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Case 1: Epidemiology, Presenting Symptoms and Patient Burden

Case 1 Background

A 32-year-old Black female is on the schedule of your dermatology clinic with the complaint of sudden hair loss on her scalp. You have a discussion regarding the differential diagnosis of alopecia with a first-year dermatology resident to prepare him for the visit. He recalls that traction alopecia and central centrifugal cicatricial alopecia (CCCA) may be more common in Black women than in others.

Case 1 Question1:

What one of the following is the estimated point prevalence of alopecia areata among Black people in the United States as of 2023?

- a. 0.2%
- b. 0.5%
- c. 0.75%
- d. 1.0%

Rationale

The correct answer is: a) 0.2%

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- 2023 United States based cross-sectional study of 1,093,176 patients in the Explorys database
 - Overall point prevalence of 0.18% (176 per 100,000 patients)
 - Ethnic differences
 - Asian (0.41%)
 - Black (0.23%)
 - Hispanic/Latino (0.21%)
 - Multiracial/other (0.31%)
 - White (0.17)
 - Sex differences
 - Female (0.20%)
 - Male (0.15%)
- 2020 Meta-analysis of 94 trials studying the global prevalence of alopecia areata
 - Overall lifetime prevalence was 2.11%
 - Age differences
 - Children and adolescents (1.83%)
 - Adults (1.64%)
 - Differences over time
 - Studies before 2000 (1.01%)
 - Studies between 2000-2009 (1.76%)
 - Studies after 2009 (3.83%)

Faculty Commentary

Brett King, MD: What's interesting in the epidemiology of alopecia areata is that, as there has been increasing interest in the disease in the past handful of years, we have dived deeper into the epidemiology to understand it better. What we have learned is interesting. On the one hand, the lifetime prevalence is approximately what we thought it was, based on studies back in the 1990s, that is about 2% of people over our lifetime will have alopecia areata. But what we have learned more recently, that maybe we didn't know as well back then, was the differences in different populations. And very recent work has suggested that



the point prevalence of alopecia areata might be greater in patients of Asian descent relative to Black patients, relative to Hispanic and White patients.

This doesn't necessarily change the way we practice medicine. It doesn't change the way that we think about alopecia areata, but it simply highlights that we need to be mindful, in every single patient that stands before us for help, to recognize that alopecia areata is possible in them. So, even in patients such as Black patients in whom we think of maybe scarring alopecias as being more common than in everybody else, we must not stop to think that they also have alopecia areata as much as other populations or maybe even more than some.

Natasha Mesinkovska, MD: So, what do we know about alopecia areata among different races and ethnicities? Well, we're just really skimming the top of that topic. Why do I say this? We know that, in the United States of America, African Americans are at an increased risk for developing alopecia areata in comparisons to Asian Americans and Caucasians. Although the initial studies were showing that maybe Asian Americans had a lower risk than Caucasians, new data that is emerging is saying maybe that is not true and that they're also having increased rates of alopecia areata. The whole topic of Hispanics as an ethnicity in the United States is definitely not studied enough, but the data from South America does show alopecia areata is a condition that is highly prevalent. So, how do we keep this area advanced and how do we learn more? Depending on who we are, depending on how we're made, depending on the type of hair we have, we do have different ways to take care of our scalp and take care of our bodies. So, as the data is coming in for the new medications, more and more details are needed as to how certain races and how patients of color are affected by the medications.

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Case 1 Background (continued)

The resident sees the patient and notes the following in the patient's electronic health record.

Chief complaint: Sudden scalp hair loss starting about 2 months ago.

History of present illness: Patient reports first noticing the small, round patches of hair loss on her scalp about 8 weeks ago. The patches have progressively increased in size and number. Patient denies pain, itching, or redness associated with the hair loss. There is no history of trauma. She has tried multiple over-the-counter and herbal hair growth products without any success.

