Reversal of myelodysplasia with pituitary hormone replacement

Introduction

This article presents an unusual case of myelodysplasia secondary to panhypopituitarism which was corrected with cortisol and thyroxine replacement.

Discussion

This 61-year-old man had a pancytopenia with bone marrow studies consistent with myelodysplasia. He also had panhypopituitarism secondary to a large non-functioning pituitary adenoma. The myelodysplastic picture resolved with steroid and thyroxine replacement, suggesting that the myelodysplasia was secondary to the panhypopituitarism.

The anterior pituitary has an established role in the regulation of erythropoiesis and panhypopituitarism is commonly associated with a normocytic anaemia. A retrospective study by Nishioka and Haraoka (2005) demonstrated anaemia in 32% of patients with panhypopituitarism which resolved with hormone replacement. The role of anterior pituitary hormones in the regulation of myelopoiesis and thrombopoiesis is less clear. In the same study of patients with panhypopituitarism, leukocyte and platelet counts were lower than in control subjects, but did not change after hormone replacement.

Thyroid hormones (Moriyama and Fisher, 1975) and testosterone (Dainiak et al, 1978) both stimulate erythroid progenitors directly, increase erythropoietin production and potentiate the action of erythropoietin. Growth hormone stimulates erythroid and granulocyte colony formation through insulin-like growth factor-1

Dr Ishan Mehta is Senior House Officer in Endocrinology in Diabeticare, Hillingdon Hospital, The Hillingdon Hospitals NHS Foundation Trust, Uxbridge, Middlesex UB8 3NN

Dr Ketan Patel is Consultant in Haematology in the Department of Haematology, Hillingdon Hospital, The Hillingdon Hospitals NHS Foundation Trust, Uxbridge, Middlesex

Dr Mark Edwards is Consultant in Endocrinology and Acute Medicine in Diabeticare, Hillingdon Hospital, The Hillingdon Hospitals NHS Foundation Trust, Uxbridge, Middlesex

Correspondence to: Dr I Mehta (idmehta@doctors.org.uk)

CASE REPORT

A 61-year-old man presented to primary care with a longstanding history of fatigue and episodic frontal headache. His fatigue had worsened over several years, resulting in impediment to occupational and social activities. He noted a reduced appetite with minimal weight loss as well as a loss of libido and erectile dysfunction. He also remarked upon a reduced ability 'to fight off colds and flus'.

He complained of a longstanding history of episodic frontal headache that had been attributed to migraine for which he took sumatriptan. Over the 6 months before presentation, he noticed increasing frequency and severity of headaches, with pain also radiating occipitally. There was never any associated aura, visual disturbance, dizziness or alteration in consciousness.

Blood tests performed in primary care showed white blood cell count 2.9x10^9/litre (neutrophils 1.5x10^9/litre), haemoglobin 118 g/dl, platelets 138x10^9/litre, thyroxine 5.20 pmol/litre (normal range 7.5–21.1 pmol/litre), thyroid-stimulating hormone 10.93 mIU/litre (normal range 0.34–5.6 mIU/litre). The full blood count was repeated a month later and showed white blood cell count 2.4x10^9/litre (neutrophils 1.0x10^9/litre), haemoglobin 113g/dl, platelets 122x10^9/litre.

He was referred to haematology with a persistent pancytopenia and bone marrow studies were performed. Bone marrow aspirate demonstrated several features of dyserythropoiesis including binucleate forms, irregular nuclei and nuclear cytoplasmic asynchrony. Dysgranulopoiesis was also observed but with no excess of blasts. The trephine biopsy revealed a mildly hypoplastic bone marrow with a cellularity of 45%. Myelopoiesis was shifted to the left with giant metamyelocytes, segmented polymorphs and megakaryocytes with variability in lobulation with several hypolobate forms. There was no evidence of infiltration. Bone marrow cytogenetics demonstrated a normal karyotype. This was all in keeping with myelodysplastic syndrome with multilineage dysplasia.

During routine haematology follow-up, thyroid function testing was repeated which showed thyroxine 4.60 pmol/litre (normal range 7.5–21.1 pmol/litre) and thyroid-stimulating hormone 10.00 mIU/litre (normal range 0.34–5.6 mIU/litre) and the patient was referred to endocrinology. Further endocrine testing was performed: 9am cortisol 41 nmol/litre (normal range 200–750 nmol/litre), testosterone <0.40 nmol/litre (normal range 6.1–27.1 nmol/litre), luteinizing hormone 0.4 IU/litre (normal range 1.2–8.6 IU/litre), follicle-stimulating hormone 1.5 IU/litre (normal range 0–19 IU/litre) and prolactin 206 mIU/litre (normal range 56–278 mIU/litre). A short synACTHen test was impaired with: time 0 minutes 47 nmol/litre, time 30 minutes 181 nmol/litre and 60 minutes 213 nmol/litre.

