60-Year-Old-Female with Hair Loss After Treatment for Reactive Lymphoid Hyperplasia

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Abstract

Radiation therapy, both for treatment and diagnosis, is becoming increasingly prevalent in medical practice. Alopecia is a potential side effect that warrants substantial consideration, with many patients claiming this as the most distressing aspect of their procedure, and some even stating they would forgo curative treatment due to potential alopecia. Hair loss is typically localized to the area of treatment and occurs in a dose-dependent fashion a few weeks after exposure to radiation. In addition to the cumulative dose of radiation that a patient receives, severity of hair loss may also be increased by the method of radiation delivery, patient-related factors such as smoking, and the use of certain antineoplastic agents. Diagnosis is based on clinical presentation and a history of radiation exposure, with dermoscopy findings for lower doses being similar to that of alopecia areata. Although most cases will spontaneously resolve within 6 months, prevention and treatment options do exist for refractory cases of alopecia. Newer treatment delivery methods that reduce off-target radiation, preventative therapies, topical medications, injections, surgery, and transplantation have all been used with some success. Of note, scalp cooling has not been shown to be an effective prevention strategy in alopecia due to radiation.

Keywords

Radiation · Radiotherapy · Alopecia · Scalp cooling · Minoxidil

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S. C. Trotter, S. Sampath (eds.), *Clinical Cases in Alopecia*, Clinical Cases in Dermatology, https://doi.org/10.1007/978-3-031-15820-9_19

Fig. 19.1 Hypopigmented patches with scarring alopecia present on the frontal scalp. Note the presumed new areas of reactive lymphoid hyperplasia in her eyebrows

A 60-year-old female reported hair loss after her scalp was treated for reactive lymphoid hyperplasia about 5 years ago. She stated that after her treatment ended, she had a rash on the scalp for about 3 weeks that then resolved. The area healed with pigmentation changes and her hair did not grow back. Her eyelashes were not affected by treatment but she has new lesions in her eyebrows of about 6 months duration.

On physical examination, there is complete hair loss of the central and frontal scalp. There are areas of hypopigmentation and hyperpigmentation mixed with pink and white macules and plaques. Of note, there are indurated, pink plaques of the eyebrows, consistent with new areas of reactive lymphoid hyperplasia. The eyelashes are intact (Fig. 19.1). The fingernails were normal in appearance.

Based on the clinical case description, what is the most likely cause of her alopecia?

1. Intralesional corticosteroids
2. Topical imiquimod
3. Intralesional methotrexate
4. Radiation

Diagnosis

Radiation

Discussion

Radiotherapy is becoming increasingly prevalent, with over 50% of cancer patients eventually receiving some form of radiation treatment [1]. Patients also receive radiation as part of fluoroscopic procedures, such as cerebral angiography, which

can have similar adverse event profiles [2]. Although alopecia occurs less frequently after radiation exposure than after chemotherapy, its effect on a patient's quality of life can be profound [3]. In one study, almost 20% of respondents said that alopecia was the most distressing side effect of their radiation treatment, and over 10% stated they would reject curative radiation treatment if it was associated with alopecia [4].

Alopecia after radiation follows a dose-response pattern and typically begins after cumulative exposures of 2 gray (Gy) or more [5]. Initially, the hair loss is that of anagen effluvium, in which damage to actively dividing matrix cells in the anagen follicles causes shedding of dystrophic hairs [6]. At lower doses, hair loss is expected to begin 1–3 weeks after exposure and spontaneously resolve within 2–6 months. However, severe, cicatricial alopecia can result from higher dose-exposures, with a 50% probability of toxicity found to be around 43 Gy [7]. This dose may be lower in pediatric patients, with a small study showing permanent radiation-induced alopecia resulting from doses as low as 21–30 Gy [8].

The mechanism of this damage is complex, involving an inflammatory cascade triggered by irradiated skin and endothelial cells [9]. In addition to the total exposure and type of radiotherapy used (proton versus photon), the severity of hair loss can be increased by other patient-related factors such as smoking, poor nutrition, autoimmune conditions, and the use of certain antineoplastic agents [2]. Ultimately, this can result in permanent damage to epithelial stem cells in the bulge region and fibrosis of the affected area [10].