Past medical history:

- No significant past medical history
- No known allergies
- No history of autoimmune diseases

Family history:

- Mother has a history of thyroid disease
- No known family history of alopecia areata
- No known family history of other autoimmune diseases

Social history:

- Nonsmoker
- Occasional alcohol use (1-2 drinks per month)



- Works as a manager at a local spa
- No recent changes in diet, exercise, or lifestyle

Review of systems:

- General: No weight loss, fever, or fatigue
- Skin: No rashes or other skin changes
- Nails: No pitting or other abnormalities
- Joints: No joint pain or swelling
- Endocrine: No symptoms of thyroid dysfunction

Current medications

- Ethinyl estradiol/desogestrel 0.03/0.15 mg oral contraceptive taken once daily
- Naproxen 220 mg 1-2 tablets as needed for occasional headache

Case 1 Question 2:

What information from the history is common in patients presenting with alopecia areata?

- a. Lack of autoimmune disease
- b. Lack of pitting in the nails
- c. Sudden hair loss
- d. Use of hormonal therapy (oral contraceptives)

Rationale

The correct answer is: c) sudden hair loss

- Alopecia areata is a common, inflammatory, nonscarring type of hair loss.
- There are significant variations in the clinical presentation among patients, ranging from one or a few small, wellcircumscribed patches of hair loss to complete loss of scalp, face, and body hair
- Patients commonly present with a sudden onset of a patch or patches of hair loss
 - o Focal
 - Well-circumscribed patches
 - No signs of significant inflammation or scarring
- Fingernail involvement
 - o 10% to 30% of patients have nail changes
 - Can be pitting or longitudinal ridging, brittle nails, or onycholysis
- Positive hair pull test is a sign of active disease
- Alopecia areata subtypes
 - AA incognita diffuse shedding
 - Alopecia totalis (AT) complete loss of all hair on the scalp
 - Alopecia universalis (AU) complete loss of all hair on the scalp, face, and body
 - Ophiasis band-like alopecia involving the posterior hairline and extending to the ears
 - Sisaipho hair loss centrally, similar in clinical appearance to androgenic alopecia
- There is no data on oral contraceptives contributing to alopecia areata

Faculty Commentary

Brett King, MD: The answer here is sudden hair loss. And among the choices, lack of autoimmune disease, lack of pitting in the nails, sudden hair loss or use of hormonal therapy, sudden hair loss is for sure the common element in patients with alopecia areata. And this is notably different than other forms of hair loss. Perhaps the other one in which we think of relatively acute onset diffuse shedding is telogen effluvium. However, even in telogen effluvium, patients do not wake up one day and have truly absent hair in patches on their scalp or face or body. That is truly a hallmark of alopecia areata and helps us to distinguish it from the other forms of hair loss. Again, the differential diagnosis in patients with hair loss is quite broad and can include central



centrifugal cicatricial alopecia (CCCA), frontal fibrosing alopecia, (FFA), lichen planopilaris (LPP), androgenetic alopecia, and telogen effluvium and we always need to be mindful of that differential. But again, sudden onset of loss in a patch or patches is really a hallmark of alopecia areata and we do not really think of these other things as necessarily being more, well are certainly not more common than sudden hair loss in patients with alopecia areata.

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Case 1 Background (continued)

The resident also notes the following during the physical examination:

- General: Well-nourished, well-developed female in no acute distress.
- Scalp: Multiple well-demarcated, round patches of hair loss on the scalp, ranging from 1 to 3 cm in diameter. No erythema, scaling, or scarring observed.
- Eyebrows and eyelashes: no hair loss
- Hair Pull Test (scalp): Positive around the affected areas.
- Skin: No other lesions or abnormalities noted.
- Nails: Normal appearance, no pitting or ridging.

The patient was also tearful, stating that she has a hard time going to work because they do not allow any type of hat or hair covering. She worries about what her clients may think and has missed work due to the hair loss.

Case 1 Question 3:

According to a recent retrospective observational study, compared to matched controls, persons with alopecia areata are at higher risk for depressive episodes, recurrent major depressive episodes, and anxiety. Which ethnic group has the highest risk of AA-associated anxiety disorders?

