Non-scarring alopecia

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Disclosures

• Consultant – Sagimet Biosciences, Pfizer Inc, Radicle Science, Pelage Pharmaceuticals
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• Speakers Bureau – Pfizer Inc.

Off-label use of medication will be discussed
Objectives

- Define non-scarring alopecia
  - Define normal hair
- Diagnosis of non-scarring alopecia
- Cases/management
- Treatment highlights
  - Minoxidil – Topical vs. Oral
  - 5-alpha reductase inhibitors in men and women
  - JAK inhibitors for alopecia areata
What’s normal about hair?

• Grows about 1 cm a month
• 10% in telogen (resting phase)
• 100-150,000 hairs per head
  • Blondes have more, red heads have less
  • Those of Asian and African descent also have thicker hair and less density
• About 100-200 hairs a day may be lost normally
  • Substantial interindividual and seasonal variation
  • If it’s not normal for the patient, then I accept that it is not normal
Sinclair Hair Shedding Scale

40% of women not complaining of hair loss rated excessive shedding with washing/hair styling; 60% of women with FPHL reported excess shedding


Normal hair cycle

1. Permanent hair removal can only occur during this active growth stage.
2. Club hair transitions upwards toward skin pore and dermal papilla begins to separate from follicle.
3. Dermal papilla fully separates from follicle.
4. Dermal papilla moves upwards to meet hair follicle once again and hair matrix begins to form new hair.
7-year-old girl with short anagen hair

Short anagen hair  Short anagen hair  Short anagen hair
Non-scarring alopecia

**Diffuse**
- Androgenetic alopecia
- Telogen effluvium
- Senescent alopecia
- Permanent chemotherapy induced alopecia
- Diffuse alopecia areata
- Trichotillomania sometimes
- Non-scarring alopecia associated with systemic lupus erythematosus

**Patchy**
- Alopecia areata
- Trichotillomania
- Post-operative (pressure-induced) alopecia
- Temporal triangular alopecia
- Anagen effluvium
- Non-scarring alopecia associated with systemic lupus erythematosus
- Early traction alopecia
- Early tinea capitis
- Early discoid lupus
Number of Patients by Diagnosis

Between 7/19/2022 and 7/19/2023

Telogen effluvium (ICD-10-CM: L65.0): 155
Alopecia areata (ICD-10-CM: L63.*): 198
Androgenetic alopecia (ICD-10-CM: L64.*): 685
Non-scarring hair loss, unspecified (ICD-10-CM: L65.9): 443
Approach to the patient
The hair loss appointment (dreaded by many)

- Every minute counts
- Everyone has a long story
- A questionnaire may help, but may also encourage the long story
- A little empathy goes a long way
- Physical exam is important, look closely!
Diagnosing alopecia

• History and physical
  
  • Timing/duration, presence of increased shedding, pattern of loss, symptoms
  
  • Scarring or non-scarring – dermoscopy helps
  
  • Miniaturized hairs, exclamation point hairs, scale, erythema, regrowth
  
  • Hair pull test – 2 or more throughout scalp likely abnormal, regardless of last wash *
  
  • Take photos **

• Laboratory evaluation – I don't always check
  
  • CBC, ferritin (>40)***, TSH; sometimes testosterone (free and total), DHEA-S, prolactin
  
  • I typically do not order ANA unless other symptoms or family history

• Histopathology (often at patient request)
  
  • Two 4mm punch biopsies, one for horizontal sectioning and one for vertical sectioning.

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Cases
Case 1

• 65 year old woman complains of 15 years of thinning hair especially over the crown of her scalp. There may be occasional pruritus, no pain or burning. There is no appreciable increase in shedding.
Androgenetic alopecia

- Very common – may be considered normal variant, especially in men.
- In women, somewhat controversial, but one could consider three categories:
  - Puberty to age 40 = androgenetic alopecia, more likely androgen-mediated
  - ~Age 40-60 = female pattern hair loss, less clearly androgen-mediated, though often perimenopausal
  - Over age 60 = senescent alopecia, not likely androgen-mediated
- May be important in determining treatment options
- All show similar histopathology
Norwood-Hamilton classification


Pathophysiology

Normal

Rapid miniaturization over one cycle

Progressive miniaturization over several cycles
Case 2

- 31-year-old woman presents with 2-3 weeks of excessive hair loss. “Clumps” of hair are noted by the patient. She has mild burning of her scalp.
- She got married 4 months ago, but has been trying to get pregnant for 10 months with fertility workup and IUI (intrauterine insemination), but no hormones. 6 months ago, she had surgery for a septate uterus. She also had COVID-19 infection 3 months ago.
Telogen effluvium (acute)

