

Good's syndrome in a patient with cytomegalovirus retinitis

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Thymoma-related adult-onset immunodeficiency or Good's syndrome is an uncommon condition. This case, of a 50-year-old woman who was human immunodeficiency virus-negative and developed herpes zoster and severe cytomegalovirus retinitis 6 months after removal of a thymoma, is the first to be reported in Hong Kong. Immunological investigations revealed no B cells, hypogammaglobulinaemia, a low CD4 count, and a low CD4/CD8 ratio. We recommend that immunological investigations, including T-cell subsets, B cells, and quantitative immunoglobulins, should be part of the routine diagnostic evaluation of patients with thymoma and infections.

Introduction

We report a case of a patient who presented with opportunistic infections, herpes zoster, and cytomegalovirus (CMV) retinitis, and a low CD4 count. Although this picture was compatible with acquired immunodeficiency syndrome (AIDS), she was later diagnosed with thymoma-related immunodeficiency—Good's syndrome (GS).

Case report

A 50-year-old Chinese woman, who was a non-smoker and non-alcohol drinker, and married with two children, was incidentally found to have a mediastinal mass in June 2006. A sternotomy was performed, and a well-encapsulated thymic tumour of 15 cm was found arising from the right inferior pole of the thymus. No palpable nodules were detected in the right lung, and neither deposits nor effusions were found in the pleura or its cavity. A thymectomy was performed and a histological examination revealed a Masaoka stage IIa thymoma (World Health Organization [WHO] classification type AB). Microscopic foci of capsular invasion were present, but the resection margin was clear. Radiotherapy was given postoperatively in October 2006.

In November 2006, our patient developed blurred vision in both eyes while travelling in mainland China. The visual impairment in her left eye progressed rapidly to total blindness within 1 day. She returned to Hong Kong and was subsequently referred to our hospital for management. Just before admission she developed herpes zoster skin lesions on her left flank (T10 dermatome).

When first seen by our hospital ophthalmologists in December 2006, she was found to have severe panuveitis in both eyes, with greater involvement in the left. Initial blood tests including a full blood count, liver and renal function tests, were unremarkable. A diagnostic posterior vitrectomy with vitreous biopsy was performed and a polymerase chain reaction examination of the vitreous sample was positive for CMV DNA and negative for herpes simplex virus 1 and 2, Epstein-Barr virus, herpes zoster virus DNA, and mycobacterium tuberculosis. Further investigations found no antibodies for human immunodeficiency viruses (HIV) 1 and 2 and syphilis; and no anti-nuclear factor and anti-DNA autoimmune markers but an immune status workup did show significant abnormalities (Table); the CD4 T cell count was low, as was the CD4/CD8 ratio, B cells were absent and she had low levels of immunoglobulins G, A, and M.

She was given intravenous ganciclovir at 5 mg/kg every 12 hours for 2 weeks, which was then changed to oral valganciclovir 900 mg daily. Her right eye retinitis improved dramatically, returning to normal visual acuity but the visual loss of her left eye was deemed beyond salvage.

The valganciclovir was continued and co-trimoxazole prophylaxis and monthly immunoglobulin replacement therapy were added. Her CD4 cell count remained low 2 months after diagnosis.

Key words

Agammaglobulinemia; Cytomegalovirus retinitis; immunologic deficiency syndromes; Opportunistic infections; Thymoma

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Discussion

Good's syndrome was first reported in 1954 by Robert Good, who described an adult with both thymoma and hypogammaglobulinaemia.¹ It is classified as an immunodeficiency associated with thymoma by the WHO/International Union of Immunological Societies.²

In the United States, the incidence of thymoma is 0.15 cases per 100 000, based upon data from the National Cancer Institute Surveillance, Epidemiology, and End Results (SEER) program.³ Most patients are aged between 40 and 60 years, with a slight male predominance. Thymomas can be associated with a variety of parathyroid syndromes including myasthenia gravis, pure red cell aplasia and hypogammaglobulinaemia or GS.

In contrast to most other primary immunodeficiency states, GS usually presents in the fourth or fifth decade of life, although it can very rarely also occur in children. Male and female patients are equally affected in GS.⁴ Hence, it is described as an adult-onset immunodeficiency syndrome occurring in patients with thymoma defined by hypogammaglobulinaemia, low or absent B cells, variable defects in cell-mediated immunity with a CD4 T lymphopaenia, an inverted CD4/CD8+ T-cell ratio and reduced T-cell mitogen proliferative responses.^{4,6} The immunodeficiency may precede or follow the diagnosis of a thymoma.⁵ In our patient, it developed 6 months after thymectomy.

