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AN UPDATE ON TREATMENTS FOR LICHEN PLANOPILARIS

Lichen planopilaris (LPP) is an immune-mediated cicatricial alopecia that is often challenging to treat. In LPP, hair follicles are selectively destroyed by a chronic lymphocytic inflammatory process, leading to irreversible scarring and permanent hair loss (**Figure 1 and 2**). Several variants of LPP have been described in the literature including the classic form, the Graham-Little-Piccardi-Lassueur syndrome, frontal fibrosing alopecia, and recently, a new clinical variant, lichen planopilaris diffuse pattern.[1]

LPP is associated with a high burden of disease and causes significant psychological distress to patients. In addition to visible hair loss, many patients experience burning, itching, and scalp tenderness which contribute to the quality of life impairment associated with the condition. The understanding that it is an incurable disease and that there are no consistently effective treatment options can also make coping with LPP difficult for patients. A recent retrospective review of 215 women with LPP with a mean age of 59.8 years found a high incidence of depression (45.7%), anxiety (41.8%), and sleep disturbance (29.2%).[2]

When approaching the management of LPP, patient selection and clear communication around treatment expectations are essential. Patients most likely to benefit from treatment are those with active disease—the presence of perifollicular scale and erythema, progressive hair loss, symptoms, and an inflammatory process on scalp biopsy compatible with LPP indicate that the condition is active. Conversely, end-stage lesions of LPP are unlikely to respond to treatment. With respect to treatment expectations, patients should understand that the goal of therapy is to stop disease progression and alleviate symptoms. Due the scarring nature of LPP, hair regrowth in areas of existing alopecia is not expected.

Treatment of LPP remains difficult. Due to a lack of high-quality evidence on therapies and the unpredictable clinical course of the disease, the best approach to the treatment of LPP is currently unclear. The absence of consistent methods to assess the response to treatment in the literature has also contributed to uncertainty about treatment efficacy. As a result, treatment varies widely.

Traditional first-line therapy for limited disease involves the use of topical and intralesional corticosteroids. Common systemic therapies include hydroxychloroquine and systemic antibiotics such as doxycycline. Despite the initial effectiveness of these treatments, relapses are common.[2,3] As a result, a range of other therapeutic options has been investigated. In addition to the treatments discussed in this article, data suggest that methotrexate, cyclosporine, oral retinoids, pioglitazone, and 5-alpha reductase inhibitors such as finasteride and dutasteride could be helpful in the treatment of LPP.

The objective of this article is to review recent data published in the literature on therapeutic modalities for LPP.

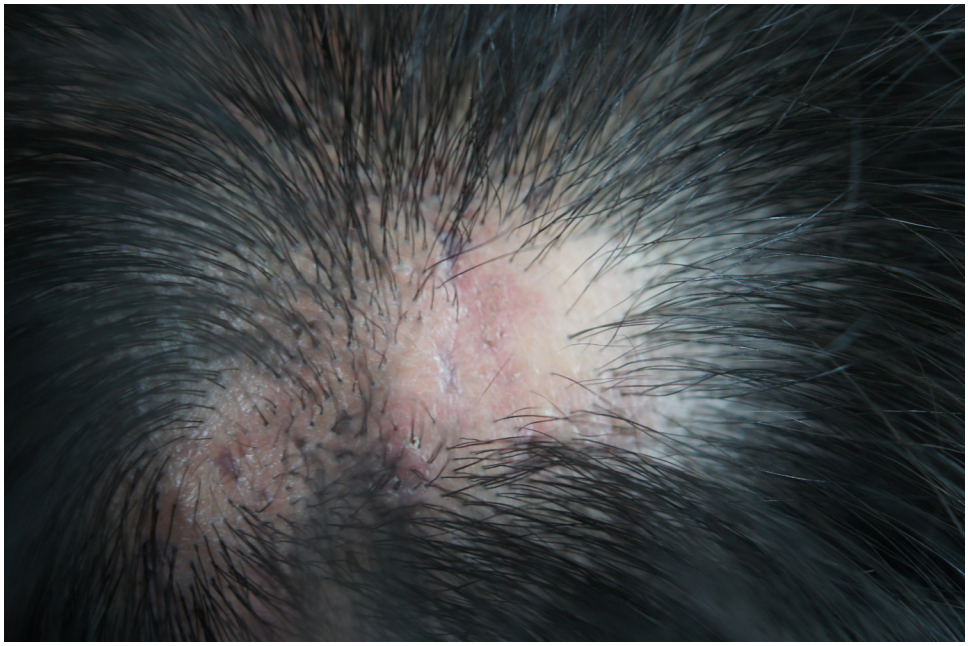

Figure 1. Lichen planopilaris of the scalp characterized by perifollicular scale, perifollicular erythema, and scarring

