Successful treatment with photodynamic therapy in a patient with nasal mucocutaneous leishmaniasis undergoing treatment with TNFα inhibitor

Treatment with anti-TNFα has been associated with an increased risk of leishmaniasis infections [1]. Cutaneous leishmaniasis (CL) is the most common form, occurring in 90% of patients; mucocutaneous leishmaniasis (MCL) affects approximately 5% and visceral leishmaniasis is less frequent, observed mainly in immunosuppressed patients [2].

Photodynamic therapy (PDT) has been shown to be effective against CL, but is not recommended in cases of MCL [3, 4].

A 53-year-old woman was investigated with rheumatoid arthritis, who had been taking treatment with adalimumab and methotrexate over the past five years. She presented with a progressive nasal deformity after a rhinoplasty, two years ago. She received several oral and topical antibiotics and steroids with progressive worsening.

She underwent an otorhinolaryngological examination to investigate mucosal and nasal skin involvement; a biopsy was performed. The histopathological study of the nasal mucosa showed an absence of epithelium, lymphohistiocytic proliferation and diffuse Donovanĭs intracytoplasmic bodies compatible with MCL. A polymerase chain reaction (PCR) test using the nasal tissue and serological testing confirmed the diagnosis of leishmaniasis (it is not possible to identify the subtypes of leishmania based on these tests performed in our centre). Serologies of HIV, HBV, and HCV were negative. Facial computerized tomography showed thickening of the right mucosa and nostril.

Adalimumab and methotrexate were discontinued and the patient was started with intravenous liposomal amphotericin B, 3 mg/kg daily. Acute renal failure developed on the fifth day with creatinine at 1.5 mg/dL (basal creatinine: 0.73 mg/dL). Treatment was discontinued and acute kidney failure was resolved. One month later, she still had oedema, erythema and nasal deformity involving the upper lip, as well as a granulomatous lesion inside the right nostril (*figure 1A*).

PDT treatment was started, with the application of 16% methyl aminolevulinate (MAL) cream applied over a 10-mm margin, covered with occlusive dressing and protected from light. After an incubation period of 1.5 hours, the lesion was irradiated using a red light-emitting diode lamp (Aktilite ®) at λ 630 nm and fluence 37 /cm^2. The patient was not anaesthetised. PDT was well tolerated due to a short incubation time. Two more sessions were performed with a two-week interval, increasing the incubation time up to three hours in the last session. She achieved complete clinical recovery one month after finishing the last session (*figure 1B*). It was well tolerated except in the last session. She developed an intense inflammatory reaction to *Staphylococcus aureus* superinfection, and was treated with amoxicillin with good response. The otorhinolaryngological examination was repeated after PDT, confirming complete response. After six months of follow-up; she remains asymptomatic; the PCR test for leishmania was negative.

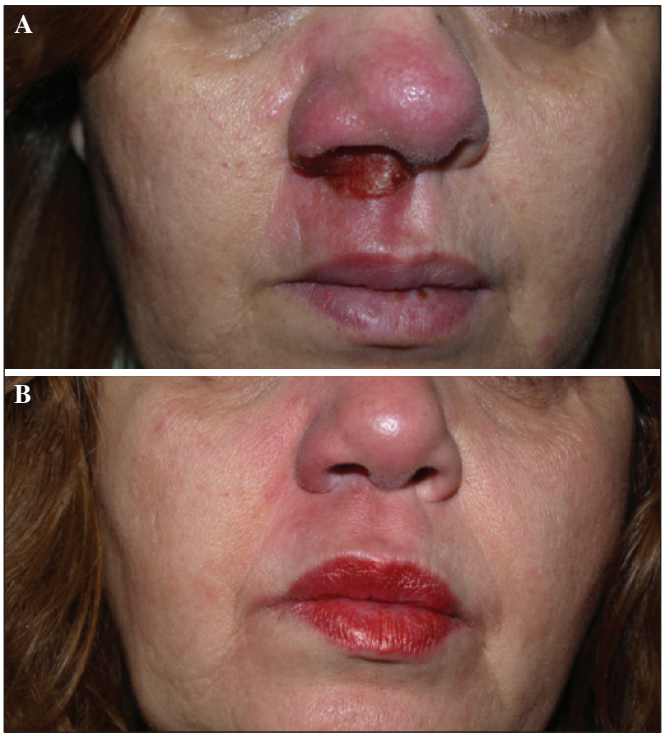

Figure 1. A) Oedema and erythema, nasal deformity involving the upper lip, with deviation of the septum to the left. **B**) Results one month after the third session of PDT.

PDT has been successfully used for cutaneous leishmaniasis with grade of recommendation B and quality of evidence I [3]. However, to the best of our knowledge, PDT has never been used for MCL. The parasiticidal mechanism is a non-specific phototoxic effect, inducing an inflammatory response and damaging host cells without a direct effect of the protozoan parasite [5, 6]. For all CL cases reported in the literature, the incubation time was three hours and the number of sessions varied depending on the study, from three to seven sessions; one case needed two sessions per week over 12 weeks to reach complete remission [7-10].

