Subacute thyroiditis in a renal allograft recipient

J. Pascual¹, L. Orofino¹, E. Hernández¹, F. Liano ¹, R. Garcia-González² and J. Ortuflo¹

Servios de ¹Nefrologia y ²Anatomia Patológica, Hospital Ramón y Cajal, Madrid, Spain

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Introduction

Subacute thyroiditis was originally synonymous with granulomatous or giant-cell thyroiditis, so called de Quervain's thyroiditis [1]. This quite frequent entity is characterized by transient thyrotoxicosis, painful and tender goitre, elevated sedimentation rate (ESR), and markedly decreased tracer activity in thyroid scan [1,2]. Despite its frequency in the general population, immunosuppressed patients suffer this disease very rarely, and to our knowledge, no well-documented cases have been reported occurring in solid-organ allograft recipients. Successful treatment of severe cases with steroids probably explains this very low frequency, as these patients are chronically treated with immunosuppressants. Herein we present a case of subacute thyroiditis arising in a renal allograft recipient taking prednisone and cyclosporin who had concomitant urinary tract infection.

Case report

A 49-year-old woman with end-stage renal failure secondary to chronic interstitial nephritis had been maintained in haemodialysis for 10 months before receiving a cadaveric renal transplant in April 1992. Initial immunosuppressive protocol included prednisone and cyclosporin (oral dose 10 mg/kg per day). One rejection episode was successfully treated with seven methylprednisolone pulses (250 mg) on day 7. HLA-DR was: A24, A2, B35, B44, Bw4, Bw6, Cw4, DR5, DRw52, and DQw3. For almost 3 years she had good graft function (serum creatinine (SCr) 1.6–1.7 mg/dl) and maintenance immunosuppression was held with prednisone (10 mg/day) and cyclosporin (5 mg/kg/day). In February 1995 she presented with a 2-week history of fever (up to 38.5°C), neck swelling and tenderness, sore throat, and mild weight loss. One day before admission, she had complained of right cervical pain and right otalgia. In addition, mild dysuria, frequent voiding, and bilateral lumbar discomfort appeared. On admission she was thin, temperature 38°C, her peripheral pulse was regular at 100/min and blood pressure was 140/90 mmHg. The thyroid gland was palpable, firm, and tender, mainly on the right lobe. The skin over the gland was unremarkable and oropharyngeal examination, laryngoscopy, bilateral otoscopy, and the remainder of the examination were normal. Admission laboratory data included the following: haemoglobin level 9.6 g/dl, haematocrit 27.6%, white blood cell count 5700/mm³, platelet count 30200/mm³, ESR 138 mm/h, SCR 1.7 mg/dl, blood urea 94 mg/dl, serum sodium 139 mmol/l, potassium 4.4 mmol/l, chloride 108 mmol/l, calcium 10.4 mg/dl, phosphorus 5.2 mg/dl, serum iron 50 µ/ml, and transferrin 214 mg/dl. Bilirubin, transaminases, and alkaline phosphatase were normal. Whole-blood through cyclosporin level was 177 ng/ml. Plasma-free T₄ was 3.38 ng/dl (normal range 0.80–2.20) and TSH was 0.02 1 U/ml (0.31–5.56). Antinuclear, antithyroglobulin, antimitochondrial, antimicrosomal antibodies, TSH binding inhibitor, and thyroid-stimulating antibody were negative.

Urine culture, undertaken with a sample obtained the day after admission, during a peak fever (38.5°C) yielded more than 100000 c.f.u. of multisensible Escherichia coli. Neck ultrasound showed that the thyroid was enlarged, specially the right lobe (anteroposterior diameter 20.9 mm). Both lobes were diffusely hypoechoic and no nodules or calcifications were found. A thyroid scan performed with 10 mCi of Tc-99m pertechnetate showed markedly diminished tracer activity with very poor visualization of the thyroid gland. Thyroid cytological specimens obtained with fine-needle aspiration showed inflammatory cells, with multinucleated giant cells (Figure 1).