- premature conversion of anagen hairs to telogen; or following prolonged anagen
- surgery, parturition, fever, drugs, dieting, or traction; primary scalp problem (i.e., psoriasis)
- Shedding occurs 3-5 months after the event, though sometimes as soon as a few weeks
- Shedding should last 3-6 months and then visible regrowth/recovery may take 3-6 months or more
- Rx: treat underlying problem, topical minoxidil, laser comb, or simply monitor
### DRUG-INDUCED ALOPECIA

| Telogen phase | Anticoagulants: heparin > warfarin  
|              | Anticonvulsants: carbamazepine, valproic acid, phenytoin  
|              | Antidepressants: imipramine, desipramine, maprotiline, fluoxetine  
|              | Antihypertensive agents:  
|              | β-blockers: acebutolol, propranolol  
|              | ACE inhibitors: captopril, enalapril  
|              | Diuretics: spironolactone  
|              | Antimicrobials: gentamicin, thiamphenicol, fluconazole  
|              | Antithyroid drugs: carbimazole, thiouracils  
|              | Colchicine  
|              | Interferons  
|              | Lipid-lowering agents: clofibrate, cholestryamine  
|              | Lithium  
|              | NSAIDs: piroxicam, naproxen, indomethacin, ibuprofen  
|              | Oral contraceptives  
|              | Retinoids  
|              | Others: allopurinol, cimetidine, L-dopa, amphetamines, pyridostigmine, bromocriptine  

| Anagen phase | Antineoplastic agents (see Table 22.8)  
|             | Others: arsenic, bismuth, gold, thallium

Table 22.7 Drug-induced alopecia. ACE, angiotensin-converting enzyme.

From Bologna, Jorizzo & Rapini: Dermatology 2e. © 2008 Elsevier, Ltd.
Case 3

- 54-year-old woman with 10 years of increased shedding of hair with “bald spots”. She is on no medications.
- She reports sensitivity of the scalp and redness.
- The shedding is constant.

Chronic telogen effluvium

- diffuse generalized shedding with thinning of scalp hair; longer than 6 months
- 30–60 years of age, mostly women
- hair loss starts abruptly
- fluctuating course and diffuse thinning of the hair all over the scalp with bitemporal and vertex prominence
- Often no discernible cause
- Terminal: vellus hair ratio = 8:1 or more
- may respond to minoxidil
- May be a precursor to androgenetic alopecia/FPHL/senescent alopecia
Treatment for diffuse thinning

- Treat scalp problems (i.e., seborrheic dermatitis)
  - Zinc pyrithione shampoo or other antiseborrheic shampoos
  - Ketoconazole shampoo (1% OTC, 2% Rx)
  - Clobetasol shampoo (helpful if concern for other dx); other topical steroids
- Hair growth promoters
  - Topical (2% (women's) or 5% solution (men's) or foam (men's or women's)) or low dose oral minoxidil (0.25 mg to 2.5 mg daily)
  - Topical bimatoprost or latanoprost
  - Laser comb, band, or cap
- If applicable, antiandrogen therapy
  - Spironolactone (young women)
  - Finasteride, dutasteride (postmenopausal)
  - Flutamide, bicalutamide (rarely, postmenopausal)
- Microneedling, platelet rich plasma therapy
- Hair restoration surgery – select cases
32 year old female
Spironolactone 150 mg daily
Minoxidil 0.625 mg daily
Ketoconazole shampoo 2% three times a week
On drospirenone-ethinyl estradiol OCP
Case 4

• 45-year-old woman with 6 months of hair loss “in patches” with no pain.
• She was on vacation when it started.
• No medications, no other medical problems.
• No body hair loss noted.
Alopecia areata

- Non-scarring patchy alopecia
- Autoimmune cell-mediated process thought to be due to loss of immune privilege in the anagen hair bulb
- Genetic polymorphisms have been identified
- Path: “swarm of bees” (lymphocytes) around the hair bulb; the key, however, is markedly increased telogen/catagen
  - Anagen to telogen/catagen ratio nearly 1:1;
  - normal is 10:1


### Table II. Alopecia Areata Scale

<table>
<thead>
<tr>
<th>Severity</th>
<th>Extent of scalp hair loss</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mild AA</td>
<td>20% or less scalp hair loss</td>
</tr>
<tr>
<td>Moderate AA</td>
<td>21%-49% scalp hair loss</td>
</tr>
<tr>
<td>Severe AA</td>
<td>50%-100% scalp hair loss</td>
</tr>
</tbody>
</table>

If mild or moderate, increase AA severity 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
- Diffuse (multifocal) positive hair pull test consistent with rapidly progressive AA

