SHORT REPORTS

Primary thyroid failure with concomitant thyroxine binding globulin deficiency

The interpretation of thyroid function test results may be complicated by abnormalities in the concentrations of thyroid hormone binding proteins. We report a case of primary thyroid failure in which estimation of the correct replacement dose of thyroxine was complicated by simultaneous deficiency of thyroxine binding globulin (TBG).

Case report

A 48 year old man was referred in 1976 to his local rheumatology clinic with a one year history of aching arms and legs. Rheumatoid arthritis was tentatively diagnosed. During follow up further symptoms of postural ankle oedema and stiffness of the wrists developed and his general practitioner noted features suggesting myxoedema. Retrospective questioning elicited that he had dryness of his skin, a preference for warm weather, and a six month history of hoarseness of his voice.

Investigations showed: total thyroxine concentration less than 10 nmol/l (0.8 µg/100 ml) (normal 60-140 nmol/l; 4.7-10.9 µg/100 ml); total triiodothyronine less than 0.5 nmol/l (0.3 ng/ml) (1.6-3.0 nmol/l; 1.0-2.0 ng/ml); thyroid hormone distribution index* 3.6 (1.2-2.0); free thyroxine index less than 0.4 (1.1-2.7); thyroid stimulating hormone 290 mU/l (<13 mU/l); total protein 89.5 g/l (67-82 g/l); albumin 46.6 g/l (37-49 g/l); globulin 42.9 g/l (24-37 g/l); thyroid microsomal antibodies positive; and tanned cell agglutination test negative.

Treatment was started with 50 µg thyroxine daily, and the replacement dose was gradually increased to raise the total thyroxine and triiodothyronine concentrations into the normal range, but this was never achieved. The replacement dose was not titrated against the plasma thyroid stimulating hormone concentration at any stage. His condition improved with 100 µg thyroxine a day, and he was discharged from the clinic.

In 1980 he was referred to our department for reassessment of his thyroid state because thyroid biochemical findings remained abnormal. He had no symptoms of thyroid disease and was clinically euthyroid taking 100 µg thyroxine daily. Thyroid function tests gave the following results: total thyroxine concentration 21 nmol/l (1.6 µg/100 ml); total triiodothyronine 0.7 nmol/l (0.5 ng/ml); thyroid hormone distribution index 2.8; and thyroid stimulating hormone 9 mU/l. The thyroxine was stopped, and several weeks later the following results were obtained: total thyroxine concentration less than 10 nmol/l (0.8 µg/100 ml); total triiodothyronine 0.5 nmol/l (0.3 ng/ml); thyroid hormone distribution index 3.0; thyroid stimulating hormone 104 mU/l; and thyroxine binding globulin 0.4 mg/l (normal 6-16 mg/l). Rocket immunoelectrophoresis failed to detect a peak of TBG. Screening of his mother had shown TBG deficiency (concentration 5.4 mg/l).

Thyroxine was restarted at 150 µg daily, and he subsequently remained euthyroid. Plasma thyroxine and triiodothyronine concentrations were ignored, and the plasma thyroid stimulating hormone concentration alone was used as an indicator of biochemical state.

Comment

This case shows the difficulty in interpreting results of thyroid function tests in patients with low or undetectable concentrations of TBG. The very high thyroid hormone distribution index both before and during replacement treatment should have suggested TBG deficiency. The total concentrations of bound thyroxine and triiodothyronine were low not only because of the patient's undoubted primary thyroid failure but also because of his concomitant TBG deficiency. In the absence of other severe non-thyroidal illness and any of the diseases commonly associated with low TBG values, and in view of the proved maternal TBG deficiency, this condition was presumably hereditary in our patient. Interestingly, with adequate replacement doses of thyroxine the plasma total thyroxine concentration varied between 20 and 26 nmol/l (1.6 and 2.0 µg/100 ml), which is characteristic of TBG deficiency.¹

TBG deficiency was first reported in 1959.² Its incidence was estimated to be one in 7900 in a neonatal screening programme in the United States.³ The difficulties in initially diagnosing TBG abnormality and in managing it when it is combined with thyroid disease have been well described.¹ Relative TBG deficiency has previously been

associated only with hyperthyroidism.⁴ As far as we are aware this is the first reported case of acquired primary thyroid failure in a patient with TBG deficiency.

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Department of Nuclear Medicine, General Infirmary at Leeds, Leeds LS1 3EX

I R WAKEFIELD, BSC, MRCS, registrar

D A HUNTER, BSC, MRCP, registrar

S R GOODALL, MSc, senior biochemist

C J HAYTER, BSC, FRCP, consultant physician

Correspondence to: Dr I R Wakefield.

