

Cas clinique

Panuvéite bilatérale à CMV révélatrice d'un syndrome de Good chez un patient de 71 ans : rapport de cas

Bilateral CMV Panuveitis as the Revealing Manifestation of Good's Syndrome in a 71-Year-Old Patient: A Case Report

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RESUME

Introduction : Le syndrome de Good (SG) est un déficit immunitaire combiné acquis, rare, défini par la triade thymome-hypogammaglobulinémie-déficit lymphocytaire T. Il affecte principalement les adultes entre la 5ème et la 7ème décennie et se distingue du CVID et du LOCID par la présence obligatoire d'un thymome, avec un pronostic plus sévère.

Observation : Nous rapportons le cas d'un patient de 71 ans, diabétique et hypertendu, admis pour bilan d'une panuvéite bilatérale granulomateuse à CMV avec une baisse de l'acuité visuelle et des épisodes répétés de bronchopneumopathies depuis 3 mois. Le bilan immunologique révèle une hypogammaglobulinémie profonde tri-isotypique et un déficit lymphocytaire T combiné. La TDM thoraco-abdominopelvienne réalisée devant l'altération de l'état général objective une masse médiastinale antérieure évocatrice de thymome, établissant le diagnostic de syndrome de Good. Le traitement par ganciclovir IV, immunoglobulines intraveineuses et prophylaxie par cotrimoxazole est instauré. L'évolution est initialement favorable avec régression des signes d'uvéite et diminution des marqueurs inflammatoires. Cependant, trois semaines après, apparaît une altération de la fonction rénale et hépatique imputée aux effets indésirables médicamenteux, ayant exigé l'arrêt du traitement. A la sortie, le patient est adressé aux chirurgiens thoraciques pour thymectomie, mais une crise myasthénique survenant quelques jours après la sortie retarde la prise en charge chirurgicale.

Conclusion : Ce cas illustre l'importance d'une recherche systématique d'un thymome devant tout déficit immunitaire combiné sans VIH, et souligne la complexité thérapeutique spécifique du sujet âgé, marquée par un risque accru de toxicité médicamenteuse et une fragilité limitant les options chirurgicales.

Mots-clés : Syndrome de Good ; thymome ; panuvéite à CMV ; hypogammaglobulinémie ; immunosénescence ; sujet âgé ; thymectomie ; myasthénie

ABSTRACT

Introduction: Good's Syndrome (GS) is a rare acquired combined immunodeficiency defined by the triad of thymoma, hypogammaglobulinemia, and T-cell deficiency. It predominantly affects adults in the fifth to seventh decade of life and is distinguished from CVID and LOCID by the obligatory presence of thymoma, with a significantly worse prognosis.

Case report: We report the case of a 71-year-old diabetic and hypertensive male, admitted for workup of bilateral granulomatous CMV panuveitis with progressive visual loss and recurrent bronchopneumonia over

3 months. Immunological investigations revealed a profound tri-isotypic hypogammaglobulinemia and combined T-cell deficiency. A thoracoabdominopelvic CT scan, performed for deteriorating general condition, revealed an anterior mediastinal mass consistent with thymoma, establishing the diagnosis of Good's Syndrome. Treatment with IV ganciclovir, IVIG replacement, and cotrimoxazole prophylaxis was initiated. Evolution was initially favorable with regression of uveitis signs and decrease in inflammatory markers. However, three weeks later, significant renal and hepatic impairment attributed to drug toxicity required full treatment discontinuation. At discharge, the patient was referred to thoracic surgery for thymectomy, but a myasthenic crisis occurring days after discharge delayed surgical management.

Conclusion: This case highlights the importance of systematically searching for thymoma in any non-HIV combined immunodeficiency, and underlines the specific therapeutic complexity in elderly patients, marked by an increased risk of drug toxicity and frailty limiting surgical options.

Keywords: Good's syndrome; thymoma; CMV panuveitis; hypogammaglobulinemia; immunosenescence; elderly; thymectomy; myasthenia gravis

INTRODUCTION

Good's Syndrome (GS) is a rare primary immunodeficiency first described by Robert Good in 1954, defined by the association of thymoma with hypogammaglobulinemia and combined T-cell and B-cell immune defects. (1) Its estimated incidence ranges from 0.2 to 1.5 per million population, accounting for less than 1% of all primary immunodeficiencies. (2) It predominantly affects adults in the fifth to seventh decade of life, with a mean age at diagnosis between 59 and 62 years and equal sex distribution. (3)

