Current Treatment of Alopecia Areata

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The number of alopecia areata (AA) clinical trials with Jak inhibitors of cytoplasmic tyrosine kinases, including Jak1, Jak2, Jak3, and tyrosine-protein kinase has increased significantly since the last Research Summit. This fact means that the conversation about current treatments for AA now also needs to include a discussion of traditionally used off-label therapies as well as evolving therapies as with Jak inhibitors.

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Introduction

The first step in selecting a treatment for a patient with alopecia areata (AA) is to ascertain what bothers the patient or the patient's parents. Is it scalp hair loss or eyebrow, eyelash, or beard hair loss? For some patients who have adapted to scalp hair loss, the primary reason for requesting a treatment may be that the hair loss he or she is experiencing in a nonscalp area is what is most bothersome. For other patients, it may be the nail involvement and dealing with fragile, brittle nails or when seeing hair falling out and present everywhere, developing anxiety or depression. Dealing with the unpredictability of AA, whether it be recurrent episodes, lack of responsiveness to prescribed treatments, or ongoing hair loss despite a commitment to a treatment plan, is challenging. This unpredictability needs to be discussed in the context of the pathophysiology of AA when developing treatment plans.

Medical and social history

Before prescribing a treatment plan to a patient with AA, a thorough medical history, including medication and supplement use, as well as current and past treatments of his or her AA, needs to be recorded. Scalp and hair care habits, including the use of cosmetic camouflage techniques and scalp or eyebrow prostheses, should be noted as many patients with extensive scalp hair loss discontinue shampooing their scalp and only use bar soap or nothing. This behavior may result in compromised scalp health and a scalp folliculitis, which could impact the success of prescribed topical or oral therapies. Supplement use is common, and when patients develop hair loss, it is not uncommon for patients to take even more supplements, and in particular biotin, despite its use not having been shown to be beneficial for normal, healthy hair, or in individuals with no biotin deficiency (Lipner, 2018; Walth et al., 2018).

Discussing how AA affects the patient in their social and/or home environment is also an integral part of the treatment of this disease. In a recent survey by the National Alopecia Areata Foundation of 641 subjects, just over 50% reported that having AA impacted their physical activities, and 20% felt that having AA impacted their relationships and social activities.

Clinical examination

The examination should include an assessment of all hair-bearing areas as well as both finger and toenails. Scalp vellus, indeterminate and terminal fibers, and the presence or absence of scale, erythema, folliculitis, or atrophy should be noted. Photography can be used to document disease extent, and the Severity of Alopecia Tool score can be used as a tool to objectively measure scalp hair loss and treatment outcomes (Olsen et al., 2018). Disease activity at the time of clinical examination can be ascertained by the presence or absence of positive hair pull tests. Both finger and toenails should be examined, and abnormalities such as pitting, dystrophy, onycholysis should be noted.

After the medical history, medication and supplement use, and disease extent and activity have been ascertained, the conversation can turn to a discussion about autoimmune diseases with a focus on AA. It is important for patients and family members to understand AA is an autoimmune disease and that this disease can spontaneously resolve, persist, reoccur, or progress, even in some situations while on therapy. There are currently no clinically significant biomarkers to predict when AA may flare but finding biomarkers is a subject of current research (Jabbari et al., 2016). Before proceeding to specific treatment recommendations, this is a good point in the visit to review the basics of what we know about AA (Table 1) and to introduce the patient and his or her family to the National Alopecia Areata Foundation.

Laboratory testing

Laboratory testing is not mandatory but may be helpful based on the results of the history and physical examination. If the patient is prescribed a systemic medication, then safety monitoring laboratory studies may be indicated. To ensure the absence of other easily treated medical conditions commonly associated with hair loss, thyroid function studies, hematologic and iron profiles, as well as Vitamin D levels, are commonly checked.

Choosing a treatment for AA

There are several non–Food and Drug Administration (FDA) approved treatments used to treat AA. Treatment recommendations should take into account the patient's age, location of the hair loss, disease extent and activity, presence of other medical or psychological problems, and in some cases, the results of a scalp biopsy (Hordinsky, 2013). As many new therapies are currently being evaluated, patients with

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Table 1. Basic Facts about AA to Share with Patients

Facts
AA affects 1.7−2.1% of the population.
50-80% of cases are sporadic.
Both males and females of all ages and races can be affected.
AA is immune-mediated and is characterized by an attack on the anagen phase of the hair cycle.
Disease associations may vary around the world and include vitiligo, thyroid disease, atopy (allergic rhinitis, asthma, atopic dermatitis).
Current genetic research suggests the same genes involved in AA also play a role in rheumatoid arthritis, type 1 diabetes, celiac disease.
AA is a multifactorial condition with a concordance rate of 42−55% for monozygotic twins and 0−10% for dyzogotic or fraternal twins.