AA, Alopecia areata.
Therapeutic ladder for alopecia areata; depends on severity

• Topical or intralesional corticosteroids – for mild disease
• Topical immunotherapy (DPCP, squaric acid) - for mod-severe
• Topical or oral minoxidil – for any severity
• Topical anthralin cream – mod-severe
• Systemic corticosteroids – severe or rapidly progressive
• Excimer laser - localized
• Systemic immunosuppressants
  • JAK inhibitors***, cyclosporine, methotrexate
• Other options, less evidence
  • Fexofenadine, platelet rich plasma therapy, simvastatin-ezetimibe
Topical corticosteroids and minoxidil foam
Max dose oral tofacitinib
5 mg twice daily
Patchy alopecia
recurred within 2 weeks
of reducing dose
Tofacitinib 5 mg twice daily
Baricitinib 4 mg daily x 1 year

Baricitinib 4 mg daily x 6 months
Case 5

- 43 year old woman with 5 years of hair loss, increased shedding in shower, overall thinner, but also in patches
- Initially denies itch, but then states that sometimes there is itching and she “removes it”
- Exam reveals diffuse thinning and miniaturized hairs, but also broken off hairs of different lengths in a somewhat patchy distribution
Trichotillomania

• DSM-5 diagnosis: Obsessive Compulsive spectrum, body focused repetitive behavior
  • (1) recurrent pulling out of one's hair, resulting in hair loss
  • (2) repeated attempts to decrease or stop the hair pulling
  • (3) significant distress or impaired functioning related to the hair pulling
  • (4) no underlying medical condition or other mental disorder that explains the hair loss/pulling

• Very common; characterize as a “habit”
• Refer to the TLC foundation (www.bfrb.org)
• Behavior modification therapy (habit reversal, cognitive behavior therapy)
• N-acetylcysteine (1200-2400 mg/day), olanzapine, SSRIs
Treatment highlights

• Minoxidil – topical vs. oral
• 5-alpha reductase inhibitors in men and women
• JAK inhibitors for AA
Minoxidil

- Topical minoxidil still with best efficacy and safety data
- Small RCT showed non-significant benefit of 1mg daily over 5% solution once daily (p=0.09; n=52)
- 10-40 mg for hypertension – 80% hypertrichosis
  - Postural hypotension, fluid retention, tachycardia, pericarditis, and nausea
- 0.25-5 mg daily for hair loss – 20% with any AE
  - (out of 1404 pts, multicenter analysis) 15% hypertrichosis
  - Lightheadedness, fluid retention/leg edema, tachycardia, headache, periorbital edema, and insomnia


5 alpha reductase inhibitors

• Finasteride 1 mg daily FDA approved for men with AGA
• Dutasteride 0.5 mg daily approved in Japan, South Korea for AGA in men
• Generally more effective than topical or oral minoxidil in male AGA*
• Adverse effects: sexual dysfunction, gynecomastia, depression, effects on fertility
• Lower risk of morbidity in prostate cancer, no difference in mortality**
• Dutasteride is present in the semen, finasteride can be absorbed through skin


36 year old male
Dutasteride 0.5 mg daily
Ketoconazole 2% shampoo every other day
Platelet rich plasma therapy
5 alpha reductase inhibitors in women

• Off-label use in women
• Finasteride 1 mg daily not effective in post menopausal women*
• Higher dose finasteride (2.5 mg or 5 mg daily) and/or dutasteride may be effective in women**
• No clear link with breast cancer in men or women


### JAK inhibitors for alopecia areata

<table>
<thead>
<tr>
<th>Medicine</th>
<th>Dosage</th>
<th>Age</th>
<th>Indications</th>
<th>JAK Targets</th>
</tr>
</thead>
<tbody>
<tr>
<td>Baricitinib*</td>
<td>2-4 mg daily</td>
<td>Age 18 and over</td>
<td>AA and RA</td>
<td>JAK 1 and 2</td>
</tr>
<tr>
<td>Ritlecitinib*</td>
<td>50 mg daily</td>
<td>Age 12 and over</td>
<td>AA</td>
<td>JAK3 and TEC</td>
</tr>
<tr>
<td>Tofacitinib</td>
<td>5 mg twice daily, 11 mg XR daily</td>
<td>Age 2 and over</td>
<td>JIA, RA, PsA, UC</td>
<td>JAK1, 3; also 2</td>
</tr>
<tr>
<td>Ruxolitinib**</td>
<td>topical</td>
<td>Age 12 and over</td>
<td>AD, vitiligo</td>
<td>JAK1, 2; also TYK2</td>
</tr>
<tr>
<td>Upadacitinib</td>
<td>15-30 mg daily</td>
<td>Age 12 and over</td>
<td>AD, AS, UC, RA AD</td>
<td>JAK1, 2; also 2, TYK2</td>
</tr>
<tr>
<td>Abrocitinib</td>
<td>100-200 mg daily</td>
<td>Age 12 and over</td>
<td>AD</td>
<td>JAK1; also 2, TYK2</td>
</tr>
</tbody>
</table>
Baricitinib

