the presence of a low transferrin level is explained by this abnormal tumour ferritin having the capacity to bind 30% of the serum iron.

Excessive serum levels of ferritin may lead to an increased iron transfer to hepatic cells.³ In this patient the localisation of excessive iron is consistent with such an effect mediated by tumour ferritin. This in turn may have produced a stimulus to intestinal iron absorption.¹

Although haemochromatosis will increase the risk of primary tumour development⁵ it is an unlikely occurrence in this case. The atypical iron distribution limited to liver and spleen, lack of family history, and high iron binding capacity are against the diagnosis of primary haemochromatosis. Probably the bronchial carcinoma produced an abnormal ferritin that resulted in excessive iron absorption from the gastrointestinal tract and increased iron deposition in the liver and spleen.

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Inhibition of stress-induced hyperprolactinaemia

Evidence suggests that there is dual control of inhibition and stimulation of prolactin secretion.¹ Inhibition appears to predominate under basal conditions and is probably mediated through dopamine. There is less certainty about the stimulatory pathway, but surges of prolactin secretion occur in some physiological and stressful states, such as sleep, nipple stimulation, general anaesthesia, and insulin-induced hypoglycaemia. This stimulatory pathway may include serotonin neurotransmission, since administration of L-tryptophan or 5-hydroxytryptamine—precursors in central serotonin synthesis—noticeably increases the serum prolactin concentration, which is blunted by serotonin antagonists.² Furthermore, the stress release of adrenocorticotrophic hormone by hypoglycaemia may be serotonin mediated.³ We therefore investigated whether serotonin neurotransmission mediated the release of prolactin in a young woman with stress-induced galactorrhoea.

Case report

A 19-year-old woman had had irregular menses before taking an oral contraceptive containing 0.1 mg mestranol for six months. During this period her ankles were fractured in a road accident, although there was no head or chest trauma. A few hours after the accident she developed breast engorgement and spontaneous bilateral galactorrhoea, which persisted. Her menses did not return when the contraceptive was stopped, and she noticed continued minor breast discharge. Five months later she underwent general anaesthesia for an orthopaedic procedure and again noted breast engorgement, which persisted for three weeks. She was not taking medication and was euthyroid. Sellar tomography showed nothing abnormal and the basal serum prolactin concentration was normal.

The stress response was reproduced by inducing hypoglycaemia with insulin 0.1 U/kg intravenously so that prolactin was released, and then giving thyrotrophin-releasing hormone 250 µg intravenously two hours later. This enabled the response of prolactin to a stimulus acting directly on the pituitary to be assessed. Because the stress pathway was thought to be serotonergic she was given cyproheptadine 8 mg by mouth seven-hourly for 21 hours, after which hypoglycaemia was induced and thyrotrophin-releasing hormone given as before (see figure).

The patient was treated with bromocriptine 2.5 mg twice daily, and within four weeks she had her first menstrual period. The galactorrhoea disappeared, and the menses have continued regularly.

Response of serum prolactin to hypoglycaemia and thyrotrophin-releasing hormone (TRH) before and after treatment with cyproheptadine. Serum glucose concentrations (in mmol/l) are given in parentheses.

Conversion: SI to traditional units—serum glucose: 1 mmol/l $\approx$ 18 mg/100 ml.

Comment

The patient twice developed stress-induced breast engorgement and also exhibited the syndrome of post-pill amenorrhoea with galactorrhoea. This syndrome may or may not be associated with an increased prolactin concentration. The oestrogen dose may have caused hyperplasia of the prolactin-secreting cells of the pituitary,¹ which in turn may have caused the increased secretory response to stressful stimuli. Even though the basal serum prolactin concentration was consistently within the normal range she exhibited a dramatic rise in concentration in response to induced hypoglycaemia; this excessive stress response may have caused the post-trauma and post-anaesthesia breast engorgement. The inhibition by cyproheptadine of this hyperactive response to hypoglycaemia suggests that it may be mediated by serotonin neurotransmission, although cyproheptadine also has mild antihistaminic and anticholinergic actions. Hypoglycaemia-induced cortisol secretion is inhibited by cyproheptadine, and this is clinically useful in treating Cushing's disease.³ There is an increase in hypothalamic serotonin content with insulin-induced hypoglycaemia, but, since both the hypothalamus and the pituitary contain serotonin, it is not yet known where the reaction that causes prolactin release occurs. Serotonin infused directly into the pituitary portal vessels failed to release prolactin, which suggests that the reaction takes place in the hypothalamus.⁵ Moreover, the fact that cyproheptadine did not interfere with the direct action of thyrotrophin-releasing hormone on prolactin release suggests that serotonin-mediated stress release of prolactin takes place at a functional level above the pituitary.

It is not known, however, whether the surge of prolactin in response to stress is mediated by a prolactin-releasing factor or by inhibition of the prolactin-inhibiting factor. Further studies are necessary to investigate the physiology of stress-induced prolactin release and to establish the exact role of serotonin neurotransmission.

Dr H Friesen kindly performed the prolactin assays.
Requests for reprints should be sent to Dr B Corenblum.

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