The immunological deficits seen in GS affect both humoral and cellular immunity, and fit the criteria for a combined immunodeficiency. In contrast to X-linked agammaglobulinaemia (XLA) and common variable immune deficiency (CVID), opportunistic infections associated with disorders of cell-mediated immunity are commonly seen in GS. The B-cell lymphopaenia typical of GS is not usually seen in CVID. Distinct classification is required, as the prognosis for GS patients is worse than that for XLA and CVID.⁷

Good's syndrome is the underlying cause in 1 to 2% of patients with primary antibody deficiency who are on immunoglobulin replacement treatments. In patients with thymoma, the incidence of hypogammaglobulinaemia is 10%.² The cause and pathogenesis of GS remain unknown; a bone marrow defect is suggested by the B- and T-cell lymphopaenia, while an autoimmune pathogenesis has also been suggested.⁸

Patients with GS may present initially with a mediastinal mass or with recurrent infections. They have increased susceptibility to bacterial, fungal, viral, and opportunistic infections related to both humoral and cell-mediated immune deficiencies. Sino-pulmonary infections with encapsulated

帶有巨細胞病毒視網膜炎的Good's綜合徵病例報告

Good's綜合徵（成年發病的免疫缺乏合併胸腺瘤）很少見。本病例報告在香港屬首次發表。患者為一名50歲女性，人類免疫缺陷病毒測試呈陰性。她在切除胸腺瘤6個月後出現疱疹病毒，以及嚴重巨細胞病毒視網膜炎。免疫測試顯示患者沒有B淋巴細胞，血丙種球蛋白減少，CD4細胞減少，和低比例的CD4/CD8細胞。當病人有胸腺瘤和感染，我們建議把免疫測試納入常規的診斷檢測，包括T淋巴細胞亞群、B淋巴細胞、以及免疫球蛋白數量。

TABLE. Lymphocyte subset profiles by flow cytometry and immunoglobulin levels

Profile	Value	Reference range
White blood cells (μL)	3810	4024-9866
Lymphocytes (μL)	888 (23.3% total white blood cells)	1158-3378
B-cell (CD19) (μL)	0 (0% lymphocytes)	103-666
T-cell (CD3) (μL)	809 (91.1% lymphocytes)	764-2620
CD4 T cells (μL)	83 (9.4% lymphocytes)	354-1526
CD8 T cells (μL)	677 (76.3% lymphocytes)	318-1457
CD4/CD8 ratio	0.12	0.71-2066
Immunoglobulin G (g/L)	2.04	8.19-17.25
Immunoglobulin A (g/L)	0.09	0.7-3.86
Immunoglobulin M (g/L)	<0.05	0.55-3.07

bacteria (*Haemophilus influenzae* and *Streptococcus pneumoniae*) and enteric infections (enteric bacteria or *Giardia lamblia*; although in most cases no definite pathogens are identified) are very common.⁵ As with people infected with the HIV, gastro-intestinal and retinal CMV infections are frequently reported in people with GS.^{5,9} Other opportunistic infections observed include herpes zoster, recurrent herpes simplex infections, babesiosis,¹⁰ CMV encephalitis,¹¹ and *Pneumocystis carinii* pneumonia.¹² Appropriate microbiological investigations and prophylactic antibiotics are warranted. We gave co-trimoxazole to our patient according to the regimen recommended for AIDS patients as her CD4 cell count was less than 200 cells/mm³. Because of the T-cell defect, the use of live vaccines in GS poses a significant risk.

While most researchers agree that the immunodeficiency in GS is related to the associated thymoma, there is no reported case of reversal of the immunodeficiency after thymoma resection. Thymectomy, however, usually has a favourable effect on associated conditions like myasthenia gravis and pure red cell aplasia.

It has been reported that intravenous immunoglobulin can improve infection control, reduce hospitalisation, and decrease use of

antibiotics,⁵ and is recommended as a means of maintaining appropriate immunoglobulin G levels for all GS patients.¹³

Immunological investigations, including T-cell subsets, B cells, and quantitative immunoglobulins, should be considered part of the routine diagnostic evaluation in patients with thymoma and infections. If the initial results are normal, repeated investigations

should be considered every second year because cases of progressive immunodeficiency have been described.¹⁴

Good's syndrome is a condition receiving increasing attention. This is the first reported local case and we hope to raise awareness of this condition as early recognition and management can improve prognosis.

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