• First approved drug for alopecia areata (6/2022)
• JAK1 and JAK2 inhibitor
• For adults with severe alopecia areata
• 2 mg or 4 mg daily
• Adverse events – upper respiratory tract infection, headache, nasopharyngitis, acne, urinary tract infection, elevated serum creatine kinase
• Serious adverse events in 2.1% (4mg) and 2.2% (2mg); 1 pt had MI

Ritlecitinib

• 50 mg daily approved 6/2023; available as of 8/2023
• For ages 12 years and older
• JAK3 and TEC inhibitor
• Most common adverse events – headache, nasopharyngitis, nausea, upper respiratory infection, acne
• Serious adverse events in 2-3% (all groups); 1 with PE

SERIOUS INFECTIONS

Patients treated with OLUMIANT are at risk for developing serious infections that may lead to hospitalization or death (see Warnings and Precautions (5.1) and Adverse Reactions (6.1)). Most patients with rheumatoid arthritis who developed these infections were taking concomitant immunosuppressants such as methotrexate or corticosteroids.

If a serious infection develops, interrupt OLUMIANT until the infection is controlled.

Reported infections include:

- Active tuberculosis, which may present with pulmonary or extrapulmonary disease. OLUMIANT should not be given to patients with active tuberculosis. Patients, except those with COVID-19, should be tested for latent tuberculosis before initiating OLUMIANT and during therapy. If positive, start treatment for latent infection prior to OLUMIANT use.
- Invasive fungal infections, including candidiasis and pneumocystosis. Patients with invasive fungal infections may present with disseminated, rather than localized, disease.
- Bacterial, viral, and other infections due to opportunistic pathogens.

The risks and benefits of treatment with OLUMIANT should be carefully considered prior to initiating therapy in patients with chronic or recurrent infection.

Patients should be closely monitored for the development of signs and symptoms of infection during and after treatment with OLUMIANT including the possible development of tuberculosis in patients who tested negative for latent tuberculosis infection prior to initiating therapy [see Warnings and Precautions (5.1)].

MORTALITY

In a large, randomized, postmarketing safety study in rheumatoid arthritis (RA) patients 50 years of age and older with at least one cardiovascular risk factor comparing another Janus kinase (JAK) inhibitor to tumor necrosis factor (TNF) blockers, a higher rate of all-cause mortality, including sudden cardiovascular death, was observed with the JAK inhibitor [see Warnings and Precautions (5.2)].

MALIGNANCIES

Lymphoma and other malignancies have been observed in patients treated with OLUMIANT. In RA patients treated with another JAK inhibitor, a higher rate of malignancies (excluding non-melanoma skin cancer (NMSC)) was observed when compared with TNF blockers. Patients who are current or past smokers are at additional increased risk [see Warnings and Precautions (5.3)].

MAJOR ADVERSE CARDIOVASCULAR EVENTS

In RA patients 50 years of age and older with at least one cardiovascular risk factor treated with another JAK inhibitor, a higher rate of major adverse cardiovascular events (MACE) (defined as cardiovascular death, myocardial infarction, and stroke) was observed when compared with TNF blockers. Patients who are current or past smokers are at additional increased risk. Discontinue OLUMIANT in patients who have experienced a myocardial infarction or stroke [see Warnings and Precautions (5.4)].

THROMBOSIS

Thrombosis, including deep venous thrombosis and pulmonary embolism, has been observed at an increased incidence in patients treated with OLUMIANT compared to placebo. In addition, there were cases of arterial thrombosis. Many of these adverse events were serious and some resulted in death. In RA patients 50 years of age and older with at least one cardiovascular risk factor treated with another JAK inhibitor, a higher rate of thrombosis was observed when compared with TNF blockers. Avoid OLUMIANT in patients at risk. Patients with symptoms of thrombosis should discontinue OLUMIANT and be promptly evaluated. [see Warnings and Precautions (5.5)].
Pearls and summary

• Clinical exam – use your eyes and your dermatoscope
• Treat the scalp – we are dermatologists
• Manage expectations
• Topical or oral minoxidil can be used for any type of hair loss
• Traditional and conservative treatments can be effective, but newer treatments can be used safely if needed
• Much research ongoing, but drug vehicle will be key
Thank you!

Feel free to email with questions: cgoh@mednet.ucla.edu

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