When the result of urine culture was available on the 3rd hospitalization day, treatment with norfloxacin (200 mg every 12 h) was started. After only 24 h, all the symptoms disappeared, including fever, neck pain, otalgia, and urinary and lumbar complaints.
Thyroiditis in a renal allograft patient

Fig. 1. Fine-needle aspiration cytology of the thyroid during subacute thyroiditis (MGG stain). (A) A polymorphic inflammatory background with scattered multinucleated giant cells and a few degenerative follicular cells (×25). (B) A multinucleated giant cell with epithelioid nuclei (×40).

Norfloxacin treatment was maintained for 10 days, and urine cultures were then negative. Immuno-suppressive regimen was not modified during admission. On an outpatient basis, 3 weeks after admission, the patient showed normal plasma-free T4 (1.84 ng/dl) and slightly low TSH (0.121 U/ml), and was asymptomatic. Three months later, thyroid hormones and thyroid scan were completely normal.

Discussion

Subacute thyroiditis is characteristically a self-limiting disease with unknown etiology, which usually lasts weeks or months and is followed by complete recovery [1]. Diagnostic criteria for subacute thyroiditis were met in our renal allograft patient: elevated thyroxine concentration, suppression of thyroidal isotope uptake, increased ESR, transient painful goitre and absence of antithyroid antibodies [1,2]. Symptoms include asthenia, malaise, pain over the thyroid and referred to the lower jaw, ear, or occiput. These symptoms may smoulder for weeks before the diagnosis is suspected. Physical findings include exquisite tenderness of the thyroid, which may be predominantly unilateral, as in our patient. Two laboratory findings are characteristic: a high ESR and a markedly diminished tracer activity in thyroid scintigraphy [2]. The remaining tests yield results depending on the stage of the disease in which they are obtained. Early, many patients (such as ours) are mildly thyrotoxic owing to leakage of hormone from the gland. Serum T4 is high and TSH undetectable. Later, as glandular hormone is depleted, the patient may pass through a hypothyroid phase, in which serum T4 is low and TSH is increased. Ultrasonographic findings are not specific, but diffuse hypoechoogenicity in the presence of extremely low tracer activity in scintigraphy usually allows a correct diagnosis [3]. Painful, tender thyroid enlargement has been described in patients with chronic thyroiditis and transient thyrotoxicosis; therefore, histological confirmation is frequently necessary [4]. Fine-needle aspiration biopsy showed multinucleated giant cells, thus confirming the diagnosis in our patient [5].

Subacute thyroiditis has been thought to be induced in genetically predisposed individuals because a strong association has been suggested between HLA-B35 and patients in whom subacute thyroiditis has developed [6,7]. Recently Cw4 antigen has also been related to genetic susceptibility in acquiring the disease [7]. Both HLA-B35 and Cw4 were found in our renal allograft patient with subacute thyroiditis. This phenotype was probably a hereditary risk factor for developing this disorder.

Older literature suggested a viral aetiology for human subacute thyroiditis [8]. The disease has several characteristics typical of viral infections, and clusters of the disease have been reported during outbreaks of viral infection [9]. Some recent findings have also suggested a role for infectious agents in the pathogenesis of thyroid disease of immune origin [8]. Our renal allograft immunosuppressed patient developed urinary tract infection secondary to E. coli concomitantly with subacute thyroiditis. Rathod et al. have described a patient with chronic bacterial sinusitis who subsequently developed subacute thyroiditis, and speculated whether this was merely fortuitous or correlated [10]. Molecular mimicry has long been one of the mechanisms by which microbes can induce immune reactions [11]. Antigenic cross-reactivity between several viruses, Yersinia and thyroid proteins and receptors have been described [8,12]. Unfortunately, such molecular studies were not performed in our patient. Adequate treatment with norfloxacin controlled urinary and thyroid symptoms within 24 h. We cannot assume that both points are related, but one could speculate on it.

The extremely low incidence of subacute thyroiditis in allograft recipients is quite surprising, taking into account the high frequency of viral infections they suffer. Interleukin-2 administered as an antineoplastic agent has recently been related to the production of subacute thyroiditis [13]. Blockade of interleukin-2 production and other cytokines is probably a major factor involved in the action of current immunosuppressants [14,15], and this probably explains the extreme rarity of subacute thyroiditis in patients chron-
ically receiving these drugs. However, our case suggests that subacute thyroiditis should be included in the differential diagnosis of a febrile allograft recipient with neck pain.

References


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