- a. Asian
- b. Black
- c. White
- d. Other

Rationale

The correct answer is: b) Black

- Patients with alopecia areata may experience, like this patient, marked impairment in psychological well-being and selfesteem, and may be more likely to suffer from psychiatric comorbidities.
- The study showed that, compared to matched controls, persons with AA had a higher risk of mental health complications
 - Depressive episodes (odds ratio (OR) 1.45)
 - Recurrent major depression (OR 1.45)
 - Anxiety disorders (OR 1.4)
 - Black population had a higher rate of anxiety disorders (OR 2.92)
 - Other studies have found a 2.5-fold increase in anxiety in patients with AA
- 51% of pediatric patients with AA met criteria for anxiety disorder



Faculty Commentary

Brett King, MD: The answer here is Black people. And this is interesting because we really understand very well that alopecia areata has a profound impact on life. We know that these patients often suffer depression and anxiety as a result of alopecia areata, or an exacerbation of preexisting depression, or anxiety as a result of developing alopecia areata. Hopefully, all of us recognize why that would be the case. If we put ourselves in this person's shoes, we're going to have that same experience of sadness and anxiety, but what's interesting about this recent work is that it's that there might be some differences in the way different populations experience alopecia areata. And again, this shouldn't surprise us, but we might not have thought that was the case. And indeed, this work highlighted that Black people with alopecia areata suffer more anxiety disorders than others, relatively speaking.

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Case 2: Diagnosis, Disease Severity, and Monitoring Case 2 Background

A 38-year-old Hispanic woman returns to the clinic with continued complaints of alopecia of the scalp. She is concerned because she wants to look her best for her daughter's quinceañera in 2 months.

History of present illness: The patient reports that the hair loss began approximately 3 months ago and has progressively worsened. She denies any itching, pain, or redness in the affected area. There are no systemic symptoms such as fever, weight loss, or fatigue.

Medical history:

- 6-year history of diet-controlled, type 2 diabetes
- Hashimoto's hypothyroidism
- Chronic headaches 1-2 per week
- History of polycystic ovary syndrome
- No known allergies
- No history of rheumatoid arthritis, psoriasis, or other autoimmune disorders

Family history:

- No family history of alopecia
- No history of autoimmune conditions

Social history

- No drug or alcohol use
- Never smoker
- Recently started a low-carbohydrate diet

Medications:

- Levothyroxine 75 mcg daily
- Acetaminophen 500 mg 1-2 every 6 hours as needed for headache



Case 2 Question 1:

What disease from this patient's medical history is a common comorbidity associated with AA?

- a. Chronic headache
- b. Hashimoto's hypothyroidism
- c. Polycystic ovary syndrome
- d. Type 2 diabetes mellitus

Rationale

The correct answer is: b) Hashimoto's hypothyroidism

- Comorbidities
 - Atopic dermatitis
 - o Helicobacter pylori infection
 - o Iron deficiency anemia
 - Thyroid dysfunction
- Vitamin D deficiency has been associated with AA
- Genome wide association studies have shown shared genetic risk loci between AA and other autoimmune disorders, such as thyroid disease, rheumatoid arthritis, celiac disease, and type I diabetes

Faculty Commentary

Natasha Mesinkovska, MD: This case is an example of a typical scenario. A relatively healthy person that comes to see us with hair loss, alopecia areata. What are the things that we have to keep in common that are associated with alopecia areata? Typically, they are autoimmune conditions, such as thyroid diseases like Hashimoto's thyroiditis in this case, but one of the things that most of us overlook is the presence of atopic dermatitis. Depending on the study, 30% or more of both adults and children will have atopic dermatitis. Other things that are common, particularly in people with darker skin types, can be vitamin deficiencies. We also have to look out for iron deficiency anemias and even *Helicobacter pylori* infections have been associated with alopecia areata. When we look at the families in these genome-wide studies, other autoimmune conditions, such as psoriasis, celiac disease, and even rheumatoid arthritis, can be present in family members.

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Case 2 Background (continued)

The physical exam of the 38-year-old Hispanic woman revealed the following:

- Scalp: A single, well-defined, nonscarring alopecic patch measuring approximately 7 cm in diameter is noted on the occipital region. The skin within the patch appears normal without erythema or scaling.
- Hair Pull Test: Negative
- Nails: No pitting or other abnormalities
- Skin: No other lesions or rashes noted



Case 2 Question 2:

Which of the following would be most beneficial to further inform the diagnosis of alopecia areata in this patient?