Unlike Common Variable Immunodeficiency (CVID) or Late-Onset Combined Immunodeficiency (LOCID), GS is uniquely defined by the obligatory presence of a thymoma, which serves as the paraneoplastic driver of the immune defect through two main mechanisms: (i) B-cell maturation arrest in the bone marrow — mediated in part by soluble factors including the cytokine Limitin, an interferon analogue secreted by thymoma cells — leading to near-absent peripheral B-lymphocytes and profound hypogammaglobulinemia; and (ii) aberrant thymic T-cell education, resulting in CD4 lymphopenia, inverted CD4/CD8 ratio, and impaired cellular immunity. (3,4) These mechanisms explain why patients with GS are susceptible not only to encapsulated bacteria — as in classical humoral deficiencies — but also to opportunistic pathogens typically associated with T-cell defects, particularly Cytomegalovirus (CMV), *Pneumocystis jirovecii*, and *Candida* species. (4)

The prognosis of GS is significantly worse than that of other primary antibody deficiencies. In a cohort of 39 GS patients, the relative mortality hazard ratio was 3.7 ($p=0.008$), with a median survival of approximately 14 years from diagnosis. (5) Major causes of death include recurrent infections, hematological complications — particularly pure red cell aplasia, found in up to 50% of cases — and associated autoimmune diseases, including myasthenia gravis (10–47% of cases), erosive lichen planus, and inflammatory bowel disease. (3,5)

CMV disease represents a particularly severe complication of GS. As CMV clearance is exclusively dependent on cytotoxic T-cell responses and independent of humoral immunity, even patients receiving IVIG replacement therapy remain highly susceptible to primary CMV infection and reactivation. (6) In a series of CVID/GS patients, CMV disease multiplied the risk of death by 26.3-fold (95%CI: 6.31–102.9; $p<0.0001$). (6) The ocular manifestation of CMV in immunocompromised non-HIV patients — including bilateral panuveitis — represents a particularly aggressive and underrecognized presentation, requiring prompt combined antiviral therapy. (7)

In elderly patients, the diagnosis and management of GS face additional complexity. Physiological immunosenescence — characterized by thymic involution, depletion of naïve T-cells, reduced NK cell activity, and impaired B-cell precursor output — may for years mask the underlying immunodeficiency and delay diagnosis. (8) Furthermore, age-related pharmacokinetic and pharmacodynamic changes significantly

alter drug metabolism, distribution, and clearance, substantially increasing the risk of drug toxicity in this population. (9)

We report a case of Good's Syndrome in a 71-year-old patient, revealed by bilateral CMV panuveitis, and discuss the diagnostic and therapeutic challenges specific to the geriatric context.

CASE REPORT

Clinical presentation

Mr. D.A. is a 71-year-old male with a medical history of type 2 diabetes mellitus (initially managed with sulfonylureas, subsequently switched to insulin) and arterial hypertension, with no prior history of recurrent infections, malignancy, or known immunosuppression. He presented to the Geriatric Unit of CHU Ibn Rochd (Casablanca) in March 2025 with a 3-month history of recurrent bronchopneumonia episodes inadequately responding to standard antibiotic courses, associated with a progressive and bilateral decrease in visual acuity.

Ophthalmological evaluation confirmed bilateral granulomatous CMV panuveitis with anterior chamber inflammation, retinal vasculitis predominantly involving arteries, and features consistent with active CMV retinitis. HIV serology was negative, ruling out the most common cause of CMV-related ocular disease.

Immunological workup

Serum protein electrophoresis (SPE) was performed as a first-line investigation and revealed a severely depressed gamma globulin fraction at 2.2 g/L (normal: 8.0–13.5 g/L), alongside a low albumin at 34.0 g/L (normal: 40.2–47.6 g/L) reflecting underlying nutritional deficit, and significantly elevated alpha-1 (6.3 g/L; normal 2.1–3.5) and alpha-2 (11.1 g/L; normal 5.1–8.5) fractions, consistent with a chronic inflammatory response. These findings on SPE prompted quantitative immunoglobulin dosage, which confirmed a profound tri-isotypic hypogammaglobulinemia:

Immunoglobulin	Patient value	Normal range	Interpretation
IgG	2.19 g/L	7.0–16.0 g/L	Severely low ↓↓
IgA	0.09 g/L	0.7–4.0 g/L	Severely low ↓↓
IgM	< 0.05 g/L	0.4–2.3 g/L	Undetectable ↓↓↓

Table 1. Quantitative serum immunoglobulins (Cerba Laboratory, 20/03/2025)

