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Infective thyroiditis in two cases of systemic lupus erythematosus

兩個系統性紅斑狼瘡病者所患的感染性甲狀腺炎

We report on two patients with systemic lupus erythematosus, both of whom developed suppurative thyroiditis. One suffered from *Staphylococcus aureus*-induced thyroiditis and the other had tuberculous thyroiditis. The occurrence of tuberculous thyroiditis in systemic lupus erythematosus has not previously been reported. The diagnoses were made by fine-needle aspiration biopsy and subsequent bacteriological confirmation. Transient alteration of thyroid function was observed in both patients. In patients with systemic lupus erythematosus who present with fever and anterior neck pain, infection of the thyroid gland should be considered, and appropriate investigations undertaken.

本文報告系統性紅斑狼瘡的兩個病例，患者都染上化膿性甲狀腺炎，起因不同，一是由金黃色葡萄球菌誘發的甲狀腺炎，另一為結核性甲狀腺炎。系統性紅斑狼瘡患者染上結核性甲狀腺炎是香港有史以來首宗報告。兩症以細針穿刺活檢診斷，及後以細菌學檢驗來確定，病者甲狀腺功能都出現短暫的變化。系統性紅斑狼瘡病者，如伴有發燒和前頸痛，應當採取適當措施診斷甲狀腺是否受到感染。

Introduction

Acute bacterial thyroiditis is uncommon and tuberculous thyroiditis is rare, because the thyroid gland is normally relatively resistant to bacterial infection.¹ The clinical features of infective thyroiditis include neck pain, fever, and tender thyroid mass, and may be difficult to distinguish from other conditions, such as de Quervain's thyroiditis. In this article, we describe two patients with systemic lupus erythematosus (SLE) who had infective thyroiditis. The cases illustrate that bacterial infection of the thyroid gland should be excluded in immunocompromised patients who present with fever and tender thyroid masses.

Case reports

Case 1

A 21-year-old woman presented to the Prince of Wales Hospital in 1995 because of a 1-week history of persistent low-grade fever and the sudden development of a tender goitre and occasional palpitations. She was known to have SLE complicated by type II mesangiocapillary glomerulonephritis and cerebral involvement. At presentation, the patient's temperature was 38°C, blood pressure was 120/80 mm Hg, and pulse rate was 110 beats per minute. She had a mild hand tremor and mild eyelid retraction. Furthermore, the thyroid gland was enlarged with fluctuance over the left lobe and was tender on palpation. Bruit and cervical lymphadenopathy were absent. The patient had been receiving an oral corticosteroid and intravenous cyclophosphamide for the SLE. One month before this admission, she had presented to her general practitioner with a fever and exudative pharyngitis. Details of the treatment given for that episode were not available. Blood culture at that presentation yielded *Staphylococcus aureus*.

The patient's white cell blood count was 11.2×10^9 /L and contained 90% neutrophils; the erythrocyte sedimentation rate (ESR) was 122 mm/h. The total thyroxine (T_4) level in the serum was initially high, at 250 nmol/L (reference

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range, 46-140 nmol/L), but it returned to normal, at 117 nmol/L, a few weeks later without specific treatment. Other indicators of thyroid function that were measured 4 weeks after presentation were all normal: the serum level of thyroid-stimulating hormone (TSH; thyrotropin) according to radioimmunoassay was 1.4 mIU/L (reference range, 0.3-4.0 mIU/L), the total tri-iodothyronine (T₃) level was 1.1 nmol/L (reference range, 1.0-3.1 nmol/L), and the T₃ (resin) uptake was 0.31 (reference range, 0.24-0.38). Tests for thyroglobulin and microsomal antibodies gave negative results. Ultrasonography of the thyroid gland revealed a haemorrhagic cyst on the left side, and radioisotope scanning demonstrated decreased uptake in the left lobe, but yielded no definite 'cold' nodules. Blood, sputum, and urine cultures were negative for organisms. Fine-needle aspiration of the thyroid yielded 6 mL of purulent material from which *S aureus* was cultured. The organism was sensitive to cloxacillin, fusidic acid, cotrimoxazole, and gentamicin. The diagnosis of acute bacterial thyroiditis leading to abscess formation was made; the thyroiditis presumably resulted from haematogenous spread from the earlier staphylococcal infection.