Treatment with TNFα antagonists has been associated with an emergence of leishmaniasis, with atypical clinical presentation and worse prognosis. According to a retrospective observational study carried out in 49 patients with leishmaniasis who were taking a TNFα antagonist, MCL was the least frequently reported clinically (10.2%). All patients with MCL were treated with systemic therapy and 65.3% discontinued treatment with TNFα antagonist [1]. Our patient required systemic treatment for a longer period of time because she was immunosuppressed, but treatment was discontinued because of side effects.

PDT offers an excellent profile of safety and cosmetic results, especially in facial areas such as the nose. Moreover, PDT offers better cosmetic outcomes in comparison with other local treatments such as surgery or cryosurgery and is better tolerated than imiquimod or intralesional meglumine antimoniate [3]. This was another reason to choose PDT in our patient.

In conclusion, we present the first MCL case treated with MAL-PDT administered after incomplete treatment with liposomal amphotericin B, who achieved complete remission following infection. PDT may be beneficial in

immunosuppressed patients with MCL and CL because it is expected to decrease the duration of systemic treatment, reducing associated side effects, and is well tolerated with excellent aesthetic outcomes. ■

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Risk of COVID-19 infection among lupus erythematosus patients and rheumatoid arthritis patients: a retrospective study in Hubei, China

Since both lupus erythematosus (LE) and rheumatoid arthritis (RA) patients need long-term treatment with immunosuppressive medications [1], they may have an increased risk of viral infection, including SARS-CoV-2 [2, 3]. Hydroxychloroquine (HCQ), a conventional drug for LE or RA, could effectively inhibit SARS-CoV-2 *in vitro*, while its clinical efficacy remains unclear [4]. Although a randomized trial showed that HCQ cannot prevent symptomatic infection after SARS-CoV-2 exposure [5], more studies are required to investigate the risk of SARS-CoV-2 infection among LE/RA patients with immunosuppressive medications. Furthermore, according to recommendations by the EULAR, the maintenance of immunomodulating and immunosuppressive therapies is suggested during the COVID-19 pandemic to avoid disease relapse. Limited data are available on the adherence to therapy in patients with LE or RA during the COVID-19 pandemic. Therefore, we explored the risk of COVID-19 infection in LE and RA patients, the possible effect of different treatments on the clinical manifestation of COVID-19, and adherence to therapy in Wuhan, China.

We conducted a retrospective cohort study in Wuhan Union Hospital via electronic medical records and one-to-one telephone correspondence during follow-up from 22nd March 2020 to 25th March 2020. A total of 338 hospitalized patients diagnosed with LE/RA from 1st January 2019 to 13th March 2020 were included (*supplementary table 1*). Three patients were admitted with severe COVID-19. One patient had close contact with a confirmed COVID-19 case, whereas the other two did not according to their self-reports. Two systemic lupus erythematosus (SLE) patients treated with HCQ were in a critical condition with COVID-19, and one RA patient without HCQ had severe pneumonia (*table 1*). One patient with SLE, concurrent with nephritis, died of respiratory failure because of COVID-19. Although it was not possible to confirm an association between autoimmunity and COVID-19, the overall occurrence of COVID-19 in our study (3/338; 0.89%) appears to be higher than Wuhan's overall infection rate (0.46%; 50,340/10,000,000 based on city-wide testing; up to June 23rd, 2020).

The incidence of COVID-19 in LE/RA patients and critical condition of three COVID-19 patients might be attributed to several factors. Firstly, these patients received long-term immunosuppressive therapy. We wonder whether their immunocompromised status may have led to COVID-19. We compared the rate of COVID-19 infection between LE/RA patients with and without immunosuppressive medications ($p>0.05$). It suggested that immunosuppressive drugs do not increase the risk of COVID-19 infection, which is consistent with previous reports [6]. A larger sample size and multicentre studies are needed to draw a definitive conclusion regarding the effect of immunosuppression therapy against COVID-19. Secondly, all of the patients were resident in Wuhan or had potential COVID-19 exposure; their onset occurred during the early stage of the epidemic in Wuhan, suggesting that patients' awareness of protection may have been lacking at that time.

In our study, 211 patients including two COVID-19 patients received HCQ at a dose below 5 mg/kg (medium duration of HCQ treatment: 11 months) (*supplementary table 2*). Due to the small sample size and retrospective method, we failed to establish a relationship between COVID-19 infection and LE or RA in patients treated with HCQ.

Thirty-two RA/LE patients discontinued previous treatments and half of them suspended treatment due to city lockdown for COVID-19. Compared with patients who adhered to medication therapy, discontinuing medication positively correlated with worse LE or RA clinical out-