Clinical Case Reports

Open Access

CASE REPORT

Chronic sinusitis in a patient with selective IgG4 subclass deficiency controlled with enriched immunoglobulins

Gérard Dine, Nadia Ali-Ammar, Said Brahimi & Yves Rehn

Hématologie clinique et biologique, Hôpital des Hauts Clos, 101 Avenue Anatole France, Troyes 10000, France

Correspondence
Gérard Dine, Hôpital des Hauts Clos, 101 Avenue Anatole France, 10003 Troyes Cedex, France. Tel: +33607513689;
Fax: +33325494722;
E-mail: gerard.dine@ch-troyes.fr

Funding Information
Funding support was provided by a CSL Behring Institutional Grant.

Received: 3 June 2014; Revised: 20 October 2015; Accepted: 14 May 2016

***Clinical Case Reports* 2017; 5(6): 792–794**

doi: 10.1002/ccr3.936

Key Clinical Message

A 71-year-old female patient with no major history of infection had presented with recurrent chronic purulent sinusitis over the past 3 years. These recurrent infections started in 2000 with otolaryngologists' support before diagnosis of IgG4 deficiency be asked. The patient was treated with increasingly extensive courses of antibiotics and underwent several maxillary and sphenoidal sinus washouts. She continued to present with purulent nasal discharge containing *Staphylococcus epidermidis*. The blood and immune work-ups were normal. Her antinuclear antibody count was 1/320, with no unusual types. The total immunoglobulin (Ig)E, serology, CD4 count, and lymphocyte B phenotype results were all normal. No humoral immune deficiency was detected. The analyses confirmed an underlying specific IgG4 deficiency with values of 3–4 mg/L over 4 months. The patient was treated in March 2011 with prophylactic antibiotic therapy, sinus drainage, and IV infusions of enriched immunoglobulins (IVIg 10%) administered at the outpatient clinic every 4 weeks for 3 months. The IgIV treatment was not interrupted. Her general condition improved within a few months, with her IgG4 levels rising to 44 mg/L. The IVIg infusions were well tolerated. The purulent nasal discharge was controlled, and the antibiotics were stopped. The follow-up visits at 2 and 9 months after introduction of IVIg showed that her IgG4 level had improved, rising to 15 and 11 mg/L, respectively, although it had not yet returned to normal. The infusions were then given every 3 weeks. At her last visit, the patient's clinical condition had substantially improved. She was able to start using the subcutaneous Ig concentrate form (20% SCIg), 15 g every 2 weeks, leading to a clear improvement in her clinical condition, with stabilization of her otolaryngologists' symptoms and signs. The complete blood count was normal, IgG4 were stable at 40 mg/L, and the other immunoglobulins and IgG subclasses were normal. It was then possible to reduce the SCIg dose to 10 g every 3 weeks, while continuing to monitor her clinical condition and laboratory test results. This is one of the rare cases of selective IgG4 subclass deficiency treated with immunoglobulins. Treatment resulted in a significant improvement in IgG4 levels versus pretreatment levels. The first improvement noted was the stabilization otolaryngologists' infections particularly purulent nasal discharge.

Keywords

Chronic sinusitis, IgG4 subclass deficiency, immunoglobulins, intravenous form, sinus infections, unusual disorder

Context

Primary immune deficiencies (PID) are a heterogeneous group of disorders affecting the different components of the immune system [1]. They are most often diagnosed in children [2]. Immunoglobulin (Ig)G subclass deficiencies are a form of PID. Although generally asymptomatic, those affected are at higher risk of chronic or recurrent sinus and lung infections than the rest of the population [3]. Intravenous immunoglobulins (IVIg) have been available since the end of the 1970s and are the mainstay of treatment for PID, including the IgG subclass deficiencies. IVIg therapy is administered by healthcare professionals in a hospital setting.

A subcutaneous immunoglobulin (SCIg; Hizentra®, CSL Behring, USA) has been developed for the treatment of PID. This form dispenses with the need for a venous line and can be administered by patients themselves at home [2].

Case History/Examination

A 71-year-old woman had presented with recurrent episodes of purulent sinusitis over the past 3 years. Her first infection occurred in 2000.

She did not have a major history of infection.

Methods and Results

The patient was prescribed increasingly long courses of antibiotics and had undergone several maxillary and sphenoidal sinus drainage. However, she continued to present with a purulent nasal discharge containing *Staphylococcus epidermidis*.

The blood and immune work-ups were normal. The antinuclear antibody count was 1/320 and no unusual types were detected. Total IgE, the CD4 count, and lymphocyte B phenotype analysis were all normal. No humoral immune deficiency was observed.

An underlying IgG4 deficiency was confirmed with levels of 3–4 mg/L observed over a four-month period.

Investigation/Treatment

Treatment with intravenous immunoglobulins

The patient was treated with prophylactic antibiotic therapy and sinus washouts. Immunoglobulins were administered intravenously (10% IVIg; Privigen®, CSL Behring, USA), 25 g as an infusion over a day, every 4 weeks for 3 months at the outpatient clinic.

The patient's general condition improved within a few months, with IgG4 levels rising to 44 mg/L and control of the purulent nasal discharge. The antibacterial treatment was stopped.

IVIg treatment was well tolerated. Her renal and hepatic functions were normal and no allergic manifestations were reported.

The follow-up visits at 3 and 9 months after introduction of IVIg showed that the IgG4 count had improved but not yet reached normal values. The IVIg infusions were then performed every 3 weeks until the introduction of the IgSC substitution.