The patient was treated with intravenous antibiotics, namely cloxacillin and fusidic acid. Vancomycin was subsequently added to the regimen because of the unsatisfactory response. Fine-needle aspirations of the thyroid were performed on three further occasions with repeated cultures positive for *S aureus*. Because the thyroid mass continued to enlarge, open drainage and packing were performed, although this was complicated by poor wound healing. The patient remained febrile and her mental state deteriorated while antibiotic therapy was being continued. Computed tomography of the brain gave normal results, but lumbar puncture showed pleocytosis. Ziehl-Neelsen staining and culture of cerebrospinal fluid were negative for acid-fast bacilli and other organisms. A trial of antituberculous drugs was started for suspected tuberculous meningitis, but the fever did not subside. Cardiac arrest developed approximately 1 month later and the patient failed to respond to resuscitation. Post-mortem examination revealed tuberculous meningitis in addition to the thyroid abscess. No other source of staphylococcal infection could be identified.

Case 2

A 19-year-old woman was diagnosed to have SLE in 1994 and had skin, joint, and renal manifestations of SLE—namely, facial skin rash, polyarthritis, neutropenia, and proteinuria of 1.10 g/d (reference level, <0.15 g/d). She was admitted to the Prince of Wales Hospital in 1995 because of a 4-day fever, pain over the anterior neck region that worsened when she swallowed, sore throat, malaise, and weight loss. She had been receiving prednisolone at a dosage of 20 mg/d. Her temperature was 39°C and pulse rate was 100 beats per minute. She had a prominent malar rash and vasculitic lesions over the palms, as well as a small, tender, and diffuse goitre mainly over the right side

of the neck. There was no bruit or thrill. Clinical examination revealed that the patient was euthyroid. Furthermore, her haemoglobin level was 87 g/L, total leukocyte count was 4.6×10^9 /L, and ESR was 60 mm/h. The serum level of TSH, as measured with an immunochemiluminescent assay, was 3.02 mIU/L (reference range, 0.30-4.00 mIU/L). Thyroglobulin and microsomal antibodies were negative, and the chest X-ray was normal. Ultrasonography of the thyroid showed two hypo-echoic lesions—indicating fluid collections—of 8 cm and 2 cm in diameter within the right lobe of thyroid.

The patient was treated for acute bacterial thyroiditis with intravenous cloxacillin and cefuroxime, but the goitre continued to increase in size. Ultrasound-guided needle aspiration yielded 0.5 mL of purulent material. Cytological examination revealed necrotic material and Ziehl-Neelsen staining showed numerous acid-fast bacilli. The diagnosis was amended to tuberculous thyroiditis due to *Mycobacterium tuberculosis*, and the patient was treated with antituberculous drugs, which consisted of isoniazid, rifampicin, pyrazinamide, and streptomycin, according to recommended guidelines, for a total of 1 year. Sputum and urine were repeatedly examined for acid-fast bacilli but none were detected.

During treatment, the TSH level transiently fell to 0.09 mIU/L and the concentration of free T₃ fell to 1.7 pmol/L (reference range, 3.3-8.2 pmol/L)—features suggestive of euthyroid sick syndrome. This was followed by transient elevation of the TSH level to 16.70 mIU/L, but with normal free T₃ (4.4 pmol/L) and free T₄ concentrations (9.2 pmol/L; reference range, 7-21.8 pmol/L). The patient remained clinically euthyroid during the whole treatment period and has been doing well after completion of the course of antituberculous therapy.