- a. Measurement of serum antinuclear antibody (ANA)
- b. Hair pluck trichogram
- c. Trichoscopy of the affected area of the scalp
- d. Measurement of blood thyroid stimulating hormone (TSH)

Rationale

The correct answer is: c) trichoscopy of the affected area of the scalp

- Diagnosis
 - o Based on clinical examination, trichoscopy of the scalp lesion and, if needed, skin biopsy
 - Clinical examination
 - Lack of scarring
 - Lack of inflammation
 - Positive pull test
 - Anagen effluvium
 - o Trichoscopy
 - Exclamation mark hairs
 - Tapering hairs
 - Black dots
 - Scalp biopsy indications
 - Solitary patch recalcitrant to treatment
 - Diffuse alopecia
 - Possibility of cicatricial alopecia
 - Scalp biopsy
 - Single biopsy taken at the edge of a patch
 - Sectioned both horizontally and vertically
 - o Blood ANA or TSH may help determine comorbidities, but are not needed for diagnosis

Faculty Commentary

Natasha Mesinkovska, MD: Alopecia areata is a clinical diagnosis. Very rarely will you, as a clinician, have to do a biopsy and, as we know, biopsies are not fun for either us or the patients. So, how do we improve our clinical skills? Using a dermatoscope is something that we're very comfortable with. I think the term trichoscopy, meaning looking at the hair, may confuse and intimidate us. What I would suggest is the following: you pull out the dermatoscope and you look closely at the area that has hair loss and the edges. I would even rub the edges to see if any hair falls off instead of doing the classical pull test. So, what are we looking for in these areas of hair loss? Usually, they're going to be the 2 types of dots. The yellow dots, which are just dilated infundibula with sebum in there and they are present in 60% to 90% of cases, depending on who you listen to, but they are going to be there in acute and chronic cases. Then there are going to be these little black dots, almost like these broken hairs, and my favorite, these little exclamation point hairs. So, these are things that can help us with our clinical exam. Other things that I always suggest is to look at the eyebrows, eyelashes and pay attention to the nails. In the nails, we are looking for pitting and any kind of dystrophy.

Brett King, MD: It's really important that we allow ourselves to not know. Dermatology happens fast. We do not always have a lot of time with patients and so we walk into the room and I think sometimes we feel pressure that we need to know the answer. We do not always know the answer and it's okay to do a biopsy. We want, first and foremost, to treat the patient, and we can't do that if we do not know the diagnosis. We do not want to say that somebody has alopecia areata, a reversible nonscarring form of



hair loss, when they actually have CCCA, an irreversible, scarring form of hair loss. Sometimes the only way we're going to separate these things is with a biopsy. Do not hesitate to do that.

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Case 2 Background (continued)

Further examination of the alopecic patch shows that it covers 5% of the posterior region of the patient's scalp.

Case 2 Question 3:

Based on the physical examination findings in this 38-year-old Hispanic woman, how severe is her alopecia areata?

- a. Mild
- b. Moderate
- c. Severe

Rationale

The correct answer is: a) mild

- Severity of Alopecia Tool (SALT) score
 - The SALT score ranges from 0 (no terminal hair loss) to 100 (100% terminal hair loss, ie, no terminal hair on the scalp)
 - Severity of AA, based on SALT score, may be categorized as
 - Mild = SALT score ≤20
 - Moderate = SALT score 21-49
 - Severe = SALT score ≥50
 - SALT looks at hair loss and does not consider quality of life, extra-scalp involvement, or psychosocial impact
 - Alopecia Areata Scale (AASc)
 - Recently published scale that includes psychosocial impact and extra-scalp involvement
 - Similar scalp hair loss severity scale as above, only modified by the presence of other important disease factors
 - o If mild or moderate, can increase the rating by 1 level if 1 or more of the following is present
 - Negative impact on psychosocial functioning resulting from AA
 - Noticeable involvement of eyebrows or eyelashes
 - Inadequate response after at least 6 months of treatment
 - o Diffuse (multifocal) positive hair pull test consistent with rapidly progressive AA

Faculty Commentary

Natasha Mesinkovska, MD: At presentation, determining whether the severity of alopecia is mild, moderate or severe can be tasking. By definition, most experts agree that mild is anything that is less than 20% of hair loss on the skull. However, think about a patient that comes in and all of the hair loss is not on the scalp. That is why there are criteria now that helps us modify this mild, moderate and severe category that exists. And these criteria are good for us to remember in case we have to make a case for insurance to cover our patient's treatment or just to simply understand for ourselves, the family, or the school, any accommodation the patient may need as an indication of the severity of the condition. What are some of these factors? So, if somebody has a certain type of severity, it gets upgraded if they have eyebrow and eyelash hair loss, if the disease is active or if it affects them psychosocially. And you do not need an expert - you can tell if the patient is impacted.



