How I Treat Alopecia in Patients with Cancer

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INTRODUCTION

Hair loss in patients with cancer can have a profound impact on quality of life. In a study of patients with breast and gynecologic cancers, 50% of patients with alopecia reported that it limited their ability to pursue leisure activities, and 14% reported they would consider rejecting curative cancer therapies associated with alopecia.[1] In this review, we discuss the differential diagnosis, clinic features, and treatment considerations for addressing alopecia in patients with cancer.

EVALUATION

History inquiry involves the onset of hair loss, areas of scalp involvement, associated inflammatory symptoms, widespread involvement of facial or body hair, nail changes, medication history and other triggers. Physical examination investigates density of hair, thinning pattern and inflammatory changes. History taking and physical exams are summarized in Table 1.. While a scalp biopsy is not warranted to diagnose most forms of cancer treatment-related alopecia, it should be considered to rule-out an inflammatory alopecia if signs of inflammation are present.

<table>
<tr><th>History</th><th>Physical Exam</th></tr>
<tr><td rowspan="3">Onset
Areas of the scalp involved
Type of hair change (shedding or thinning)
Associated scalp symptoms (itch, pain, flaking)
Involvement of the eyebrows, eyelashes, or body hair
Presence of nail changes
Medication history
History of other triggers, including recent surgeries or hospitalizations, psychosocial stress, and history of hypothyroidism or iron deficiency</td><td>Density of hair
Pattern of thinning (focal, diffuse, androgenetic)
Signs of inflammation (erythema or scaling)
Eyebrows, eyelashes, nails</td></tr>
<tr><td>Trichoscopic Exam</td></tr>
<tr><td>Miniaturization
Loss of follicular ostia
Signs of inflammation</td></tr>
</table>

Table 1. *Elements of history and physical exam for cancer treatment-induced alopecia.*

DIFFERENTIAL DIAGNOSIS AND TREATMENT

Telogen Effluvium

Telogen effluvium (TE) is a form of nonscarring alopecia marked by widespread hair shedding without accompanying scalp symptoms. It is a reactive process triggered by metabolic stress, hormonal changes, or medications. Particular triggers to consider in patients with cancer are surgeries, starting or stopping hormonal mediations (for example, discontinuing contraceptives with a new diagnosis of breast cancer), and psychosocial stress. A pull test of 40 hairs, yielding at least four hairs, is consistent with TE. In instances where there are suspicions of underlying hypothyroidism or iron deficiency, laboratory testing may be performed.

Acute TE follows a self-limited course, with treatment focusing on correcting the underlying cause. Additionally, topical minoxidil can be employed by patients for a period of 6-12 months to aid in the restoration of hair density.[2]

Chemotherapy-Induced Alopecia

Alopecia occurs in approximately 65% of patients who receive chemotherapy, including alkylating agents, anthracyclines, antimetabolites, vinca alkaloids, and taxanes.[3] Chemotherapy-Induced Alopecia (CIA) is a subtype of anagen effluvium; hair in the anagen phase is sensitive to chemotherapeutic agents because it rapidly proliferates.

On examination, CIA presents as widespread, rapid shedding. Patients experience patchy or diffuse alopecia, predominately in the frontal or temporo-occipital hair lines, where there is increased friction from sleep and head coverings.[4] The eyelashes and eyebrows may be involved, especially in patients receiving taxanes.[4] Trichoscopic features of CIA include

the presence of broken hairs and scattered black dots.[4]

CIA can progress to complete alopecia within a few months of onset.[3-5] After the anti-cancer therapy is discontinued, CIA is typically reversible within 2 to 6 months,[3-5] though it may be persistent or permanent. We reassure patients with CIA that they are likely to regrow their hair, and we encourage the use of topical minoxidil in the first 6 months following chemotherapy to speed recovery.[6]

