Panhypopituitarism in Association with Interferon-Alpha Treatment

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ABSTRACT

A 30-year-old woman presented in March 2000 with a six-year history of oligomenorrhoea followed by amenorrhoea. She was a known hepatitis B carrier and received interferon-alpha therapy from 1994 to 1997. She developed oligomenorrhoea three months after commencing interferon therapy. Endocrine investigation showed panhypopituitarism. Magnetic resonance (MR) imaging showed a 2 x 3 mm cyst at the posterior aspect of the anterior pituitary gland. She was treated with cortisol, thyroxine and sex hormone replacement. Repeat MR imaging 10 months later showed the same pituitary cyst with no interval change. In conclusion, a case of irreversible panhypopituitarism, associated with interferon-alpha therapy, is reported.

Keywords: amenorrhoea, interferon-alpha, oligomenorrhoea, panhypopituitarism

INTRODUCTION

Interferon-alpha therapy has been widely used in the treatment of hepatitis and chronic myelogenous leukaemia. It has been reported to cause various endocrine abnormalities, in particular thyroid dysfunction(1,2). Some of these problems are reversible while some may run an irreversible course. Pituitary involvement has rarely been reported although there are two previous reports of hypopituitarism(3,4). However, there is a possibility of under-recognition due to difficulty in assessment.

CASE REPORT

A 30-year-old woman presented to our institution in March 2000 for investigation of secondary amenorrhoea. She had menarche at the age of 11 years, followed by regular menses until 1994. She presented to a private practitioner in 1994 with epigastric discomfort, and was incidentally found to be a hepatitis B carrier. She was put on interferon-alpha therapy continuously from 1994 until 1997 by doctors in the private sector. The reason for this prolonged interferon-alpha therapy was not clear to us and no explanation was available. She developed oligomenorrhoea three months after commencement of interferon-alpha therapy. She developed amenorrhoea starting from January 1999. She visited a gynaecologist, was told to have hyperprolactinaemia and was given bromocriptine. However, she remained amenorrhoeic despite bromocriptine treatment, and stopped taking it from November 1999.

Physical examination revealed normal secondary sexual characteristics. Visual fields were normal and she was otherwise well. The prolactin concentration was 485 mIU/L (normal <650 mIU/L) at the time of referral to us. Serum oestradiol was 173 pmol/L while follicle-stimulating hormone and luteinising hormone concentrations were 5.9 IU/L and 1.4 IU/L, respectively, suggesting hypogonadotropic hypogonadism. Further investigations were arranged at the next visit. Free thyroxine T4 concentration was low at 8.9 pmol/L.
developed oligomenorrhoea a few months after commencing interferon-alpha therapy, which further progressed to amenorrhoea four years later. This suggested a progressive destructive process. She had panhypopituitarism at the time of presentation to us. The small 2 mm cyst is unlikely to explain her hypopituitarism. The raised AFP may suggest the possibility of germinoma. However, the gradual decrease of AFP and lack of a corresponding lesion on MR imaging did not support this possibility. The raised AFP is likely due to underlying liver cirrhosis.

A short-term study has shown an activation of the pituitary-adrenal axis with interferon treatment but long-term data are not available\(^{[8]}\). Hypopituitarism has previously been reported to both run a reversible or irreversible course after interferon-alpha therapy\(^{[3,4]}\). In our case, this patient did not show recovery of pituitary function despite discontinuation of interferon-alpha for more than three years. It should be noted that the patient reported by Sakane et al\(^{[9]}\) received interferon-alpha treatment for three months only and ran a reversible course. On the other hand, our patient received interferon-alpha treatment for more than three years and the patient reported by Concha et al\(^{[10]}\) received interferon-alpha for one year. Both of them ran an irreversible course. The difference in treatment duration may explain the irreversibility of the hypopituitarism. A prospective study of the thyroid dysfunction in patients receiving interferon alpha therapy has also shown that some of the processes were irreversible in some of the patients\(^{[10]}\).

In summary, this lady developed irreversible panhypopituitarism in association with interferon-alpha therapy. This case emphasises the importance of the possibility of autoimmune endocrine disease, including irreversible hypopituitarism, occurring in association with the use of interferon alpha therapy.

**REFERENCES**