Magnetic resonance imaging of the brain showed an expanded pituitary fossa with a 29x21x20 mm lesion, consistent with a large pituitary adenoma that had undergone previous haemorrhage and was associated with chiasm compression (*Figures 1* and *2*). Visual field testing demonstrated a bitemporal superior visual field defect and optical coherence tomography scanning showed bilateral nerve fibre layer loss.

Treatment for the hypopituitarism was started, initially with hydrocortisone 20 mg at 8am, 10 mg at 2pm, 10 mg at 8pm and subsequently thyroxine 50 μg daily in addition. The patient underwent transphenoidal adenectomy, which was uncomplicated. Following surgery, hydrocortisone and thyroxine replacement, the patient's full blood count normalized within 3 months: white blood cell count 8.3 x10^9/litre (neutrophils 5.8x10^9/litre), haemoglobin 132 g/litre, platelets 186x10^9/litre, and his blood film showed no evidence of myelodysplasia. He was later started on testosterone and his hormone replacement was titrated appropriately. On repeat testing, his visual fields had normalized. Clinically the patient's fatigue and headaches were abolished and he reported feeling 'like a new man'.

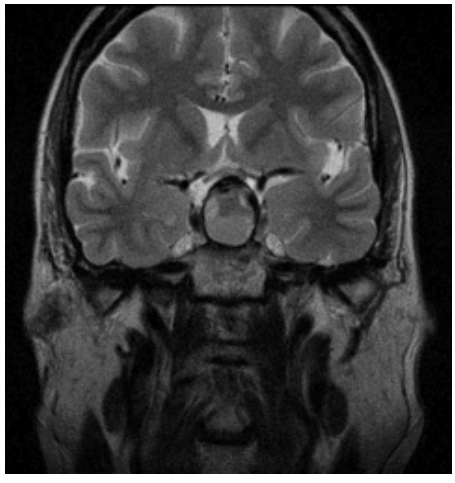

Figure 1. Magnetic resonance imaging of the brain (coronal view).

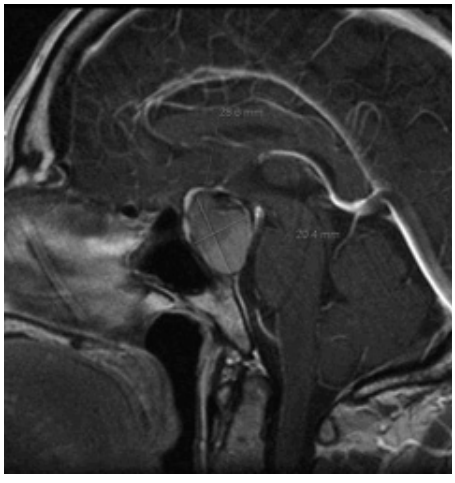

Figure 2. Magnetic resonance imaging of the brain (midsagittal view).

(Merchav et al, 1988). Steroid hormones directly stimulate erythropoiesis, but the mechanism is unclear.

Although normocytic anaemia is common, pancytopenia is a rare idiosyncratic response to panhypopituitarism with evidence limited to isolated case reports and predominantly associated with Sheehan's syndrome (Fatma et al, 2011). A case reported by Hallstensen et al (2001) demonstrated the normalization of both erythropoiesis and myelopoiesis following the administration of cortisol in a patient with hypopituitarism presenting with anaemia and neutropenia.

Holmes et al (2011) reported a similar case to this, with pancytopenia secondary to a macroprolactinoma, but with no myelodysplastic features. To the authors' knowledge, this is the first reported case that demonstrates not only pancytopenia but also myelodysplasia in the context of panhypopituitarism secondary to a pituitary macroadenoma. The resolution of the myelodysplasia with cortisol and thyroxine replacement in this patient suggests that one or both of these hormones play a role in regulating myelopoiesis. **BJHM**

Dainiak N, Hoffman R, Maffei LA, Forget BG

LEARNING POINTS

- Panhypopituitarism should be considered as a rare cause of pancytopenia.
- In patients with abnormal haemopoiesis secondary to hypopituitarism, replacement of pituitary hormones may correct the haematological abnormalities.

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