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Case 3: Treatment Options

Case 3 Background

A 29-year-old Chinese man presents with a 2-month history of multiple hair loss patches on the scalp. History of present illness:

- The patient noticed the first patch of hair loss approximately 2 months ago.
- Since then, additional patches have appeared, varying in size.
- The patches are nonpainful and nonitchy.
- No associated redness, scaling, or other skin changes.
- No history of similar episodes in the past.

Medical history:

- History of gout.
- No known allergies.
- No history of autoimmune diseases.

Family history:

- No family history of alopecia areata.
- No history of autoimmune conditions.

Social history:

- Smokes 3-4 cigarettes a day.
- Occasional alcohol consumption.
- Works as a software engineer.
- No recent significant stressors reported.

Current medications:

• Allopurinol 300 mg daily

Physical examination:

- Multiple well-demarcated, round patches of hair loss on the scalp. No erythema, scaling, or other skin abnormalities in the affected areas.
- Hair pull test is positive at the periphery of many of the patches.
- Half of the right eyebrow is missing.
- Nails have pitting.
- Trichoscopy revealed black dots on the scalp and several exclamation mark hairs.
- SALT score 35.

The diagnosis of severe alopecia areata is made. The patient is very worried about his hair loss and is anxious that he is going to lose more hair.



Case 3 Question 1:

Which characteristic of this 29-year-old Chinese man is correlated with a reduced possibility of remission?

- a. Adult onset
- b. Extensive hair loss
- c. Pitting nails
- d. Positive pull test

Rationale

The correct answer is: b) extensive hair loss

- Indicators of remission
 - Alopecia areata does not destroy hair follicles.
 - Spontaneous hair regrowth is possible.
 - In particular, for patients with mild AA, spontaneous remission may be as high as 80% within 1 year of development of patches
 - Spontaneous remission is rare in patients with severe AA, occurring in 2% to 5% of patients
 - The best indicator of remission is the extent of hair loss at diagnosis
 - 14%-25% of patients will progress to alopecia totalis or universalis
 - Relapse rate can be as high as 85%.
 - A less favorable prognosis (lack of remission or increased severity of disease) has been observed with the following:
 - Childhood onset with ophiasis
 - Nail changes
 - Family history of AA
 - Concurrent atopy
 - Concurrent autoimmune disease
 - Long-standing or extensive alopecia

Faulty Commentary

Brett King, MD: Of the answer choices, extensive hair loss is more closely correlated with a reduced possibility of remission. The recent clinical trials in patients with alopecia areata probably highlight this the best and really give us the most concrete data. I think that we have long had an understanding that patients with more severe disease, with more extensive hair loss, probably have a lower rate of spontaneous remission. Even though we may have thought that, every chapter that reviews alopecia areata, everything written about it always says that it is a waxing and waning disorder. But again, recent clinical trials, particularly with severe alopecia areata or patients with 50% to 100% scalp hair loss, very clearly show that the rate of spontaneous remission in patients with this severe alopecia areata is close to zero, ranging from 2% to 8% of patients over 24 to 36 weeks. Really very low. We want to think about that when we're speaking to patients. Because patients will frequently say, "Well, doctor, what if I do nothing?" The answer is if they're sitting there with 80% scalp hair loss, we can say that over the next 9 months, your chances of spontaneously regrowing your hair are very, very low, probably much less than 10%. The data is really important to us in clinical practice.

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Case 3 Background (continued)

The 29-year-old Chinese man returns in 2 months with increasing hair loss. The SALT score is now 55 and the patient wants to discuss his treatment options.

Case 3 Question 2:

Which one of the following medications would be the most appropriate systemic therapy for this patient?

