A stepwise approach to the adult immunodeficiency evaluation for the rhinologist

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Purpose of review
Patients with an immunodeficiency may present to their Rhinologist with a history of recurrent, severe, and chronic infections. Therefore, it is essential for the Rhinologist to have a basic understanding of clinically relevant immune deficiencies.

Recent findings
After describing different types of immunodeficiencies, their presentations, and management strategies, an evaluation algorithm is described.

Summary
Through a collaborative approach, Rhinologists and Clinical Immunologists can provide comprehensive medical care to patients with immunodeficiencies.

Keywords
antibiotics, immunodeficiency, immunoglobulin replacement therapy, recurrent infections, vaccinations

INTRODUCTION

Understanding and evaluating the immune system is relevant to the clinical practice of Rhinologists as patients with immunodeficiencies can present with recurrent, chronic and severe infections of the head and neck [1,2]. Often, patients may present to their Rhinologist before they have seen a Clinical Immunologist. Hence, it is important for Rhinologists to have knowledge of the immune system and the different presentations of immunodeficiencies. This article will focus on the presentation and management of adults who are evaluated by Rhinologists.

The immune system is complex and contains many different parts, including the innate, humoral and cellular immune systems [1,3▪]. Innate immunity involves complement system, phagocytes, natural killer (NK) cells, and physical barriers. Humoral immunity encompasses B cells (B-lymphocytes) and antibodies while cellular immunity includes T cells (T-lymphocytes). An abnormal immune system can be either hypo or hyper functioning. Therefore, when one part of the immune system is not functioning normally, it can manifest as recurrent infections and/or autoimmune disorders. Suspicion for an immunodeficiency should be considered when a patient presents with a history of recurrent, chronic, or severe infections, frequent courses of antibiotics, or missing significant amounts of work or school due to illness [2]. Requirement of sinus surgery or myringotomy tubes as an adult can also be a signal of a possible immunodeficiency [4▪].

PRIMARY IMMUNODEFICIENCY

There are both primary immunodeficiencies (PIDs) and secondary immunodeficiencies (SIDs) [5▪,6▪]. PIDs are also known as inborn errors of immunity (IEIs). They consist of over 450 disorders and are due to genetic mutations [7▪]. Knowledge of genetic defects associated with PIDs has dramatically increased over the past 40 years [8▪]. It is estimated that about 1 in 10 000 people are affected by PIDs [9▪,10]. Also, it is thought that many individuals remain undiagnosed [9▪,10]. As the understanding and treatment strategies for PIDs advances, patients with PIDs are experiencing increased longevity and improved quality of life. This progress can result in

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KEY POINTS

- Knowledge of the immune system and how to evaluate for a possible immunodeficiency is relevant to the clinical practice of Rhinologists.
- Evaluation for a possible immunodeficiency is performed through a combination of history and laboratory evaluation.
- Based on the type of immunodeficiency, there are different treatment strategies that may be utilized.
- Through collaboration, Rhinologists and Clinical Immunologists can provide comprehensive medical care to patients with immunodeficiencies.

adult patients who may present with a history of an immunodeficiency that was diagnosed in childhood.

Specific antibody deficiency (SAD) is a common PID seen in patients with chronic rhinosinusitis (CRS) [11]. SAD is a form of humoral immunodeficiency, and it is a disorder of antibody function in which an individual is not able to make antibodies after a person receives a polysaccharide vaccine. Patients with SAD have normal cellular immune function and have normal immunoglobulin levels. One study estimated that 24% of individuals with CRS had SAD in comparison to 11% of healthy patients [11]. SAD is associated with increased incidence of sinopulmonary infections and antibiotic use. Additionally, SAD severity, defined by the number of protective postvaccination pneumococcal titers, can be associated with lower airway disorders and increased antibiotic use [11].

One of the most common PIDs in adults is common variable immunodeficiency (CVID) [11]. One in 25 000 people are estimated to have CVID. CVID affects men and women equally and is typically diagnosed between 20 and 40 years [12,13,14▪]. CVID is defined as low quantitative immunoglobulins, specifically low IgG and either low IgA or IgM, and poor response to vaccines [14▪]. In contrast, hypogammaglobulinemia is defined as low immunoglobulin levels [14▪].