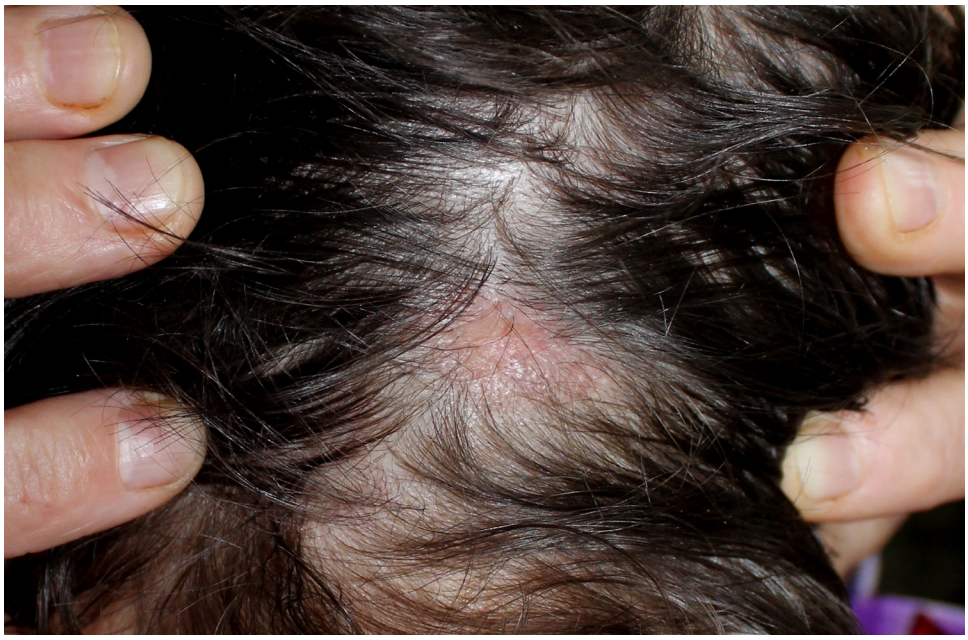

Figure 2. A case of lichen planopilaris in a female patient

ORAL MINOXIDIL

Oral minoxidil is a systemic vasodilatory agent which has demonstrated efficacy in the treatment of androgenetic alopecia and chronic telogen effluvium. A recent retrospective review evaluated the role of low dose oral minoxidil (LDOM) in increasing hair thickness in patients with LPP.[4] LDOM was started at a dose of 0.25 to 1 mg and gradually uptitrated over a minimum treatment duration of 6 months. Subjects' change in global hair thickness was assessed before and after LDOM treatment. The study found that hair thickness improved in 39% of patients, remained stable in 53% of patients, and worsened in only 8% of patients. LDOM was generally well-tolerated, with mild adverse events such as hypertrichosis, postural hypertension, tachycardia, and weight gain being reported in a minority of patients.

The study concluded that LDOM can help to maintain or improve hair thickness in most patients with LPP, with an acceptable safety profile. The increase in background hair thickness generated by LDOM might provide better concealment of adjacent areas of hair loss, thus reducing patient disease burden. Although there were limitations of the study, including its small sample size (n = 51) and retrospective design, LDOM may be a promising therapeutic option to add to the treatment armamentarium for patients with LPP.

MYCOPHENOLATE MOFETIL

While the pathophysiology of LPP remains poorly understood, the disease is thought to result from a T-lymphocyte-mediated cytotoxic immune reaction to

follicular antigens. Mycophenolate mofetil (MMF) is an antimetabolite that blocks de novo guanine nucleotide synthesis by inhibiting inosine monophosphate dehydrogenase. Both T and B lymphocytes lack purine scavenger mechanisms and consequently, their DNA replication pathways are inactivated by MMF. Recently, a systematic review and meta-analysis was published regarding the outcomes of MMF in LPP.[5] Based on a total of six studies comprising 94 LPP patients, the pooled proportion of any good response (either partial or complete) was 69.2% (95% CI 47.8 – 77.0). Side effects occurred in 16.9% of cases, which included elevated liver function tests, edema, hyperlipidemia, anaemia, herpes zoster infection, photosensitivity, and urinary tract infection. Based on these findings, it was concluded that MMF is reasonably effective and well-tolerated in the treatment of LPP, with fewer associated adverse events than other immunosuppressive medications such as cyclosporine. Although the current evidence for MMF remains limited, it appears to be a potential therapeutic option for patients with severe or recalcitrant LPP who have failed hydroxychloroquine and other immunosuppressants.

