Extended Abstract

Paraneoplastic syndromes associated with thymoma beyond Myasthenia gravis: extended abstract

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Background

Paraneoplastic syndromes can occur in context with thymomas. While Myasthenia gravis is the most often diagnosed one, there are some others that are frequently not diagnosed or misdiagnosed, e.g., the Good syndrome (1). Named after Robert Good, the syndrome was first mentioned in 1954 by himself. Until now, there is no written consent about uniform diagnostic criteria or even a specific ICD-10 code to define the Good syndrome; it is included in ICD10:D80.8. Furthermore, therapeutic guidelines are not available; case reports, small retrospective studies and one prospective study can be found while searching for the terms 'good syndrome', 'thymoma', 'immunodeficiency' and 'hypogammaglobulinemia' on PubMed. They mostly agree on performing diagnostic investigations and offering therapy. But there is no definite recommendation.

Definition

Known as a primary syndrome of immunodeficiency (IUIS 2017, International Union of Immunological Societies Expert Committee for primary immunodeficiency diseases), Good syndrome has no unified criteria to be diagnosed. The reviewed literature claims that the Good syndrome occurs in patients with thymoma, a malignant tumor of the thymus gland in the anterior (prevascular) mediastinum (2-4). The patients suffer from reduced to absent B cells in the peripheral blood and hypogammaglobulinemia ranging from one to all immunoglobulins being reduced. Recurrent infections of the upper and lower respiratory tract are caused by microorganisms, e.g., bacteria like *Haemophilus influenzae*, *Streptococcus pneumoniae*, *Staphylococcus aureus*, *Salmonella spp.*, *Cambylobacter jejuni*, viruses like *Herpes simplex*, *Human herpesvirus 8 (Cytomegalovirus)*, *Varicella zoster* and fungi/protozoa like *Candida albicans*, *Giardia lamblia*, *Pneumocystis carinii* and many others (5). Additionally, there are other paraneoplastic syndromes like myasthenia gravis, pure red cell aplasia, alopecia, lichen ruber planus, xerosis cutis, pemphigus, onycholysis, alveolitis and thrombocytopenia. Besides the effects on B cells, low $CD4^+$ T cell levels and an inverse $CD4/CD8^+$ T cell ratio occur (2,5). There is no significant difference between the sex of the patients. The age of patients with the primary diagnosis of a thymoma varies, but most commonly these tumors are detected in the fifth decade of life (2,5,6). The histological classification of thymomas following the WHO classification shows type B thymomas as more common in patients with a paraneoplastic syndrome than others (1).

Therapy

There is no proven therapy for Good syndrome patients, neither a standard operating procedure (SOP) for diagnosis nor a therapeutic regime. Pathological laboratory values can be misinterpreted e.g., as anemia, lymphopenia, thrombocytopenia, neutropenia caused by cytotoxic side effects of the chemotherapy in treating thymomas or by immunosuppression of other paraneoplastic syndromes. Patients who are suspected to have a Good syndrome with no evidence for thymoma in the chest imaging e.g., CT should get another control scan half a year later or a FDG-PET scan as there may be a microthymoma already causing a paraneoplastic syndrome very early.

Regarding reduced or absent immunoglobulins which

are found in patients with this paraneoplastic syndrome, it should be part of the baseline diagnostics to check levels of IgG, IgA and IgM in certain intervals as well as B and T cell subsets and the T cell ratio. Due to infections with different pathogens, vaccination status should be updated with relevant vaccinations e.g., against pneumococcus, influenza or SARS-CoV-2. Infections must be avoided by vaccinations, isolation and treatment with antibiotics, antifungal and antiviral drugs if possible.

As a therapy attempt, immunoglobulins should be replaced intravenously or subcutaneously. This treatment may have an additional immunomodulatory effect on the paraneoplastic Good syndrome. Decreased laboratory parameters, such as erythrocyte or platelet numbers, should be replaced by erythrocyte or platelet concentrates or their production should be stimulated.

Summary

The Good syndrome is a thymoma associated immunodeficiency syndrome with reduced or absent B and T cells, IgG, IgA and IgM levels. Infections occur due to bacterial, fungal or viral pathogens.

As there is no SOP for diagnosis or therapy, it is important to think about the Good syndrome as a possible reason for specific symptoms occurring in thymoma patients.

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