- a. Cyclosporine
- b. Methotrexate
- c. Prednisone taper
- d. Ritlecitinib

Rationale

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The correct answer is: d) ritlecitinib

European Expert Consensus Statement on the Systemic Treatment of Alopecia Areata (2024)

- A SALT score \geq 20 is a general indication for systemic therapy
 - Alopecia Areasta Scale score of moderate to severe
- Wait-and-see approach
 - Regrowth rate in placebo arms of trials involving patients with severe AA is rare (0% to 8%)
 - \circ Wait-and-see approach is not recommended for patients qualifying for systemic therapy

Non-Acute Systemic Treatment of Alopecia Areata





Ritlecitinib

- Efficacy results from the phase 2b-3, randomized, double-blind, controlled ALLEGRO trial in patients aged 12-65
 - У
- % of patients with SALT score ≤20 at 24 weeks
 - Placebo: 2%
 - Ritlecitinib 50 mg: 23% (*P*<0.0001)
- 48-week results
 - 90% sustained SALT<20
 - 48% of patients achieved SALT<20
 - 40% to 50% of patients who had eyebrow/eyelash involvement at baseline saw improvement
- Baricitinib
 - Efficacy from the phase 3, randomized, double-blind, controlled BRAVE-AA1 trial in adults aged 18-65 y
 - % of patients with SALT score ≤20 at 36 weeks
 - Placebo: 6.2%
 - Baricitinib 2 mg: 22.8% (*P*<0.001 vs placebo)
 - Baricitinib 4 mg: 38.8% (*P*<0.001 vs placebo)
 - 52-week results of continued use of baricitinib
 - % of patients with SALT score ≤20 (BRAVE-AA1, BRAVE-AA2 trials, respectively)
 - Baricitinib 2 mg (21.2%, 24.4%)
 - Baricitinib 4 mg (40.9%, 36.8%)
- Deuruxolitinib
 - Efficacy from the phase 3, randomized, double-blind, controlled THRIVE-AA1 trial in adults aged 18-65 y
 - % of patients with SALT score ≤20 at 24 weeks
 - o Placebo: 0.8%
 - Deuruxolitinib 8 mg BID: 29.6% (*P*<0.001)
- Other immune modulators (cyclosporine, methotrexate, and azathioprine)
 - No information from large, randomized, placebo-controlled trials

Faculty Commentary

Brett King, MD: The correct answer is ritlecitinib. And for anybody who thought about methotrexate or cyclosporine or prednisone, we know why we think that. In the world that we are all coming from not very long ago, those were the therapies that we had to treat patients with severe alopecia areata. But now, in a world of ritlecitinib and baricitinib and deuruxolitinib, we have an opportunity for what I call reliably effective therapies. That is medicines that we know that, over the course of 1 to 2 years of treatment of patients with 50% to 100% scalp hair loss, that we're going to help up to 50% of them or more grow their hair back. We do not have any data for cyclosporine, methotrexate or prednisone that says that those medicines have efficacy rivaling the medicines ritlecitinib, baricitinib and deuruxolitinib. Therefore, ritlecitinib is the right answer here.

Natasha Mesinkovska, MD: We tend to focus on *Janus* kinase (JAK) inhibitors for alopecia areata and many of us ask, well what happened with all the old therapies, cyclosporine, methotrexate, azathioprine? My opinion, personally, is even before JAK inhibitors showed their efficacy, the efficacy of all of those was very limited, but the side effects were not. And I think if, in today's climate, some of these medications were to be tested in an attempt to gain approval for alopecia areata, they would definitely not fare well and maybe will be inferior to the JAK inhibitors.



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Case 3 Background (continued)

The 29-year-old Chinese man and his dermatologist discuss starting JAK inhibitor therapy. The clinician reviews the benefits and limitations of JAK inhibitor therapy with the patient.

Case 3 Question 3:

What would be a safety concern with starting a JAK inhibitor in this patient?

- a. Alcohol use
- b. Drug-drug interaction with allopurinol
- c. Hyperkalemia
- d. Smoking history

Rationale

The correct answer is: d) smoking history

- The prescribing information for all 3 JAK inhibitors approved for AA includes several warnings and precautions related to cardiovascular events and malignancies. Consequently, caution should be used in patients with a history of tobacco smoking or who have other cardiovascular or cancer risk factors.
- While there are drug interactions with JAK inhibitors, they do not interact with allopurinol.
- Prior to initiating JAK inhibitor therapy, laboratory evaluation, eg, complete blood count with differential, liver function, and kidney function, is recommended.

