summary

A case of congenital adrenal hyperplasia presenting with pigmentation of Addisonian type with a history of involuntary infertility is described. Adrenal function tests strongly suggest a deficiency in the enzymatic system affecting 21-hydroxylation.

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A CASE OF "SEIZURES INDUCED BY MOVEMENT"

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THE phenomenon of seizures precipitated by movement has been recognised at least since 1901 when Gowers described three patients, but it is rare. Mathews (1958) reported four cases of "tonic seizures" apparently occurring in the course of disseminated sclerosis, three of which began with movement, walking, turning over in bed or overbreathing. In his discussion of the causation he considers central tetany and excitation or inhibition of the pyramidal or extrapyramidal system by discharge from a subcortical focus, a supplementary motor area or brain stem. The disorder has also been found in association with epidemic encephalitis as described by Wilson (1930) and by Sterling (quoted by Wilson). Twelve cases with no other disease were collected by Lishman, Whitty and their colleagues (Lishman, Symonds, Whitty and Willison, 1962; Whitty, Lishman and FitzGibbon, 1964). They also reviewed the literature and supported the view that it is a form of "reflex epilepsy", though it is unknown whether from discharge from the basal ganglia or the premotor cortex. In support of the latter, Falconer, Drive and Serafetinides (1963) cured a similar, but not identical case, by excision of a scar from the cortex.

We here describe a case which exemplifies most of the features of this bizarre condition because it easily may be thought to be hysterical but, if recognised, can be treated effectively with anticonvulsants.

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Case Report

The patient was a fat messenger boy aged [illegible] years. He had no significant past history until two weeks before admission when, while riding a bicycle, he experienced an unpleasant sensation "like electricity" in his left arm which lasted about half a minute. It was followed by generalised sweating; there was no incontinence nor loss of consciousness. Since then he had had several more attacks, averaging about three a day. They always affected his left side only and were transient. In a typical attack, he felt it starting about ten seconds before his hand clenched; then the elbow flexed and he pressed his index finger against the teeth. Sometimes the left leg was involved similarly with inversion of the foot. The sensation spread to the ear but the face was not affected. After some 45 seconds the spasm ceased and he relaxed, obviously relieved. He had found that it helped to hold his arm straight with the right hand.

In the ward he lay still in bed as he found that the spasm was precipitated by movement. At length he was persuaded to get up which he did, anxiously hyperventilating, and after two steps he had an attack as described. In spite of the appearance of strong muscular contraction, it was easy for an observer to straighten the fingers. In between attacks clinical examination was normal.

Investigations: CSF, WR and skull X-ray were normal. Hb and ESR normal; WBC 12,000, 13% eosinos (this is not usually noticed). Angiography was thought unjustified in view of the family history.

Treatment was begun with chlordiazepoxide (Librium) 10 mg. t.d.s. because it has a mild anticonvulsant as well as a sedative effect. After two days he had no more seizures. Electroencephalogram on the third day showed that there was a mild overall dysrhythmia of a nonspecific variety,