

A woman with multiple autoimmune diseases: pathologic correlations and complications

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RESUMEN

Se reporta el caso poco común de una mujer joven con trastornos autoinmunes (incluyendo tiroiditis, miastenia gravis, enfermedad de Crohn y eritema nodoso). El tratamiento con esteroides se complicó con una infección severa del tracto urinario superior. La correlación clínico-patológica entre las diferentes complicaciones autoinmunes amerita discusión, así como el apoyo eventual del tratamiento con inmunosupresores, el cual agrega riesgos significativos adicionales a estos factores predisponentes. Los médicos responsables deben estar informados de que estos pacientes pueden presentar trastornos múltiples, concurrentes o subsecuentes y que las complicaciones por infección severa son de especial importancia.

Palabras clave:

Tiroiditis, miastenia gravis, timectomía, enfermedad de Crohn, eritema nodoso, autoinmunidad, infección sistémica

SUMMARY

A very uncommon case report of a young woman suffering from multiple autoimmune-dysreactive disorders (including thyroiditis, myasthenia gravis, Crohn's disease, and erythema nodosum), while undergoing steroid therapy, was complicated by a severe upper urinary tract infection. The pathogenetic and clinical association between the different autoimmune-dysreactive complications deserves discussion, as well as the eventual supporting role of the immunosuppressive treatment, which might contribute significantly to these risk factors. Clinicians who are engaged in the management of these patients should be aware that multiple, concurrent or subsequent disorders may occur in these subjects, and also severe infectious complications may be of relevant concern.

Key words:

Thyroiditis, myasthenia gravis, thymectomy, Crohn's disease, erythema nodosum, autoimmunity, systemic infectious complications

Introduction

Broad pathologic associations including autoimmune thyroiditis, myasthenia gravis, thymectomy (performed for the control of the neurological disease), Crohn's disease, and a wide range of autoimmunity disorders (i.e. systemic lupus erythematosus, ulcerative colitis, biliary cirrhosis, rheumatoid arthritis, lichen planus, and vitiligo), associated with immune system imbalances, are already known since 1960s, although the majority of clinical reports has been represented by anecdotal cases.¹⁻⁶ On the other hand, the association with other immune-mediated disorders (i.e. erythema nodosum), and the increased risk to develop severe infectious complications, need major attention, since both pathogenetic and clinical relations with the development of systemic infectious complications remain still unknown (concurrent immune system impairment, iatrogenic immunosuppression, or other).

An exemplary case of multiple autoimmune-dysreactive disorders associated with erythema nodosum and a severe upper urinary tract infection is reported, to shed light on an enlarged spectrum of immune-mediated complications possibly accompanying these disorders.

Case report

A young, 26-year-old female patient, with an already known post-thyroiditis hypothyroidism, polycystic ovaries, and a diagnosis of myasthenia gravis posed since four years, two months before hospitalization developed an ileal-colonic Crohn's disease treated with systemic corticosteroids. After the occurrence of irregular hyperpyrexia (with septic-like body temperature spikes reaching 40 °C, and preceded by intense chills), not responsive to an empiric combination of oral cephalosporins and clarythromycin (which probably prompted

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an allergic-toxic diffuse maculo-papular, itching skin rash), the patient was moved to our Division of Infectious Diseases, where she underwent an extensive workup. Upon admission, a frank leukocytosis (total white blood cells 23,550 cells/ μ L), with neutrophilia (88.3%), was associated with an evident increase of erythrocyte sedimentation rate (ESR) (96, first hour), an increased platelet number (669,000 cells/ μ L), mild alterations of serum liver enzymes, an hemorrhagic conjunctivitis, and a painful, swelling erythema-nodosum-like picture involving the extensor site of both lower limbs. An emerging dysuria and lumbar pain, assessed by both ultrasonographic and contrast-enhanced CT scan of the abdomen, detected a severe, left multifocal pyelonephritis, in association with an urinalysis typical of upper urinary tract infection, and the repeated isolation from urine of *Escherichia coli* strains which proved susceptible to the large majority of tested antimicrobial compounds, in absence of any other significant cultural, serological, laboratory, and/or instrumental data. After the suspension of prior, empiric antibiotic regimens carried out with co-amoxiclav, and subsequently with i.v. ticarcillin-clavulanate, an antimicrobial chemotherapy initially performed with i.v. full-dose cefotaxime and metronidazole for 8 days, was changed at the time of discharge with oral ciprofloxacin and the resumption of steroid therapy, shared with the Gastroenterologists who are following-up our patient due to the recent bowel inflammatory disease. Neither recurrences nor sequelae of the acute infectious complication, nor other autoimmune-dysreactive disorders, were registered during the subsequent, 18-month follow-up.

Discussion

A broad spectrum of predisposing conditions pose selected subjects already suffering from autoimmune-dysreactive disorders at an increased risk to develop even severe infectious complications. The frequent, prolonged immunosuppressive treatments may be associated with multiple immune system disturbances often disclosed just during the diagnostic workup of these underlying syndromes.

When patients with autoimmune diseases are of concern, the concurrence of multiple, dysreactive pathologic conditions involving different organs and systems is proportionally frequent. In our case, an autoimmune thyroiditis, a myasthenia gravis, a Crohn's disease, and an erythema nodosum have been already diagnosed in a young woman aged 26 (in particular, to the best of our knowledge an erythema nodosum was never reported until now concurrently with myasthenia gravis).

Internal Medicine physicians, and all Rheumatological, Dermatological, and Infectious Disease specialists, as well as consultants asked to contribute to the diagnosis, staging, and management of each single complication and the entire syndrome, have to consider that each single manifestation

may be part of the proteiform, systemic features of all linked disorders and their possible complications.

In particular, an infectious etiology may take advantage from the chronic administration of corticosteroids or other immunosuppressive agents.⁷ Moreover, infectious complications may be supported by an already imbalanced immune system response characterized by an increased Th1-like response, which is opposed to the increased Th2 response typical of these autoimmune disorders.^{6,8} This laboratory picture occurs in patients who suffer from an association of chronic inflammatory bowel syndrome and myasthenia gravis with an increased overall incidence, when compared with that of the general population.^{9,10}

In particular, a relationship has been established between inflammatory bowel diseases and thymus disorders.¹¹ From a pathogenetic point of view, the intrathymic process of T-lymphocyte maturation is altered during myasthenia gravis,¹² while intrathymic B-lymphocyte abnormalities may also contribute to support the onset of autoimmune disorders.¹³

In many cases like that presented by us, the co-existence of multiple, concurrent illnesses may lead to a delayed differential diagnosis and a delayed, adequate management of infectious diseases which are potentially severe, and may lead to permanent sequelae.

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