Faculty Commentary

Brett King, MD: The answer here is smoking history. And the way we understand that answer is that all JAK inhibitors have a boxed warning and, in that boxed warning, we have cautions regarding malignancy risk and cardiovascular risk, that is MI or stroke. And when we go back to the study that gave us the boxed warning for all JAK inhibitors, that was the ORAL Surveillance study, a study of tofacitinib in older patients with moderate-to-severe rheumatoid arthritis. It was clear—and numerous post hoc analyses of the ORAL Surveillance study have again continued to add data in support of this notion—that current or past



smokers are at greater risk of these, and I want to say this very clearly, rare events. Even in the ORAL Surveillance study, these events were very uncommon. But again, if we were to identify the patients in that study who were driving those events, they were current or past smokers. So here in this case, we want to think about this aspect of the patient's history, and we would want to share that data with the patient so that they could make the best decision that they possibly could for themselves. Also, we might use it as a way to tell a current smoker or to help a current smoker perhaps move away from or to stop smoking, which would just be better for their health in general.

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Case 4: Shared Decision Making

Case 4 Background

A 14-year-old Black female presents with a 3-month history of progressively worsening alopecia of the scalp and eyebrows. She is accompanied by her mother and father.

History of present illness:

- The patient first noticed small patches of hair loss 3 months ago.
- The hair loss has progressed rapidly, with larger patches now visible.
- The patches are nonpainful and nonitchy.
- No associated redness, scaling, or other skin changes.
- No history of similar episodes in the past.

Medical history:

- No significant past medical history.
- No known allergies.
- No history of autoimmune diseases.

Family history:

- No family history of alopecia areata.
- Mother has rheumatoid arthritis.

Social history:

- Lives with parents and 2 siblings.
- Attends middle school and is active in sports.
- Has recently missed school and other events due to hair loss.

Physical examination:

- Multiple well-demarcated, round patches of hair loss on the scalp.
- SALT score of 55.



- Trichoscopy shows several exclamation mark hairs and signs of regrowth with short, thin hairs.
- No erythema, scaling, or other skin abnormalities in the affected areas.
- Hair pull test is positive at the periphery of the patches.
- Eyebrows show patches of hair loss.
- Nails are normal without pitting or other abnormalities.
- Patient is tearful when describing the hair loss and missing social functions.

Case 4 Question 1:

Which medication below is most appropriate for this patient?

- a. Abrocitinib 100 mg PO daily
- b. Baricitinib 2 mg PO daily
- c. Deuruxolitinib 8 mg PO twice daily

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d. Ritlecitinib 50 mg PO daily

Rationale

Correct answer is: d) ritlecitinib

- JAK inhibitor use
 - Ritlecitinib is approved for the treatment of severe alopecia areata in adults and adolescents 12 years of age and older
 - 15% of the population in the ALLEGRO trial were adolescents
 - Consistent results observed between the adolescent subgroup and the adult subgroup at week 24
 - Baricitinib and deuruxolitinib are approved for the treatment of severe alopecia areata in adults only.
 - Abrocitinib is not approved for alopecia areata.

Faculty Commentary

Natasha Mesinkovska, MD: When a young patient with alopecia areata comes to the office, we have to be aware of the life stages that they're going through. In this case, we have a young adolescent who has rapid hair loss, and she has lost more than half the hair on her skull. That is what Severity of Alopecia Tool (SALT) 55 pertains to, severity of alopecia, or how much hair you've lost. What are we going to do? I think the instinct in us, as a provider, is to do as little as we can and maybe try things topically, maybe try injections. But I think this is a time when we have to have the discussion because there's no algorithm that you need to fail in order to get to the JAK inhibitors in this case. If the patient is facing rapid progression, totalis or universalis is around the corner, then you have to introduce the idea of the JAK inhibitors. The only JAK inhibitor that is approved in adolescents, adults from 12 to 18, is ritlecitinib. It comes as 1 dose, it's a small capsule, 50 mg daily, that is very easy to prescribe and take. That is what I have to reiterate with you is to start the discussion and initiate the treatment.

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Case 4 Background (continued)

The dermatologist discusses starting a JAK inhibitor with the 14-year-old girl and her parents.

Case 4 Question 2:

Which one of the following laboratory measurements should be done in this patient before starting therapy with a JAK inhibitor and routinely during therapy??