Discussion

The thyroid gland is remarkably resistant to infection because of its rich blood supply, abundant lymphatic drainage, the presence of high iodine content, and its encapsulated position away from external structures.¹ Hence, acute bacterial thyroiditis is an uncommon disease, and tuberculosis of the thyroid rarely occurs. Berger et al² identified 153 cases of bacterial thyroiditis and 21 cases of mycobacterial thyroiditis in the English medical literature since 1900. The overall incidence of tuberculosis in thyroidectomy specimens has been reported to be 0.4% in a recent series.³

Tuberculosis is relatively common in Hong Kong. In 1997, a total of 7072 cases were notified to the Department of Health under the Quarantine and Prevention of Disease Ordinance.⁴ Tuberculosis affecting the thyroid gland is very rare. Local data on the number of cases of tuberculosis which involve the thyroid are not available. Among notified cases of tuberculosis in Singapore over a 10-year period,

only one case involved the thyroid gland.⁵ Our second case is the only known case of tuberculous thyroiditis seen in our hospital since it opened in 1985.

Predisposing factors for thyroid infection include a patent thyroglossal fistula,⁶ an immunocompromised state, and pre-existing thyroid diseases, such as goitre, adenoma, thyroiditis, and carcinoma.² One recent report cites a case of suppurative thyroiditis in a patient with SLE and a lethal cardiomyopathy,⁷ but there seems to be no previously reported association of tuberculous thyroiditis with SLE. Although autoimmune thyroiditis has been described in patients with SLE,⁸ this combination of diseases is relatively uncommon,⁹ and autoimmune thyroiditis does not seem to have been present in either of our cases. Thyroid disorder per se is a predisposing factor for infective thyroiditis, but there was no evidence of any pre-existing thyroid diseases or autoimmune thyroiditis in either of the patients. Their susceptibility to infective thyroiditis was likely related to an immunocompromised state secondary to SLE. Patients with SLE are well-known to be at increased risk of infection. This susceptibility can be attributed to low complement levels, loss of immunoglobulins through the nephrotic syndrome, lymphopenia, functional hyposplenism, defective macrophage function, deficiency in mannose-binding lectin, and treatment with immunosuppressive agents, such as corticosteroids and cyclophosphamide.¹⁰

Patients with acute infective thyroiditis are typically euthyroid, although thyrotoxicosis has been described in a patient with tuberculous thyroiditis.¹¹ The transient increase of T₄ levels in the first patient was likely due to secretion of preformed hormone from the inflamed thyroid gland. The patient's thyroid function normalised after 1 month. The transient suppression of TSH and free T₃ and the subsequent elevation of TSH and normalisation of thyroid hormone levels during the recovery phase in the second patient was consistent with euthyroid sick syndrome, which is commonly associated with pulmonary tuberculosis.¹² The transient elevation of TSH reflects subsequent recovery of the hypothalamic-pituitary-thyroid axis.

The classic features of neck pain, fever, and tender thyroid mass were observed in both patients, although these features are less commonly seen in patients with tuberculous thyroiditis compared with thyroiditis of other aetiology.² The most useful diagnostic tool remains fine-needle

aspiration biopsy under ultrasound guidance, to identify the causative organisms. Treatment consists of administration of appropriate antibiotics and drainage of the lesion when appropriate. Tuberculous thyroiditis require long courses of antituberculous drugs, which is similar to the treatment required by cases of tuberculosis with extrapulmonary involvement. Incision and open drainage is sometimes necessary, as was the case for the first patient in our case report. Some surgeons advocate excision of the affected area.¹³

In immunocompromised patients presenting with fever and neck pain, infective thyroiditis needs to be considered. Increased levels of C-reactive protein may alert the physician to look for an infective focus in patients with SLE who develop a fever. Definitive diagnosis of the condition requires ultrasound-guided needle aspiration followed by bacterial confirmation. Incision and drainage, with or without surgical excision, and parenteral antibiotic therapy are the mainstay of treatment.

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