Hypopituitarism in primary haemochromatosis; recovery after iron depletion

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Summary

We report a case of primary haemochromatosis complicated by anterior hypopituitarism which recovered after aggressive venesection therapy. Reversal of anterior hypopituitarism in haemochromatosis following iron depletion has not been previously described.

Keywords: haemochromatosis, hypogonadism, hypopituitarism

Hypogonadotrophic hypogonadism is a common complication of primary haemochromatosis in men and although other abnormalities of pituitary function are recognised, hypopituitarism is rare.¹⁻⁶

We describe a man with primary haemochromatosis and anterior hypopituitarism. Pituitary function recovered following regular venesections. Reversal of hypopituitarism following iron depletion has not, to our knowledge, been previously reported.

Case report

In 1984 at the age of 42 years, the patient was diagnosed as having diabetes mellitus and haemochromatosis. The diagnosis of haemochromatosis was established on the basis of serum iron studies and a characteristic liver biopsy which showed no evidence of cirrhosis. He was started on subcutaneous insulin therapy, weekly venesections removing one pint of blood and advised to abstain from alcohol. Screening did not uncover other family members with haemochromatosis.

In 1986, he complained of lethargy, absent libido, and impotence of two years duration. On examination he was hypogonadal. Endocrine investigations were consistent with hypopituitarism and, in particular, showed severe hypogonadotrophic hypogonadism (table). Computed tomography (CT) of the brain showed a normal hypothalamus and pituitary gland. He was prescribed intramuscular testosterone esters (Sustanon, Organon) building up to a maintenance dose of 500 mg every month, 100 µg oral thyroxine daily and 5 mg oral prednisolone every morning. He rapidly felt well and his libido gradually returned.

Regular venesections continued until 1988, when he became anaemic (haemoglobin 8.8 g/dl) and iron deficient (serum iron 3.2 µmol/l;

reference range 10–30). Thereafter, he was venesected intermittently according to his serum iron concentrations. In 1989, he was prescribed oral mesterolone (Pro-viron, Schering Health) 50 mg twice daily instead of Sustanon but otherwise continued on his other replacement therapy.

In 1994, he was referred to the department of medicine in Guildford, and anterior pituitary function was re-evaluated. Following withdrawal of prednisolone for 24 hours, serum cortisol increased from 467 nmol/l to 635 nmol/l one hour after intravenous administration of 250 µg Tetracosactrin (Synacthen, CIBA Laboratories) suggesting recovery of the hypothalamic-pituitary-adrenal axis. Pituitary replacement therapy was withdrawn and three months later anterior pituitary function was normal (table). He remains well on insulin and in particular continues to enjoy normal sexual function.

Discussion

In haemochromatosis, excess iron is deposited in the pituitary gland and has a particular predilection for the gonadotrophs.^{7,8} Therefore, although hypogonadotrophic hypogonadism is common, symptomatic hypopituitarism is rare.¹⁻⁶

Although considered irreversible,⁹ three cases of partial and complete recovery from hypogonadotrophic hypogonadism following regular venesections have been reported.¹⁰⁻¹² Our case is all the more remarkable, since the patient we described had extensive anterior pituitary disease in addition to marked hypogonadotrophic hypogonadism, all of which resolved following aggressive venesection therapy.

In conclusion, anterior hypopituitarism is a rare complication of primary haemochromatosis (see box on next page) but one which may recover after iron depletion. Anterior hypopituitarism complicating haemochromatosis is, therefore, a previously unrecognised cause of reversible hypopituitarism.

Learning point

Anterior hypopituitarism, a rare complication of primary haemochromatosis, may be reversible with aggressive venesection therapy

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Table Results of investigations

Investigation	1986	1994	Reference range
Testosterone (nmol/l)	0.7	18	10–30
Luteinising hormone (IU/l)	1.8	4	2–11
Follicle-stimulating hormone (IU/l)	1.0	4	1–9
Total thyroxine (nmol/l)	–	66	60–150
Free thyroxine (pmol/l)	5.0	12.4	9–24
Thyroid-stimulating hormone (mU/l)	2.1		<5
		1.52	1.5–3.5
Prolactin (mU/l)	99		<360
		206	<600
Dehydroepiandrosterone sulphate (µmol/l)	<0.1	1.9	0.7–11.5
Peak cortisol response to insulin-induced hypoglycaemia (nmol/l)	346	570	>550
Peak growth hormone response to insulin-induced hypoglycaemia (IU/l)	16.2	49.3	>20
Iron (µmol/l)	51	27	10–30
Iron-binding capacity (µmol/l)	54	51	45–70
% saturation	94	53	20–55
Ferritin (µg/l)	500		36–262
		33	15–330
Total bilirubin (µmol/l)	29	26	<20
Aspartate aminotransferase (IU/l)	48	26	<45
Gamma glutamyl transferase (IU/l)	26	24	<55
Alkaline phosphatase (IU/l)	121		30–115
		134	80–300
Albumin (g/l)	46	39	34–50
Electrocardiogram	normal		
Chest X-ray	normal		

Frequency of clinical features at diagnosis in 145 men and 18 women with primary haemochromatosis

Symptoms:

weakness and lethargy 83%
 abdominal pain 58%
 arthralgia 43%
 loss of libido or potency 38%
 amenorrhoea 22%
 dyspnoea on exertion 15%
 neurological symptoms 6%

Physical findings:

hepatomegaly 83%
 pigmentation 75%
 loss of body hair 20%
 splenomegaly 13%
 peripheral oedema 12%
 jaundice 10%
 gynaecomastia 8%
 ascites 6%

Other findings:

electrocardiogram changes 36%
 cirrhosis 69%
 oesophageal varices 9%

Laboratory findings:

increase in serum transaminase activity 62%
 abnormal serum albumin concentration or
 prothrombin time 18%
 diabetes mellitus 55%

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