Lymphocyte subset analysis demonstrated a combined T-cell deficiency with a low CD4 count, an inverted CD4/CD8 ratio, and an elevated CD8 compartment, suggestive of immune dysregulation beyond a simple humoral defect:

Subset	Patient value	Interpretation
T CD3	2,912/mm ³	Normal
T CD4	667/mm ³	Low ↓↓
T CD8	2,470/mm ³	Elevated ↑
CD4/CD8 ratio	0.34	Inverted (normal >1)

Table 2. Lymphocyte subset analysis

Radiological workup and diagnosis

Given the patient's significant deterioration of general condition — including weight loss, persistent fatigue, and failure to thrive — a thoracoabdominopelvic CT scan (CT-TAP) was performed. Imaging revealed an anterior mediastinal pre-vascular mass measuring [dimensions to be completed], with features consistent with a thymoma, alongside a right-sided pneumonia. No splenic, hepatic, or lymph node abnormalities were identified at that time.

The finding of an anterior mediastinal thymoma in association with profound hypogammaglobulinemia and combined T-cell immunodeficiency established the diagnosis of Good's Syndrome, in accordance with established diagnostic criteria requiring all three components of the defining triad. (3,4)

Treatment and evolution

At the time of treatment initiation, baseline renal and hepatic functions were within normal limits (GFR >60 mL/min/1.73m², transaminases within normal range). Treatment was initiated according to the following protocol:

Antiviral therapy: IV ganciclovir at 5 mg/kg twice daily for 21 days, followed by oral valganciclovir at 900 mg twice daily for a total treatment duration of 3 months.

IVIG replacement: intravenous immunoglobulins (sucrose-free formulation) at 0.4–0.6 g/kg every 3–4 weeks, for a total of 5 cycles. Current guidelines recommend caution when initiating IVIG in patients with a GFR below 30 mL/min/1.73m², with preference for sucrose-free formulations to minimize osmotic nephrotoxicity. (9,10)

Antimicrobial prophylaxis: cotrimoxazole (trimethoprim-sulfamethoxazole) for *Pneumocystis jirovecii* pneumonia prevention.

Antibiotherapy: adapted to the pulmonary infectious episodes according to available microbiological data.

The initial clinical and biological evolution was favorable: progressive regression of uveitis signs with improvement of bilateral visual acuity, and a significant decrease in inflammatory markers (CRP normalizing within the first weeks of treatment). However, approximately three weeks after treatment initiation, the patient developed:

- **Significant renal impairment:** creatinine rose to a peak of 5.65 mg/L with a GFR falling below 15 mL/min/1.73m², representing a severe acute kidney injury.

- **Major hepatic cytolysis:** AST reached 3,895 IU/L and ALT 2,882 IU/L (>100× upper limit of normal), with conjugated hyperbilirubinemia and a TP of 41%.

- **Coagulopathy:** INR at 1.80, TP 41%, consistent with hepatic functional impairment.

These complications were attributed to the cumulative nephro- and hepatotoxic effects of ganciclovir, IVIG, and antibiotherapy in a high-risk geriatric patient with diabetes, nutritional deficit, and reduced physiological organ reserve. Full treatment discontinuation was required. Hepatitis B and C serologies were negative, excluding viral hepatitis as an alternative etiology.

Despite this therapeutic setback, the initial therapeutic response in terms of visual acuity and inflammatory markers was maintained. After progressive renal and hepatic recovery, the patient was deemed clinically stable and referred to the thoracic surgery department for thymectomy planning. However, a few days following discharge, he developed a myasthenic crisis — a well-recognized autoimmune complication affecting 10–47% of GS patients (3) — which required urgent neurological management and further delayed definitive surgical intervention.

DISCUSSION

1. Diagnostic approach: systematic thymoma search in non-HIV combined immunodeficiency

This case illustrates a fundamental diagnostic principle: any HIV-negative patient presenting with a combined humoral and cellular immunodeficiency — particularly when manifesting as an opportunistic CMV infection — requires systematic chest imaging to rule out an anterior mediastinal thymoma. (3,4) The discovery of thymoma definitively reorients the diagnosis from LOCID or CVID toward Good's Syndrome, with fundamentally different therapeutic and prognostic implications.