Treatment options for CIA include topical minoxidil 5% foam or solution and oral minoxidil 1.25mg, with dose increases as tolerated. Minoxidil works to promote hair regrowth by causing vasodilation and polarization of smooth muscle cells on the scalp. Oral minoxidil can exacerbate underlying health conditions, and patients should be screened for personal histories of congestive heart failure, which is a side effect of doxorubicin, as well as hypotension. We counsel on the risks of orthostasis, peripheral edema, headaches, and hypertrichosis, as well as the rare side effects of pleural and pericardial effusion with oral minoxidil. Though platelet-rich plasma (PRP) injections is a treatment modality for androgenetic alopecia, to date no trials have studied its efficacy in CIA.

Endocrine Therapy-Induced Alopecia

Endocrine therapy-induced alopecia (EIA) secondary to tamoxifen or aromatase inhibitors may lead to early cessation of therapy in women undergoing treatment. EIA typically manifests after 1-2 years on endocrine therapy, mirroring the clinical presentation of androgenic alopecia (AGA) by affecting the frontoparietal and vertex regions of the scalp.[4] Trichoscopic features also ressemble AGA with miniaturization.

In addressing EIA, a variety of treatments exists, with topical minoxidil 5% or oral minoxidil 1.25 mg favored as first-line therapies suitable for the continuous duration of endocrine therapy.[7-8] Encouraging results from smaller studies also highlight the efficacy of oral/topical dutasteride and oral/topical spironolactone.[8-9] Importantly, there is a theoretical concern that oral spironolactone or 5-α reductase inhibitors may increase hormonal stimulation of estrogen receptor-positive tumors; more extensive research is needed to fully assess potential adverse effects. For this reason, we limit use of these medications to topical applications in patients with EIA. A pilot study on the effectiveness of PRP for the treatment of EIA is currently underway,[9] and we consider PRP when patients cannot tolerate minoxidil or when patients plateau. Notably, patients on combined CDK4/6 inhibitor + endocrine therapy regimens demonstrated more recalcitrant EIA compared to those receiving monotherapy, necessitating oral minoxidil, often a doses of 2.5 to 5 mg, for optimal management.[10] A summary of cancer-treatment induced alopecia is found in Table 2.

Alopecia Type	**Telogen Effluvium**	**Chemotherapy-Induced Alopecia (CIA)**	**Endocrine Therapy-Induced Alopecia (EIA)**
Causes	• Surgeries • Medication changes • Psychosocial stressors • Hormonal imbalances	• Cytotoxic agents, in particular: alkylating agents, anthracyclines, antimetabolites, vinca alkaloids, and taxanes	• Aromatase inhibitors • Selective estrogen modulators
Diagnostic Features	• Positive Pull Test of 3+ hairs with 40 hairs pulled	• Patchy areas of alopecia, especially in the frontal and temporo-occipital hairlines • May involve the majority or all of the scalp • Eyebrow and eyelash involvement	• Similar to androgenetic alopecia with areas of alopecia in the frontoparietal and vertex scalp

Trichoscopy Findings	• No variation in hair shaft diameters • May see short regrowing hairs with a tapered distal end	• Broken hairs • Black dots	• Hair follicle miniaturization
Treatment Options	• Topical 5% minoxidil for 6-12 months or until hair has regrown • Correction of underlying cause • Permissible to not use hair regrowth medications, as hair will regrow once underlying cause is removed	• Topical 5% minoxidil, especially in the first 6 months after chemotherapy • Oral minoxidil for patients who do not have contraindications* • Protein-Rich Plasma (PRP), though has not been studied in patients with CIA	• Topical 5% minoxidil or oral minoxidil during treatment • Can also consider topical dutasteride and topical spironolactone • Oral spironolactone is typically avoided in patients with a history of breast cancer • A study of the use of Protein-Rich Plasma (PRP) for the management of EIA is currently underway

*Contraindications of oral minoxidil include congestive heart failure and hypotension.

Table 2. *Summary of cancer-treatment induced alopecia*.

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