Polyglandular autoimmune syndrome type III associated with coeliac disease and sarcoidosis

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Summary: A female patient demonstrating a previously not reported constellation of polyglandular autoimmune syndrome type III (including autoimmune thyroiditis, Graves' ophthalmopathy, insulin-dependent diabetes mellitus and vitiligo), coeliac disease and sarcoidosis is described. This may be a random association but might also indicate a common immunological and/or genetic disturbance.

Introduction

Autoimmune disorders and sarcoidosis may be related and the association between sarcoidosis and autoimmune thyroid disease has long been recognized. Polyglandular autoimmune (PGA) syndromes occurring together with sarcoidosis have only been described in a few cases. However, none of these was associated with coeliac disease. We would like to report a female patient with PGA syndrome type III (autoimmune thyroid disease, insulin-dependent diabetes mellitus (IDDM), vitiligo), coeliac disease, transiently positive adrenal antibodies and sarcoidosis.

Methods

Serum microsomal antibodies and thyroglobulin antibodies were measured by complement binding reaction and passive haemagglutination, respectively. Serum adrenal, gluten (IgA/IgG), reticulin, parietal cell, smooth muscle, glomerular and mitochondrial antibodies as well as antinuclear factors were measured by immunofluorescence. The HLA haplotype was analysed in Lund's transplantation laboratory according to the method of Vartdal et al.

Case report

A female patient born in 1941, without known heredity for autoimmune diseases, was admitted in 1970 to our department due to polyuria, polydipsia and weight loss and IDDM was diagnosed. In 1976 a nodular goitre was noted, thyrotrophin was 8 mIU/l (reference range < 8), serum antibodies against microsomal antigen (titre 1/640, reference value < 1/10) and thyroglobulin antibodies (titre 1/10, reference value < 1/10) were present and L-thyroxine was instituted.

In October 1984 the patient complained of gritty foreign body sensation in the eyes associated with redness, tearing and photophobia. On examination, lid retraction, periorbital oedema, conjunctival injection and slight chemosis were noted. Exophthalmometry ad modum Krahn demonstrated readings of 12 mm in the right and 14 mm in the left eye. Eye movements and a computerized tomographic (CT) scan of the orbits were normal. The patient was euthyroid and thyroid-stimulating immunoglobulins were not demonstrated in the serum. Fine needle biopsy of the thyroid revealed autoimmune thyroiditis. The clinical diagnosis was Graves' ophthalmopathy.

In April 1985 the patient complained of epigastric discomfort and frequent diarrhoea. Anaemia (erythrocyte sedimentation rate 35 mm/hour) with sideropenia and low blood folate 18 nmol/l (reference range 70−200) but a normal bone marrow aspiration were noted. An electrophoresis of the plasma proteins showed a polyclonal rise of IgA 4.6 g/l (reference range 0.5−3.0) and a low serum albumin 33 g/l (reference range 36−48). Serum antibodies against adrenal antigen (titre 1/20, reference value < 1/10), gluten (IgA/IgG: 9.0/5.3 U/ml, reference value: 2.5/3.0 U/ml) and reticulin (titre 1/100, reference value < 1/10) were demonstrated. Hepatitis B surface antigen and serum antibodies against cytomegalovirus, parietal cell, smooth muscle, glomeruli and mitochondria as well as antinuclear factor were not detected. Islet cell antibodies were not analysed. A morning serum ACTH, a morning serum cortisol and a short synthetic ACTH stimulation test were normal. A computed tomographic (CT) scan of the abdomen including the adrenals was normal. A
chest X-ray examination demonstrated bilateral hilar lymphadenopathy but no parenchymal involvement. A mediastinal lymph node biopsy showed multiple non-caseating giant epitheloid cell granulomas compatible with sarcoidosis (Figure 1) and without evidence of malignant disease. Staining for mycobacteria and fungi was negative, as was culture of the biopsy specimen. Culture and direct microscopy of sputum and of specimens obtained by gastric lavage were negative for mycobacteria. Pulmonary function tests and arterial blood gases were normal. A Mantoux test was negative. A small bowel biopsy by Crosby capsule revealed total villous atrophy without sarcoid granulomas and was compatible with coeliac disease (Figure 2). The patient was discharged on a gluten-free diet and her condition improved markedly.

In July 1986 patchy vitiligo was observed. Normal visual acuity but deteriorating ophthalmo-pathy with protrusion (17 mm on the right, 16 mm on the left eye) and diplopia with restricted eye movements was noted. A CT scan disclosed enlargement of extraocular muscles. Oral corticosteroids were administered (prednisolone 30 mg/day) but were ineffective and in November 1986 the patient was given retrobulbar irradiation (30 Gy). The ophthalmopathy improved and corticosteroids could be finally withdrawn in May 1988. In March 1988 a chest radiograph and a new small bowel biopsy were normal. In November 1986 and in July 1990 no adrenal antibodies could be detected in the serum and a synthetic ACTH stimulation test was again normal. The HLA haplotype was A1,3; B8,40; Cw3,w7; DR3,6; DQ1,2.