Abbreviation: AA, alopecia areata.

AA should be updated about not only traditionally used therapies but also about ongoing clinical trials and the off label use of Jak inhibitors and, especially, oral tofacitinib.

Since the last Alopecia Areata Summit in 2016, the treatment of stable patchy AA continues to commonly include the use of topical or intralesional corticosteroids, 2% or 5% topical minoxidil when there is fine vellus or indeterminate hair growth present, anthralin, topical immunotherapy, or combinations such as a topical steroid with topical minoxidil. Local injections of intralesional triamcinolone acetonide ranging in concentrations from 3 to 10 mg/cc is still a preferred treatment for scalp and eyebrow AA. Topical immunotherapy with diphenylcyclopropenone or squaric acid dibutylester also continues to be another accepted therapy for AA.

In addition to the treatments already mentioned, oral immunosuppressive agents such as prednisone, methotrexate, cyclosporine, or intravenous solumedrol or Ig are sometimes prescribed for patients with alopecia totalis or alopecia universalis. For those patients with active hair shedding, oral prednisone may be prescribed to try to turn off disease activity.

For those experiencing eyelash loss, there are again no established treatments. Topical prostaglandin analogs have been studied, but this approach has not been popularized, and the presence of some hair growth is probably needed to have a successful clinical outcome (Roseborough et al., 2009).

The selection of the best treatment for the patients with AA can be challenging. A review of randomized controlled trials in AA was published in 2014. (Hordinsky and Donati, 2014). A review of 29 trials using the American College of Physicians Guideline grading system, found that the studies were of moderate quality overall and that a number of treatments were effective, particularly the use of topical and oral corticosteroids and the sensitizing agents. The majority of these studies involved adult patients. Treatment studies of pediatric AA are limited, but of the studies available for review, the use of potent topical steroids such as clobetasol propionate cream 0.05% has been found to be more effective than a lower potency topical steroid such as 1% hydrocortisone (Lenane et al., 2014). The use of immunotherapy in children, particularly in those with chronic and extensive AA, is supported as is the use of pulsed, high dose systemic corticosteroids, especially in the setting of acute hair loss.

Since the last Summit in 2016 where the use of Jak inhibitors was introduced, and study results on adult patients were presented from Columbia University, Cleveland Clinic, and Stanford and Yale Universities, there has been a surge in off label use of oral tofacitinib, currently approved in the United States for the treatment of rheumatoid arthritis. There has also been an increase in the use of compounded formulations of topical tofacitinib and ruxolitinib, as well as opportunities for patients with AA to participate in several industry-sponsored clinical trials assessing the efficacy of both topical and oral Jak inhibitors for the treatment of AA. Overall treatment response rates reported at the 2016 Summit with oral tofacitinib or ruxolitinib ranged from 54% to 75% (Craiglow et al., 2017,. 2016; Liu et al., 2017; Mackay-bibWiggan et al.,2016). The treatment response in 13 adolescents treated at Yale University was noted to be 75%. This group also reported no positive results with a compounded topical tofacitinib inhibitor.

With this surge in the use of Jak inhibitors to treat AA, part of the treatment visit needs to include a discussion of Jak inhibitors. As patients with AA learn more about Jak inhibitors, they, in turn, ask their physicians and advanced health care providers about this new potential approach. Providers concurrently need to learn about Jak inhibitors and be able to share this information with their patients. Physicians and mid-level providers need to know that the Jak family includes Jak1, Jak2, Jak3, and tyrosine-protein kinase and that this is a group of cytoplasmic tyrosine kinases which mediates signal transduction through interactions with type 1 and type 2 cytokine receptors that are critical for leukocyte activation, proliferation, survival, and function.

Finally, there can be a discussion about cosmetic camouflage with wigs or scalp prostheses. Patients can also be referred to Locks of Love, a nonprofit organization that provides hair prostheses for children younger than age 18.

Summary

Physicians and mid-level providers generally prefer topical or intralesional steroid therapy for the treatment of AA. However, after the recently published studies in which the systemic Jak inhibitors (e.g., tofacitinib or ruxolitinib) were shown to reverse the AA process, there is currently a surge of clinical trials and interest in treating patients with AA with Jak inhibitors. Concurrently, more attention is being focused on the psychological needs of patients with AA. In the meantime, other therapeutic approaches are also being examined. Some of these treatments include the use of low dose IL-2 and simvastatin and/or ezetimibe (Castela et al., 2014; Lattouf et al., 2015), administration of platelet-rich plasma (Trink et al., 2013), use of oral antihistamines, and the addition of photobiomodulation.

With all the ongoing clinical research activities in AA, the future is looking up for both children, adolescents, and adults who have this common autoimmune disease that currently has no FDA approved therapy.

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CONFLICTS OF INTEREST

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