Subcutaneous immunoglobulin treatment

The patient was then switched to a subcutaneous immunoglobulin (20% SCIg; Hizentra®) with monthly monitoring of IgG4 levels.

The SCIg were administered at a dose of 5 g every 2 weeks for 2 months during the switch from IVIg to SCIg, between the outpatient clinic and the patient's home.

The SCIg were subsequently administered at a dose of 10 g every 2 weeks in a one-hour infusion. Two infusion sites were used and the product was administered via a 50-mL pump. The flow rate at each site was 40 mL/3 h whether 13.3 mL/h whenever possible. This scheme was chosen for many reasons: schedule of the patient, organization of home care, and tolerance.

As no significant changes in the patient's renal or hepatic function were observed with the 10 g IgG dose, the SCIg dosage was increased to 15 g every 2 weeks, following a protocol similar to the 10 g dose protocol.

No tolerance issues were reported.

Outcome—Follow-up

The patient was seen twice at the outpatient clinic after switching to SCIg. Her clinical condition had clearly improved, with stabilization of her otolaryngologists' infectious manifestations. Her sinus discharge had cleared up. In view of the improvement in both her clinical condition and the infection, the originally planned surgical procedure on her frontal sinus was no longer necessary.

Laboratory tests performed in January 2013 showed that her complete blood count was normal and her total IgG level was 14.95 g/L. Her IgG4 level had stabilized at 40 mg/L. The other immunoglobulins and IgG subclasses were normal.

When she was seen again in early July 2013, her general condition was stable and the clinical examination was satisfactory. She had not experienced any major infectious episodes during the winter. Her complete blood count continued to be normal, with total IgG levels of 11.33 g/L. The other immunoglobulins were also normal. The

IgG4 level was normal (50 mg/L), as were the other IgG subclasses. For the patient's comfort, the interval between the 10 g SCIg injections was increased to 3 weeks. We continued to monitor her clinical condition and blood test results.

Discussion

This patient's immune work-up showed that she presented with an unusual immune defect involving the IgG4 subclass only, in a context of a high-risk sinus secondary infection. She also had another autoimmune disorder, thyroiditis, for which she was taking Levothyrox (levothyroxine sodium). Her case was further complicated by an atopic tendency which has now been treated. Her long-standing and refractory otolaryngologists' infection placed her at risk for pyoencephalitis, despite the numerous otolaryngologists' procedures performed. This poor clinical situation with its attendant neurological risk factors prompted us to start intravenous enriched immunoglobulin replacement therapy, which was continued for 9 months. Treatment led to an improvement seen both clinically and in her laboratory test results, although her values did not immediately return to normal. As soon as possible, she was switched to a subcutaneous form of injectable immunoglobulins. No major tolerance issues were observed, despite her atopic tendencies. She has been treated with subcutaneously injected immunoglobulins for the past year and a half. Her clinical condition has continued to improve. She no longer experiences her recurrent otolaryngologists' infections. A suspicious lesion in the frontal sinus was suggestive of unconfirmed aspergillosis. As her clinical condition had improved and this lesion was no longer visible on her imaging studies, the otolaryngologist surgical procedure scheduled prior to immunoglobulin treatment was deemed no longer necessary. Her clinical condition and laboratory test results have improved to the extent that, for her comfort, it is now possible to allow 3 weeks between injections, with regular clinical monitoring and blood tests.

Conclusion

This report on a case of a specific IgG4 deficiency demonstrates the potential value of using the intravenous form of enriched immunoglobulins to treat this rare and unusual disorder, followed by the subcutaneous form. The clinically serious nature of this selective IgG4 disorder—the only immune defect detected in this patient's blood work-up—and the lack of potential treatment alternatives prompted our team to propose enriched immunoglobulin replacement therapy. As her subclass 4 levels returned to normal and, above all, her clinical condition stabilized, dispensing with the need for further surgery and ruling out any serious threat of pyoencephalitis, our novel approach appears both effective and legitimate. No tolerance issues were reported after the intravenous or subcutaneous infusions. Our patient has been able to resume a totally normal life at home with her family. She now receives her infusions as an outpatient at home.

Acknowledgments

Funding support was provided by a CSL Behring Institutional Grant. We would like to thank Galien Health Publishing for their editorial help. We would like to acknowledge CSL Behring for their grant support CSL Behring.

Authorship

GD: was in charge of the biological and clinical diagnosis of this case and in charge of the innovative therapy decision. SB: was in charge of the biological and clinical follow-up. NAA: was in charge of the clinical follow-up of this innovative therapy in day hospital. YR: was in charge of the biological diagnosis of this case.

Conflict of Interest

None declared.

References

1. Notarangelo, L. D., A. Fischer, R. S. Geha, J. L. Casanova, H. Chapel, M. E. Conley, et al. International Union of Immunological Societies Expert Committee on Primary Immunodeficiencies. Primary immunodeficiencies: 2009 update. J. Allergy Clin. Immunol. 124:1161–1178.
2. Borte, M., P. Malgorzata, M. Serban, T. Gonzalez-Quevada, B. Grimbacher, S. Jolles, et al. 2011. Efficacy and safety of Hizentra®, a new 20% immunoglobulin preparation for subcutaneous administration, in pediatric patients with primary immunodeficiency. J. Clin. Immunol. 31:752–761.
3. Reynolds, H. Y. 1988. Immunoglobulin G and its function in the human respiratory tract. Mayo Clin. Proc. 63:161–174.