Discussion

This patient had PGA syndrome type III defined as autoimmune thyroid disease occurring together with IDDM and/or pernicious anaemia and/or vitiligo/alopecia. In the present case, autoimmune thyroiditis, Graves' ophthalmopathy, IDDM and vitiligo were concurrent, and to the best of our knowledge this is the first report of a patient with PGA syndrome type III, coeliac disease and sarcoidosis. In addition, transiently positive adrenal antibodies in serum were detected indicating that our patient might develop Addison's disease and thus fulfil the criteria for PGA syndrome type II defined as Addison's disease and autoimmune thyroid disease and/or IDDM. Whether there was a causal relationship between the treatment with corticosteroids and the disappearance of the adrenal antibodies is open to speculation.

Although the association between sarcoidosis

![Figure 1](mediastinal_lymph_node_biopsy_showing_non-caseating_giant_epitheloid_cell_granulomas_compatible_with_sarcoidosis_haematoxylin_and_eosin_x_125.png)
Figure 2  Small bowel biopsy showing total villous atrophy without sarcoid granulomas compatible with coeliac disease (haematoxylin and eosin, × 125).

and autoimmune thyroid disease has long been recognized\(^2\) the association of sarcoidosis with PGA syndromes has been reported in only a few cases almost exclusively with the PGA syndrome type II,\(^3\)\(^-\)\(^7\) except in one report describing Graves' thyrotoxicosis, pernicious anaemia and vitiligo (PGA syndrome type III) in a patient with sarcoidosis.\(^2\) However, coeliac disease was not noted in any of the aforementioned cases. IDDM was diagnosed before thyroiditis in our patient, a pattern previously observed in PGA syndromes.\(^9\)\(\text{lo}\)

Coeliac disease, also regarded as an autoimmune disease,\(^1\) has been described in association with the PGA syndrome type III.\(^4\) Coeliac disease and sarcoidosis occurring together in the same patient has recently been described in five cases\(^1\)\(^2\) and in addition a high frequency of antibodies against gliadin (41%) was found in a recent study of patients with sarcoidosis, where one of the patients with gliadin antibodies showed total villous atrophy consistent with coeliac disease.\(^1\)

Although the pathogenesis of sarcoidosis is unknown, it is probably a disease promoted by aberrations in immunological reactivity\(^1\)\(^4\) and a combination of abnormalities of some aspects of T cell function with enhanced or normal ability of B cells to produce antibodies\(^1\)\(^4\) has been documented.

The pathogenesis of autoimmune endocrine diseases involves a HLA-linked genetic susceptibility and a probable environment-induced initiating event, leading to an abnormal immune response in which both humoral and cellular mechanisms are involved.\(^1\)\(^5\) The HLA haplotype of our patient (A1,3; B8,40; Cw3,w7; DR3,6; DQ1,2) was in good accordance with the findings of HLA A1, B8, DR3, Dw3, DR4 being more frequent in patients with the PGA syndromes type II and III,\(^4\) with adult coeliac disease\(^4\) or with sarcoidosis,\(^1\)\(^6\) as compared to the general population. This indicates a common underlying genetic predisposition for these conditions.\(^4\)

In conclusion, the patient described demonstrates a previously unreported constellation of PGA syndrome type III, coeliac disease and sarcoidosis, which may be a random association but might also indicate a common immunological and/or genetic disturbance.

Acknowledgement

We wish to thank Associate Professor L. Bondesson for evaluating the histological tissue preparations and Dr J. Kurkus for the HLA analysis.
Obstructive uropathy due to extramedullary haematopoiesis in beta thalassaemia/haemoglobin E

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Summary: An 18 year old woman with beta thalassaemia/haemoglobin E developed a large pelvic tumour resulting in bilateral obstructive uropathy. Technetium-99m sulphur colloid marrow image, computed tomographic scan of the abdomen and needle biopsy of the mass confirmed the diagnosis of extramedullary haematopoiesis. Although radiation is the treatment of choice for decompression, the mass in this patient did not respond satisfactorily due to its multiple area of tumour autoinfarction. Obstructive uropathy due to extramedullary erythropoiesis has not to our knowledge been previously described.

Introduction

Extramedullary haematopoiesis, a common manifestation of severe thalassaemia, occurs as a consequence of uninhibited erythropoiesis.¹ Common sites of involvement include the posterior mediastinum, liver and spleen. Generally these extramedullary haematopoietic masses are asymptomatic, although spinal cord compression has been frequently cited.²³ A patient with beta thalassaemia/haemoglobin E in whom an unusually large pelvic extramedullary haematopoietic mass resulted in severe bilateral obstructive uropathy prompts this report.

Case report

An 18 year old woman with the diagnosis of beta thalassaemia/haemoglobin E since the age of 10

References


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Accepted: 18 June 1992
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Postgrad Med J 1993 69: 72-75
doi: 10.1136/pgmj.69.807.72

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