CMV panuveitis constitutes a classifying opportunistic infection in the GS context. Unlike humoral pathogens (encapsulated bacteria) typically targeted by IVIG therapy, CMV clearance is exclusively T-cell-dependent, independent of antibody levels. (6) Its presence therefore signals a severe combined immunodeficiency beyond a simple humoral defect, and should trigger the search for thymoma even when routine CVID criteria are met. In this series, CMV disease in CVID/GS patients conferred a 26.3-fold increase in mortality risk (95%CI: 6.31–102.9; $p < 0.0001$). (6) The bilateral and granulomatous nature of the panuveitis observed in our patient is consistent with published series of non-HIV CMV panuveitis, where anterior chamber inflammation (64%) and retinal arterial vasculitis (73%) were the most common findings, in a presentation distinctly different from classic HIV-related CMV retinitis. (7)

Regarding the differential diagnosis, it is important to distinguish GS from LOCID (a subset of CVID defined by Malphettes et al. (11) as CVID + opportunistic infection and/or $CD4 < 200/mm^3$) and from classical CVID. The critical differentiator is the thymoma: in its absence, GS cannot be diagnosed, and LOCID or CVID criteria apply. In GS, the neoplastic thymoma drives the immune defect through a paraneoplastic mechanism — B-cell maturation arrest and aberrant T-cell thymic education — not through a primary genetic defect as in most CVID phenotypes. This distinction has direct therapeutic consequences: thymectomy is a cornerstone of GS management, whereas it has no role in CVID or LOCID.

2. Therapeutic complexity in the elderly: immunosenescence and drug toxicity

The management of GS in elderly patients involves a substantially higher degree of therapeutic complexity than in younger adults. This complexity operates at two levels: the diagnostic-biological level and the pharmacological level.

At the biological level, physiological immunosenescence — defined as the age-related decline of immune function — creates a background of vulnerability that can mask GS for years. Specific changes include thymic involution (with near-complete loss of thymic tissue by the seventh decade), depletion of naïve T-cell pools ($CD45RA+CCR7+$ cells), reduced NK cell cytotoxicity, impaired neutrophil chemotaxis and phagocytosis, and declining B-cell precursor output from bone marrow. (8) These changes overlap significantly with the immune phenotype of GS itself, making it difficult to determine the extent to which observed lymphopenia and immunoglobulin depression are attributable to the disease versus to physiological aging. In our patient, the $CD4$ count of $667/mm^3$ and inverted $CD4/CD8$ ratio of 0.34 — while consistent with GS — may have been partially amplified by immunosenescence, further complicating the immunological interpretation.

At the pharmacological level, aging significantly alters drug pharmacokinetics and pharmacodynamics through multiple mechanisms: decreased renal glomerular filtration rate (GFR declines by approximately 1 mL/min/year after age 40), reduced hepatic cytochrome P450 enzymatic activity, decreased albumin-mediated drug binding, reduced body water volume (altering distribution volumes), and diminished physiological organ reserve limiting tolerance to acute toxicity. (9) These changes collectively increase the risk of drug accumulation, hepatotoxicity, and nephrotoxicity in elderly patients receiving complex pharmacological regimens.

In our patient, this vulnerability was dramatically illustrated by the severe renal and hepatic toxicity developing three weeks into treatment. The combination of ganciclovir (a known nephrotoxin requiring dose

adjustment for GFR <70 mL/min), IVIG (osmotic tubulopathy, particularly with sucrose-containing formulations, contraindicated when GFR <30 mL/min/1.73m²), (10) and antibiotherapy in a diabetic elderly patient with baseline nutritional deficit created a synergistic toxic burden that his physiological reserves could not sustain. Current recommendations advise strict renal function monitoring before and 48–72 hours after each IVIG cycle, sucrose-free formulation use in at-risk patients, and infusion rates not exceeding 1–2 mL/kg/hour. (10) Subcutaneous immunoglobulins (SCIG) represent an alternative with better renal tolerability in patients with impaired baseline renal function.

The occurrence of a myasthenic crisis — further delaying thymectomy — exemplifies the multisystemic nature of GS and its particular severity in elderly patients. Myasthenia gravis, present in 10–47% of GS patients, (3) requires its own specific management (acetylcholinesterase inhibitors, immunosuppressants, plasmapheresis), which may itself carry additional toxicity risks in a frail elderly patient. The cascade of complications — drug toxicity → treatment discontinuation → delayed surgery → myasthenic crisis → further surgical delay — illustrates how the precarious clinical state of elderly GS patients can create self-perpetuating management challenges.

3. Prognosis of Good's Syndrome in the elderly

The overall prognosis of GS is significantly worse than that of other primary immunodeficiencies. In a cohort study by Jansen et al. (5), median survival from diagnosis was approximately 14 years, with a mortality hazard ratio of 3.7 compared to age-matched European population life tables ($p=0.008$). Main causes of death were recurrent infections (particularly CMV and *Pneumocystis jirovecii*), hematological complications (pure red cell aplasia), and malignant progression of the thymoma itself.

