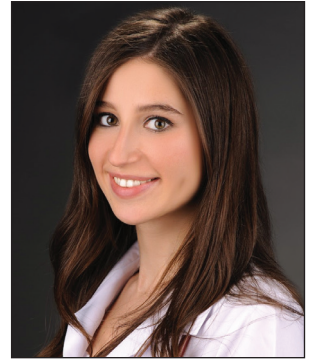


# Systemic Interferon Alfa Injections for the Treatment of a Giant Orf

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## RESIDENT PEARL

- Human orf lesions spontaneously resolve in 4 to 8 weeks; however, in immunocompromised patients, orf lesions may be persistent, atypical, and giant. We observed that surgical interventions for treatment of orfs cause a delay in the natural healing process, and other treatment options such as subcutaneous interferon alfa-2a may be used.

*Orf is a zoonotic infection caused by a parapoxvirus and is endemic in sheep and goats. It may be transmitted to humans by direct contact with infected animals. We report a case of a giant orf in a patient with chronic lymphocytic leukemia (CLL), which proliferated dramatically after surgical excision and resolved after systemic interferon alfa-2a injections.*

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**O**rf, also known as ecthyma contagiosum, is a common viral zoonotic infection caused by a parapoxvirus. It is widespread among small ruminants such as sheep and goats, and it can be transmitted to humans by close contact with infected animals or contaminated fomites. It usually manifests as vesiculoulcerative lesions or nodules on the inoculation sites, mostly on the hands, but other sites such as the head and scalp occasionally may be involved.<sup>1</sup> We report the case of an orf that proliferated dramatically and became giant after total excision. It was successfully treated with systemic interferon alfa-2a injections and imiquimod cream.

## Case Report

A 68-year-old man presented with a rapidly enlarging mass on the left hand that developed 4 weeks prior after close contact with a freshly slaughtered sheep during an Islamic holiday in Turkey. His medical history was remarkable for chronic lymphocytic leukemia (CLL), which was diagnosed one year prior. The patient had been treated with systemic prednisolone and cyclophosphamide therapies, but his disease was in remission at the current presentation and he currently was not receiving any treatment.

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On physical examination, a 2-cm, exophytic, pinkish gray, weeping nodule was observed on the proximal aspect of the right thumb. Based on the clinical findings and typical anamnesis, a diagnosis of an orf was concluded. It was decided to monitor the patient without any intervention; however, because the lesion did not resolve and remained stable, he was referred to a plastic surgeon for surgical removal after 6 weeks of follow-up.

Histopathologic examination of the excision specimen revealed pseudoepitheliomatous hyperplasia, massive capillary proliferation, and viral cytopathic changes in keratinocytes characterized by ballooning degeneration and eosinophilic cytoplasmic inclusions, which was consistent with the clinical diagnosis of an orf. Unfortunately, the lesion relapsed rapidly following excision (Figure, A). Treatment with oral valacyclovir (1 g 3 times daily) and imiquimod cream 5% (3 times weekly) was initiated. However, this treatment was unsuccessful and was discontinued after 6 weeks, as the lesion kept growing, reaching a diameter of approximately 5 cm and becoming lobulated on the surface (Figure, B). Combination therapy was started with imiquimod cream 5% (3 times weekly) and intralesional interferon alfa-2a injections (3 million IU twice weekly). The injections were so painful that the patient refused further therapy after only 2 injections. The therapy was switched from intralesional to systemic subcutaneous injections of interferon alfa-2a (3 million IU twice weekly) with concomitant imiquimod cream 5% 3 times weekly. This treatment was well tolerated by our patient with no notable side effects, except for mild fever on the night of each injection. Three weeks after the commencement of systemic injections, remarkable healing of the lesions with reduced size and exudation was noted. The frequency of injections was decreased to once weekly, which was then discontinued after 6 weeks when the lesion totally resolved (Figure, C). At 12 months' follow-up, there were no signs of relapse.

### Comment

Orf is an occupational disease that usually develops in farmers, butchers, and veterinarians; however, epidemic outbreaks of human orf are commonly observed in Turkey after the feast of sacrifice, as many individuals have close contact with the animals during sacrification.<sup>2</sup> In Turkey, orf is well recognized by dermatologists, and clinical diagnosis usually is not difficult.

Human orf has a self-limited course in which lesions spontaneously resolve in 4 to 8 weeks; however, in immunocompromised patients, such as our patient with CLL, orf lesions may be persistent, atypical, and giant, requiring early and effective



An orf on the right thumb relapsed rapidly following surgical excision (A). The lesion continued to grow after 6 weeks of therapy with oral valacyclovir and imiquimod cream 5% (B). Treatment was changed to subcutaneous injections of interferon alfa-2a and imiquimod cream 5%, which resulted in resolution after 9 weeks (C).

treatment. Treatment options for giant orf tumors in immunocompromised individuals include surgical excision,<sup>3</sup> cryotherapy, topical imiquimod,<sup>4,5</sup> topical or intralesional cidofovir,<sup>6</sup> and intralesional interferon alfa injections.<sup>7</sup> According to our clinical observations, surgical interventions for treatment of orfs usually cause a delay in the natural healing process; however, because surgical excision is a

recommended treatment option for exophytic and recalcitrant orfs, we decided to treat our patient with surgical excision, which resulted in rapid recurrence and massive proliferation. A similar case of giant orf that was aggravated after surgery has been reported.<sup>8</sup> In light of these cases, it is our opinion that treatment options other than surgery may be reasonable.

Chronic lymphocytic leukemia may show features of both humoral and cell-mediated deficiency. Patients are known to be prone to viral infections such as varicella-zoster virus, herpes simplex virus, cytomegalovirus, and human papillomavirus. A giant orf infection on the background of CLL also has been described.<sup>9</sup>

Interferons were first discovered in 1957 and named after their ability to interfere with viral replication. They represent a family of cytokines that has an essential role in the innate immune response to virus infections. Because of their antiviral properties, recombinant forms of interferon alfa are widely used with success in the treatment of chronic hepatitis B and hepatitis C virus infections. A few other antiviral clinical applications of interferon alfa include infections caused by human herpesvirus 8 (the etiological agent in Kaposi sarcoma) and human papillomavirus (the etiological agent in juvenile laryngeal papillomatosis and condyloma acuminatum).<sup>10</sup>

In a report by Ran et al,<sup>7</sup> intralesional interferon alfa injections were successfully used for treatment of giant orf lesions in an immunocompromised patient. As a result, we started treating the patient with intralesional interferon alfa-2a, but it was not well tolerated by our patient, as it was quite painful. We then decided to continue the therapy with systemic interferon alfa-2a injections, as we believed that it was a good option due to its antiviral, antiproliferative, and antiangiogenic properties. With the experimental combined therapy of systemic interferon alfa-2a and topical imiquimod, our patient achieved a complete response in 9 weeks (3 weeks of twice weekly injections and then 6 weeks of once weekly injections) and had no relapses during 12 months of follow-up.

## Conclusion

We present a rare case of a giant orf treated with systemic interferon alfa-2a injections. Because

intralesional injections are quite painful, systemic subcutaneous injections of interferon might be a good and safe alternative for recalcitrant orf lesions in immunocompromised patients. However, more studies and reports are needed to confirm its effectiveness and safety.

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