- a. Blood creatine kinase
- b. Blood electrolytes
- c. Blood glucose
- d. Complete blood count with leukocyte differential

Rationale

The correct answer is: d) complete blood count with differential

- Baseline lab tests
 - o CBC with differential, liver and kidney function tests
 - Repeat at 1 month, 3 months, and then as needed depending on prior results and risk factors
 - Test for tuberculosis
 - Hepatitis B and C panel
 - Lipid panel (not necessary for ritlecitinib)
 - Repeat at 3 months and then as needed depending on prior results and risk factors

 Pregnancy test 				
	Initial screening	1 Month	3 months	Every 3-6 Months*
	Complete blood count with differential			
	Liver and kidney function	Liver transaminases	Liver transaminases	Liver transaminases
	tests	Kidney function tests	Kidney function tests	Kidney function tests
	Tuberculosis test		Lipid panel	
	Hepatitis B & C panel			
	Lipid panel			
	Pregnancy test (if applicable)			

*Depending on prior laboratory results and patient risk factors

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Faculty Commentary

Natasha Mesinkovska, MD: When we initiate a patient on a JAK inhibitor for alopecia areata, we have to ensure that certain parameters are followed. JAK inhibitors have a boxed warning for increased risk of infections, malignancies and thromboembolic events that we have to respect and watch for. What are the things that we typically check for JAK inhibitors prior to initiation of therapy? We check a complete blood count, we check that the electrolytes are normal, and we check for certain types of infections such as tuberculosis, hepatitis B and hepatitis C. We check lipids, depending on what type of JAK inhibitor we initiate. Those are the ones that we monitor either before or after. How do you follow up on these patients and how frequently do you check labs? This is a question that a lot of providers will ask, and it depends on which medication we are prescribing. Usually, for



ritlecitinib, at 4 weeks, we check the complete blood count. For medications, such as baricitinib for example, we check lipids at 12 weeks. Whenever you're not sure, you always go to the providers' site to check for the recommended laboratory frequencies.

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Case 4 Background (continued)

The 14-year-old Black female and her parents return in 12 weeks. The patient shows a 50% improvement in scalp coverage. She still does not feel comfortable at school, but has started to participate in sports again.

Case 4 Question 3:

Which of the following referrals would be the most appropriate recommendation for the patient?

- a. Behavioral health
- b. Cardiovascular
- c. Endocrine
- d. Rheumatology

Rationale

The correct answer is: a) behavioral health

- Compared to the general pediatric population, patients with AA have higher rates of the following:
 - Separation anxiety
 - Generalized anxiety disorder
 - Social phobia
 - Major depressive disorder
 - AA lowers self-esteem and is manifested negatively in school, social life, and at home
- Higher severity of disease is correlated with a lower quality-of-life (QOL) for the parents
- Clinicians may recommend the following:
 - AA support groups
 - Clinical psychologists
 - Educational psychologists
 - Custom-made wigs
 - Not studied in pediatric patients, but have been shown to improve QOL in adults

Faculty Commentary

Natasha Mesinkovska, MD: It's just hair. How many times have we heard that? Alopecia areata is just hair. Well, actually it is a medical disease. It's a medical disease with consequences, not only when it comes from an inflammatory/immunologic perspective, but also as to the way one views themselves and the way one is viewed by the environment where they live. The psychosocial impact of this condition is tremendous.

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Particularly in young patients with alopecia areata, there is a high rate of anxiety conditions and even social phobias. Who do we turn to? We can always refer them to therapists, but also, for any patient, young and adult, there are support groups out there, there are clinical and educational psychologists that can help them navigate the disease process better.

Brett King, MD: It's really important that we not try to fix problems that we cannot fix, that somebody else can do a better job with. And our patients with alopecia areata, as we've discussed, often suffer depression or anxiety as a result of their disease or they suffer an exacerbation of their underlying depression or anxiety as a result of developing alopecia areata. And let's acknowledge the awful experience that it often is. Let's not say, "Oh well, at least you're not sick!" Let's acknowledge that it is an awful experience for many patients and let's not be afraid to say, "Have you spoken to a therapist, have you spoken to your primary care doctor about the way you are feeling? Maybe speaking to somebody might make you feel better. Maybe you need medicine to help you get through this sort of situational depression or situational anxiety." Again, let's not insist that we have the whole answer and let's take advantage of our colleagues to help us manage these sometimes-challenging situations with patients.

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