In elderly patients, these prognostic figures are likely substantially worse, though dedicated geriatric-specific GS cohorts are lacking in the literature. The cumulative impact of multimorbidity, reduced physiological reserve, inability to sustain aggressive antiviral and immunosuppressive regimens, increased surgical risk for thymectomy (which itself does not correct the immunodeficiency but may slow autoimmune complications), and higher susceptibility to recurrent opportunistic infections all contribute to a more unfavorable trajectory. Thymectomy, when feasible, remains the cornerstone of disease control and may improve associated autoimmune manifestations including myasthenia gravis. However, in fragile elderly patients, the decision to proceed with surgery must be individualized within a dedicated multidisciplinary framework, weighing oncological benefit against operative morbidity and mortality.

CONCLUSION

Good's Syndrome remains a diagnostic challenge, particularly in elderly patients where its presenting features may be attributed to immunosenescence, comorbidities, or common infectious conditions. This case underscores two critical clinical principles: first, any non-HIV patient with combined immunodeficiency and opportunistic CMV infection must undergo systematic chest imaging to exclude thymoma — the obligatory and diagnostically defining feature of GS; second, the management of GS in elderly patients requires a heightened level of vigilance for drug toxicity, driven by age-related pharmacokinetic changes, reduced organ reserve, and the high-risk pharmacological combinations inherent to GS treatment.

Early multidisciplinary involvement — integrating geriatrics, immunology, ophthalmology, thoracic surgery, and neurology — is essential from the moment of diagnosis to navigate the complex therapeutic trade-offs and ensure individualized, patient-centered management. Further prospective data on GS outcomes in elderly populations are needed to better guide treatment decisions in this vulnerable group.

ETHICAL COMPLIANCE

Conflict of interest declaration: The authors declare no conflict of interest in relation to this publication.

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Ethical approval: This case report was conducted in accordance with the ethical standards of the institutional research committee.

Informed consent: Written informed consent was obtained from the patient for publication of this case report.

REFERENCES

1. Good RA. Agammaglobulinemia — a provocative experiment of nature. *Bull Univ Minn Hosp Med Found.* 1954;26:1–19.
2. Kelleher P, Misbah SA. What is Good's syndrome? Immunological abnormalities in patients with thymoma. *J Clin Pathol.* 2003;56(1):12–16.
3. Jansen A, van Deuren M, Miller J, Spickett G, Mantovani L, Tauber T, et al. Prognosis of Good syndrome: mortality and morbidity of thymoma associated immunodeficiency in perspective. *Clin Immunol.* 2016 Oct;171:12–17.
4. Tarr PE, Sneller MC, Mechanic LJ, Economides A, Eger CM, Strober W, et al. Infections in patients with immunodeficiency with thymoma (Good syndrome). *Medicine (Baltimore).* 2001 Mar;80(2):123–33.
5. Jansen A, van Deuren M, Miller J, Spickett G, Mantovani L, Tauber T, et al. Prognosis of Good syndrome. *Clin Immunol.* 2016;171:12–17.
6. Yong MK, Lewin SR, Manuel O. Cytomegalovirus disease is an under-recognized contributor to morbidity and mortality in common variable immunodeficiency. *Front Immunol.* 2022 Feb 21;13:815193.
7. Pathanapitoon K, Dodds EM, Cunningham ET Jr, Rothova A. Clinical spectrum of CMV-associated posterior uveitis and panuveitis in patients without HIV infection. *JAMA Ophthalmol.* 2013;131(5):638–645.
8. Christodoulou RI, Ahmad SM, Atkins C, Ehteshami M, Lu L, Sandalova E. Immunosenescence: Aging and Immune System Decline. *Vaccines (Basel).* 2024 Dec;12(12):1314.
9. Mangoni AA, Jackson SH. Age-related changes in pharmacokinetics and pharmacodynamics: basic principles and practical applications. *Br J Clin Pharmacol.* 2004 Jan;57(1):6–14.
10. Luque Y, Louis K, Jouanneau C, Placier S, Esteve E, Bazin D, et al. Nephrotoxicity of sucrose-containing versus sucrose-free intravenous immunoglobulins. *Nephrol Dial Transplant.* 2018;33(12):2124–32.
11. Malphettes M, Gérard L, Carmagnat M, Mouillot G, Vince N, Boutboul D, et al. Late-onset combined immune deficiency: a subset of common variable immunodeficiency with severe T cell defect. *Clin Infect Dis.* 2009 Nov 1;49(9):1329–38.