SECONDARY IMMUNODEFICIENCY

SIDs are acquired from another cause, including infection, malignancy, and medications. SIDs can develop at different stages of life based on their cause and they can be temporary or permanent. Evaluation for HIV is important to consider, as it is an infectious cause of immunodeficiency. A history of malignancy, chemotherapy, or immunotherapy are possible causes of a SID. A history of transplant or autoimmune disorder and subsequent use of immune suppressive medications is another common cause of SIDs. Notably, the use of corticosteroids can be a cause of a SID. In turn, an individual with an immunodeficiency can be at an increased risk for malignancy and autoimmunity [9▪].

EVALUATION

Immunodeficiencies are managed in different ways depending on the aspect of the immune system that is not functioning appropriately as well as the severity [15]. When starting an evaluation for an immunodeficiency, it should be based on the type of infection(s) the patient has been experiencing [1,2,16]. Assessment of vaccine response is a key aspect of the evaluation. If a patient does not have a protective response to either the pneumococcal or tetanus vaccine, these vaccines may be given and then these levels are often repeated in 4–8 weeks [17]. The purpose of this is to both provide protection against the pathogen and measure the function of the patient's immune system by assessing whether the patient can mount a response to the particular vaccine. *Streptococcus pneumoniae* is a common bacterial cause of sinusitis, otitis media, and pneumonia. The purpose of evaluating *S. pneumoniae* titers after a patient receives the pneumococcal polysaccharide vaccine is to assess the humoral immune response to polysaccharide antigens; this vaccine is primarily T-cell independent. In contrast, response to tetanus toxoid vaccine assesses antibody responses to protein antigens. In addition, monitoring response to the tetanus toxoid vaccine evaluates the patient's cellular immunity as this vaccine is T-cell dependent, requiring a coordination of T and B cell responses [17,18]. Vaccines against *S. pneumoniae* are available in two forms: pneumococcal polysaccharide vaccine and pneumococcal conjugate vaccine [19▪]. Of note, the pneumococcal conjugate vaccine is currently part of the standard childhood vaccine series [20▪]. The pneumococcal conjugate vaccine was first approved and routinely administered to children in 2000 [19▪]. Therefore, many adults who present to see a Rhinologist may not have received this vaccine. It is now recommended that all adults 65 years and older and also those 19–64 years old with certain medical conditions receive the pneumococcal vaccine [19▪]. Regarding severity, if the immunodeficiency is mild, such as if the immunology laboratories are abnormal but clinically the patient is overall well, then these laboratories may be monitored over time. If the immunodeficiency is considered more severe, then different treatment options may be discussed. These therapies are discussed later in the article.