PLATELET-RICH PLASMA

Platelet-rich plasma (PRP) has emerged as a popular treatment option for non-scarring alopecias such as androgenetic alopecia. Until recently, its effectiveness in treating cicatricial alopecias including lichen planopilaris was largely unknown. Over the last two years, there has been increasing evidence to support its clinical benefits in the treatment of LPP.[6,7] A recent retrospective analysis examined the effect of PRP in 10 patients with LPP.[6] After an average of four treatments, four out of ten patients demonstrated improvement in LPP, defined by disease stabilization and/or attenuated symptoms, and three out of ten patients demonstrated neither improvement nor worsening. While the exact mechanism of action of PRP remains unclear, it is thought to promote hair growth via its effects on platelets, growth factors, and anti-inflammatory mediators. There have been concerns regarding the potential for PRP to cause new areas of disease (i.e., koebnerization) in patients with LPP. However, this retrospective review concluded that PRP need not necessarily be avoided for LPP patients and that it may result in clinical improvement without koebnerization. Future studies are needed to better understand the role of PRP in the treatment of LPP.

TOFACITINIB

Tofacitinib is a pan-Janus kinase (JAK) inhibitor approved for the treatment of moderate-to-severe rheumatoid arthritis, psoriatic arthritis, and ulcerative colitis. It has been used off-label in its topical and systemic forms for the treatment of various dermatologic conditions including psoriasis and vitiligo, as well as in the non-scarring alopecia, alopecia areata.[8] Two recent retrospective review studies found that tofacitinib was an effective therapeutic option for patients with LPP. Responses in both studies were evaluated based on patient-reported symptoms and physical examination findings. The first retrospective case series, published in 2018, included six females and four males and the average age at presentation was 55 years (range 33–68 years). The diagnosis of LPP was biopsy proven in five patients and was a clinical diagnosis in the remaining five patients. This study reported that eight out of ten patients treated with oral tofacitinib 5 mg twice daily or three times daily for 2-19 months as either monotherapy or adjunctive therapy had clinical improvement as measured by lichen planopilaris activity index (improvement ranged from 30% to 94%). Adjunctive therapies were used in five patients and included intralesional triamcinolone (two patients), hydroxychloroquine (one patient), intralesional triamcinolone and hydroxychloroquine (one patient), and intralesional triamcinolone and tacrolimus ointment (one patient).[9] Tofacitinib was well tolerated by all patients.

In the second retrospective review, published in 2020, topical and oral tofacitinib were used adjunctively in nine patients with LPP.[10] Three of four patients receiving topical therapy (2% cream twice daily) achieved a positive response, and all patients receiving systemic therapy (5 mg twice daily or three times daily) demonstrated a favourable response. Minor laboratory abnormalities were noted in patients on systemic therapy and included mild, transient hemoglobin and creatinine abnormalities, and mildly elevated triglyceride and cholesterol levels, but none required treatment. No other adverse events were reported. Despite these promising results, further investigation of tofacitinib in the setting of LPP is warranted.

NALTREXONE

Naltrexone is a long-acting opioid antagonist. At a low daily dose of between 1 and 5 mg, naltrexone exhibits both analgesic and anti-inflammatory effects and has been used successfully in treating a variety of inflammatory conditions. In the context of dermatology, low-dose naltrexone (LDN) has

demonstrated benefit in the treatment of pruritus, Hailey-Hailey disease, Grover disease, and Darier disease.[11] In a case series of 4 patients with LPP treated with 3 mg of naltrexone daily, a reduction in pruritus, clinically evident scalp inflammation, and disease progression was seen in all patients. Improvements were noted within 1 to 2 months of starting therapy and no adverse events were reported.[12] LDN is an interesting treatment option for LPP as it is relatively inexpensive, well-tolerated, and does not require laboratory monitoring. Further studies are required to better understand its potential role in the treatment of LPP.

CONCLUSION

In conclusion, new data continues to emerge on therapeutic options for LPP. As with other challenging and refractory dermatologic conditions, LPP will likely require a multimodal treatment approach involving the combination of therapeutic agents to achieve optimal outcomes. Although there is still a need for high quality data, the promising therapies reported in the literature in recent years will likely be a useful addition to our clinical repertoire.

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