Potential use of postcoital contraception to prevent unwanted pregnancy

Unwanted pregnancy is a major problem despite the widely available contraception services. Abortion is widely used as a solution to the management of unwanted pregnancy but is unsatisfactory economically, emotionally, and socially. Effective methods of postcoital contraception are available,¹⁻⁴ but, although they have the potential to prevent unwanted pregnancy, they have not made any impact on the number of terminations, which is increasing.⁵

To estimate the potential use of postcoital contraception we asked a consecutive sample of 100 women who were having their pregnancy terminated at this hospital about their use of contraception, their awareness of the possibility of pregnancy at the time of intercourse, and their knowledge of and attitudes to postcoital contraception.

Patients, methods, and results

The test sample consisted predominantly of young unmarried women with no previous pregnancies, although a quarter were married or living with their consort. Ninety six women considered themselves to have a stable relationship with their consort.

Patients were asked if they had considered the possibility of pregnancy within 48 hours after unprotected intercourse, when they could have sought postcoital contraception. Twenty eight women had been aware of the risk of pregnancy immediately after intercourse 15 had not used any contraceptive protection, 11 had been aware of potential contraceptive failure (usually the sheath had burst), and two had forgotten to use their normal method of contraception. Another 28 women would not have sought postcoital contraception as they believed that they had been adequately protected by contraception. Of these 28 women, 24 were pregnant due to genuine failures in their contraceptive method and four thought that they were using their method correctly. Forty four women had not considered the possibility of pregnancy at intercourse: 25 had not used any contraception, and 19 knew that they had used their method incorrectly but did not correlate this with the risk of pregnancy.

Knowledge of postcoital contraception was poor. One woman had conceived despite postcoital contraception, one had requested it but been refused, and 10, although having sufficient knowledge of postcoital contraception, had considered themselves to be protected by their existing method. Forty one women were aware of postcoital contraception but their knowledge was vague or inaccurate; the remaining 47 had no knowledge at all. When patients were told of the possibility of postcoital contraception only two expressed any concern about the method, both about contraindications to oestrogen. The remaining 98 women said that they would have used postcoital contraception if they had known of its existence or had thought of it within the effective time limit.

When asked where they would prefer to obtain postcoital contraception 78 patients said that they would prefer to go to their own general practitioner, 13 to a family planning clinic, three to a specific postcoital contraception clinic, three to an army medical centre, and one to a chemist; two had no preference. Although only three women preferred the suggestion of a specific postcoital contraception clinic, five others supported the idea in principle.

*The thyroid hormone distribution index (THDI) is inversely related to the spare capacity of specific plasma proteins for binding thyroid hormones (free thyroxine index = THDI × total thyroxine/100).

Comment

Termination of pregnancy is a problem, particularly among young unmarried women. Postcoital contraception could help to reduce the number of unwanted pregnancies, but there is uncertainty about its potential value and controversy about its desirability. Our study showed widespread ignorance about postcoital contraception, which contrasted sharply with the desire to see this method made more available. The preferred source of help was the general practitioner, and therefore general practitioners need to be made aware of the need for such a service.

This study suggests that postcoital contraception could make an important contribution in decreasing the number of terminations of pregnancies, but greater awareness of the method will be required among both patients and medical staff.

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Newells Hospital and Medical School, Dundee DD1 9SY

TRACEY A JOHNSTON, fourth year medical student
PETER W HOWIE, MD, professor of obstetrics and gynaecology

Correspondence to: Professor P W Howie.

Diagnosis by bronchoalveolar lavage of cause of pulmonary infiltrates in haematological malignancies

Interstitial lung disease in patients with malignant lymphoma often presents diagnostic problems. Transbronchial biopsy is often not diagnostic and carries an increased risk of bleeding because of coagulopathy in these patients. We recently succeeded in clarifying the underlying cause of pulmonary infiltrates in seven patients with haematological malignancies by subtyping cells recovered by bronchoalveolar lavage.

Method and results

Bronchoalveolar lavage was performed with a flexible bronchoscope by instilling 100 ml sterile 0.9% saline in 20 ml aliquots into the lung segment that was radiographically most severely affected. Lymphocytes in the lavage fluid and in blood were subtyped with commercially available mono-

clonal antibodies using the peroxidase-antiperoxidase method performed on glass slides coated with poly-L-lysine.¹ This method has proved useful in the study of multiple surface markers when cell numbers are low. Another advantage is the evaluation with a light microscope, which gives simultaneous information about cell morphology. The table gives the results in seven consecutive patients.

In four patients (cases 1-4) the diagnosis of lymphoma was definitely established by bronchoalveolar lavage. In two of these patients (cases 1 and 4) this diagnosis was entirely unexpected. Though one patient (case 1) was in a subleukaemic phase, examination of mononuclear cells from the blood showed only 5% abnormal lymphoid cells. This had not been found before by routine analysis of white cells. The other patient (case 4) was not leukaemic, and no other organs apart from the left lung were affected. In cases 1 and 2 the diagnosis of malignant lymphoma was confirmed by bone marrow biopsy (case 1, immunoblastic lymphoma; case 2, lymphoplasmacytic immunocytoma). In case 3 a bronchial biopsy showed diffuse infiltration of the bronchial mucosa by small lymphoid cells consistent with lymphocytic lymphoma. In case 4 bronchoscopic biopsies did not show lymphoma, and a histological diagnosis was not available.