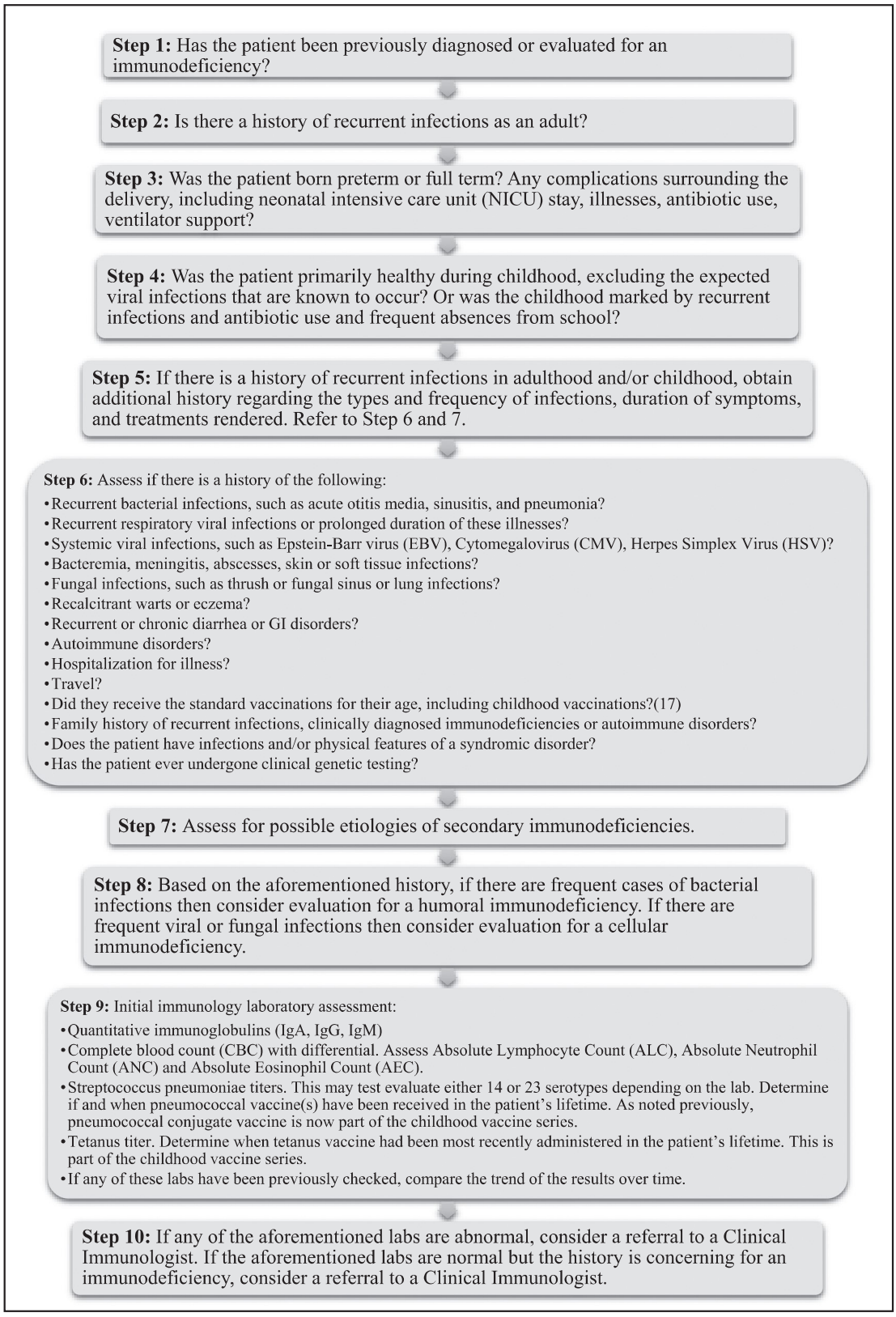

FIGURE 1. History and laboratory evaluation for immunodeficiency.

When evaluating for a possible immunodeficiency, obtaining a thorough history is fundamental. We recommend assessing for immunodeficiencies using the 10-Step algorithm depicted in Fig. 1.

If a referral to a Clinical Immunologist is ordered, we recommend providing initial counseling on immunodeficiencies with the clarification that further exploration will be performed under the care of the Clinical Immunologist. Initial counseling may include explanation that an immunodeficiency is a disorder in which the immune system is not acting as it normally should, and this can result in recurrent infections and/or autoimmune disorders. Immunodeficiency evaluations combine obtaining a thorough history with immunology laboratory testing. It may be possible that based on history and the immunology laboratories, further laboratory testing may or may not be required but this will be determined when the patient is evaluated by the Clinical Immunologist. By providing the Clinical Immunologist with the patient's history and initial immunology laboratories, this can help to advance the patient's care as the Clinical Immunologist will have this information at the first visit and so a further evaluation and/or counseling can be provided.

TREATMENT

Regarding treatment options, antibiotic prophylaxis may be considered for patients with recurrent or severe infections. Antibiotic prophylaxis may be administered daily or several days a week depending on the antibiotic that is chosen [15]. Another therapy that can be provided is immunoglobulin replacement therapy [21]. Immunoglobulin replacement therapy is a form of passive immunity in which antibodies from donors are pooled and then can be administered as infusions [22▪]. These infusions are administered either subcutaneously or intravenously. They are given weekly, biweekly, or monthly, depending on the delivery method. There are multiple formulations of immunoglobulin replacement therapy available in the United States [22▪]. The decision on when to initiate and the duration of this therapy should be made in consultation with a Clinical Immunologist. Additionally, often patients with immunodeficiencies are treated with prolonged courses of antibiotics when they have an infection. These patients also should have a lower threshold for receiving antibiotics due to their decreased ability to respond to infections compared to individuals without immunodeficiencies. Gene therapy and bone marrow transplant are also treatment strategies for some patients with immunodeficiencies [15].

CONCLUSION

Knowledge of presenting features and how to evaluate for a possible immunodeficiency is important for the practicing Rhinologist. Adult patients with immunodeficiencies may first present to their Rhinologist before they are evaluated by a Clinical Immunologist. Obtaining a thorough history of the type, frequency, duration and treatment of previous infections is essential. If the history is concerning, initiating an immunology evaluation through laboratory testing before referral to a Clinical Immunologist can advance patient care. By working together, Rhinologist and Clinical Immunologists can provide comprehensive medical care to patients with immunodeficiencies.

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Conflicts of interest

There are no conflicts of interest.

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- ▪ of special interest
- ▪▪ of outstanding interest

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