Diagnosis of alopecia due to radiation is typically based on clinical presentation (well-demarcated areas of alopecia localized to the areas of radiation treatment, typically without inflammation) and a history of exposure to radiation in the past month [2]. Dermoscopic findings at lower radiation doses are similar to those of alopecia areata, with yellow and black dots, short vellus hairs, broken hair, coiled hair, and white dots being common [6]. At higher doses associated with cicatricial alopecia, dermoscopy will show decreased hair density, white patches, and the absence of follicular openings [10].

Treatment

As alopecia can be such a concerning side effect of treatment, it is important to counsel patients on the potential timing of their hair loss and that most cases will spontaneously resolve. Additionally, management strategies do exist for radiotherapy alopecia. Some of these include preventative therapies, topical medications, injections, and surgery. The way the radiation treatment itself is delivered can also have an impact. To reduce off-target radiation and spare healthy hair, newer treatment planning strategies such as intensity modulated radiotherapy and volumetric-arc therapy (both of which employ linear accelerators and precision treatment planning to treat tumors while minimizing exposure of the scalp) can be employed [10]. Scalp cooling, which may have utility in some other conditions, has not been shown to be preventative for alopecia due to radiation [11].

Preventative therapies such as nitroxides or prostaglandin E2 prior to radiotherapy have been shown to be possibly preventative for alopecia [6]. Topical silymarin (an extract from milk thistle), subcutaneous amifostine, and oral pentoxifylline are other agents that have been studied for prevention [9]. All of these medications have antioxidant properties and are theorized to improve blood flow and inhibit fibroblast proliferation at the area of treatment. Cholecalciferol (vitamin D_3), which has some evidence for potentially regulating gene transcription and increasing the expression of keratins, appears to be preventative in some studies [12]. Less proven preventative therapies include the application of topical epinephrine or norepinephrine, which conferred up to 95% coat retention in a study of rats exposed to radiation [13].

Topical minoxidil 5% solution has been used for the treatment of persistent alopecia with moderate success. One study reported an 82% subjective response rate among patients with radiation-induced alopecia lasting longer than 6 months [10]. Minoxidil is thought to cause local vasodilation via ATP-dependent potassium channel activation, and stimulation of resting hair follicles into the anagen phase. A good response is typically achieved in 4 months with twice daily use but may take over a year if exposed to higher doses of radiation.

N-acetylcysteine, available in both topical and oral forms, is another potential therapy. Through its anti-inflammatory effects on IL-6, TNF-α, and IL-1, it is thought to reduce the cascade of cytokines that results from damaging radiation on epithelial cells [14]. By donating a cysteine and replenishing glutathione, n-acetylcysteine also exerts antioxidant effects. This reduces reactive oxygen species that could potentially damage cellular organelles.

Botulinum toxin type A injection has mixed evidence, with some case reports supporting its use to treat radiotherapy alopecia [15]. The theorized mechanism of this improvement was an increased blood flow to the tissues of the scalp, via relaxation of the musculature. One such report injected muscles around the scalp (including frontalis, temporalis, periauricular, and occipitalis muscles) at 30 injection sites every 3 months for 12 months. There was minimal effect noted at 3 months, with more modest increases in hair density and thickness noted after 12 months.

For cases of alopecia refractory to treatment, reconstructive surgical options may be considered. In pediatric patients, a variety of techniques have been reported with good success [16]. Choice of surgical technique should be guided by the pattern and location of hair loss, and include simple excision, scalp flap surgery, and tissue expansion. Transplantation can also be considered and has a success rate reported to be as high as 85% even in areas of poor vascularization. Some hair growth may be observed within 3 months after transplant, but full results are often not realized for over 1 year.

Key Points

- Alopecia due to radiation exposure follows a dose-response relationship, with transient anagen effluvium expected at doses above 2 Gy, and potential for permanent hair loss at doses above 43 Gy.

- Hair loss begins 1–3 weeks after radiation exposure and will resolve spontaneously in 2–6 months for low doses.
- As alopecia can be such a concerning side effect of treatment, it is important to counsel patients on the expected timing for appearance and resolution of this potential event.
- While no treatments have been found to be entirely effective, the use of preventative medications, topical agents, reconstructive surgery, and transplantation have all been tried with some success.

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