In the three remaining patients (cases 5-7) pulmonary infiltration with haematological malignancies was ruled out by analysis of lavage fluid cells with monoclonal antibodies. In all three cases the cell differentials in the lavage fluid were abnormal, showing a predominance of T lymphocytes as evidence of alveolitis, but atypical lymphoid or myeloid cells were not present. In cases 5 and 6 drug induced interstitial pneumonitis was the most probable diagnosis; this was supported in case 5 by the complete clearing of the lung shadowing after cyclophosphamide was withdrawn. In case 7 the decreased ratio of helper to suppressor T cells and the increase in Leu-7⁺ natural killer cells in lavage fluid suggested hypersensitivity pneumonitis due to organic dusts.^{2,3} This diagnosis was confirmed by the history (exposure to parakeets) and by positive serum precipitins against antigens of this bird.

Comment

We conclude that bronchoalveolar lavage and analysis of the recovered cells for surface markers should be considered as a non-invasive diagnostic approach in cases of pulmonary shadowing associated with malignant haematological disorders. Compared with biopsy procedures, bronchoalveolar lavage is a safe method that does not carry an increased risk of bleeding in patients with clotting defects.

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Medizinische Universitätsklinik, D-7800 Freiburg, Federal Republic of Germany

U COSTABEL, MD, clinical and research assistant

K J BROSS, MD, assistant professor

H MATTHYS, MD, professor

Correspondence to: Dr U Costabel.

Characteristics of seven patients with pulmonary shadowing and malignant haematological disorders*

Case No	Sex	Age (years)	Clinical diagnosis	Diagnosis established by bronchoalveolar lavage	Results of surface marker analysis of lymphocytes in lavage fluid (data are % of total cells recovered)
1	F	34	Suspected sarcoidosis with hilar and pulmonary involvement	B cell lymphoma of high malignancy	18% abnormal large lymphoid cells, positive for B ₁ , Ia, IgG, λ
2	M	62	Gastrectomy for malignant lymphoma 5 years previously. Subsequent progressive interstitial lung disease of unclear cause	B cell lymphoma of low malignancy (immunocytoma, lymphoplasmacytic)	60% abnormal small lymphoplasmacytic cells, positive for B ₁ , Ia, IgM, κ, OKT9, OKT10
3	M	53	Chronic lymphocytic leukaemia. Pulmonary infiltrates of unclear cause	B cell lymphoma of low malignancy (lymphocytic)	35% abnormal small lymphoid cells, positive for B ₁ , Ia, Leu-1, IgG, κ
4	F	47	Chronic pneumonia of left lower lobe	T cell lymphoma of high malignancy (immunoblastic), suppressor/cytotoxic phenotype	20% abnormal large lymphoid cells with irregular nuclei, positive for Leu-2a, OKT8, Ia, OKT11
5	F	58	B cell lymphoma (immunocytoma, lymphoplasmacytic). Interstitial lung disease of unclear cause. Treatment with cyclophosphamide + vincristine	No evidence of pulmonary B cell lymphoma. Lung disease probably induced by cyclophosphamide	62% normal lymphocytes, of which 90% were pan T cells (Leu-1/OKT3 ⁺), 60% helper/inducer (Leu-3a/OKT4 ⁺), 30% suppressor/cytotoxic (Leu-2a/OKT8 ⁺), and <1% B cells (B ₁ /IgM + D ⁺)
6	F	68	Chronic myeloid leukaemia. Pulmonary infiltrates of unclear cause. Treatment with busulfan	No evidence of pulmonary infiltrates of chronic myeloid leukaemia. Lung disease probably induced by busulfan	83% normal lymphocytes, of which 95% were pan T cells (Leu-1/OKT3 ⁺), 75% helper/inducer (Leu-3a/OKT4 ⁺), 20% suppressor/cytotoxic (Leu-2a/OKT8 ⁺), and <1% B cells (B ₁ /IgM + D ⁺)
7	F	47	Chronic myeloid leukaemia. Interstitial lung disease of unclear cause	No evidence of pulmonary infiltrates of chronic myeloid leukaemia. Hypersensitivity pneumonitis (parakeet fancier)	67% normal lymphocytes, of which 95% were pan T cells (Leu-1/OKT3 ⁺), 45% helper/inducer (Leu-3a/OKT4 ⁺), 50% suppressor/cytotoxic (Leu-2a/OKT8 ⁺), 31% NK-cells (Leu-7 ⁺), and <1% B cells

*Classification of lymphoma based on Kiel's classification.