Missed Pneumonia or Immunodeficiency?

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Tomorrow starts today

Introduction

CVID is a primary immunodeficiency that has a known association with autoimmune disorders. Although the initial presentation is recurrent sinopulmonary infectio ns, up to twenty
percent of cases report autoimmune disorders as the initial manifestation. We present a case of a patient with a history of autoimmunity who presented with a missed pneumonia.

Case Description

A 12 year old female with history of NMDAR encephalitis, autoimmune hemolytic anemia and hypothyroidism initially presented with weekly fevers, persistent uncontrollable cough, shortness of breath and intermittent post-tussive emesis. Patient was noted to present with similar symptoms 3 months prior. Upon review of the Xray from that visit, it appeared that patient likely had a lobar pneumonia left untreated. Upon further review of patient's history it was noted that she has been having 6 months sinusitis and cough. Immune labs obtained at this time indicated hypogammaglobulinemia with no antibody activity against Streptococcus pneumoniae serotypes and no change in pneumococcal titers post vaccination. This led to the diagnosis of Common Variable Immunodeficiency (CVID) . Chest x-ray and CT scan on admission
revealed lymphadenopathy and pulmonary nodules. A trans-esophageal biopsy of the mediastinal lymph nodes was obtained which was negative for non-caseating granulomas. Patient was started on monthly IVIG treatments which she has now required long term.

Discussion

While some patients can reach an autoimmune state after malignancy or a pathogenic state, many have an idiopathic propensity to autoimmunity. Out patient initially presented with NMDAR encephalitis, hypothyroidism and autoimmune hemolytic anemia.

The typical presentation of CVID is sinopulmonary infections, however there is a fraction of patients that initially present with autoimmune disorders and a later presentation of sinopulmonary infections[4]. The most common autoimmune disorders seen in CVID are autoimmune cytopenias. However rheumatologic disorders such as SLE and thyroid dysfunction have also been noted. Although autoimmune neurologic disorders are not as commonly seen in CVID, there have been case reports of patients presenting with anti-GAD[6] or a non-specific onconeuronal antibody[7] as an initial presentation. Interestingly, this is the first documented case of NMDAR encephalitis as the sole presentation of CVID.

Other causes of hypogammaglobulinemia where also considered in this patient given the medications she received for the treatment of her NMDAR encephalitis. Our patient received a total of 5 doses of Rituximab over a one-month span and was also on seizure prophylaxis for 2 years after her initial diagnosis of NMDAR encephalitis.

Although seizure medications have been known to cause hypogammaglobulinemia or cell depletion, it is often transient. Additionally, the inciting agents are typically phenytoin, carbamazepine, lamotrigine which our patient did not take. Persistent immunodeficiency after treatment with an immunomodulatory drug (PITID) is also a factor that can cause hypogammaglobulinemia.

Rituximab induced hypogammaglobulinemia is also a transient condition in which patients display reduced levels of immunoglobulin up to 6 months after treatment with rituximab. However some studies conducted on patients with immunodeficiency who received rituximab have shown a greater time to resolution or even long term persistent hypogammaglobulinemia requiring immunoglobulin replacement therapy[5]. This may indicate that patients who may require long term IVIG replacement therapy likely have an underlying immune dysfunction which can be unmasked or heightened by the use of rituximab.

Although baseline immunoglobulins were obtained prior to the start of rituximab in our patient, we believe they were falsely elevated due to multiple doses of IVIG patients received 1 month prior to measurement of baseline labs. Persistent and delayed onset hypogammaglobulinemia post-rituximab therapy has been noted in pediatric patients with CNS autoimmune disorders[9], however further study is required given the rarity of cases. An alternative explanation would be an idiopathic propensity to autoimmunity presenting itself prior to the typical symptoms seen in CVID.

Conclusions/ Key points

When to suspect immune dysfunction

- When encountering a patient with frequent sinopulmonary infections, particularly if it was not a previously noted problem, it is beneficial to assess immune function.
- Patients with history of autoimmune disorders who show frequent infection history. This is particularly seen in patients with CVID as 20% of cases present with autoimmunity as the sol presentation with later observed immun dysregulation
- PITID after treatment with particular medications in patients with autoimmune disorders or seizure history should be considered if exposure to medicine was atleast a year of symptoms. This disorder often presents as transient hypogammaglobulinemia but there are rare cases (particularly in patients with a neuroautoimmune history) where there is a need for long term IVIG replacement therapy.

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