

## Herpes Zoster Duplex and Multiplex: The Exception That Confirms the Rule<sup>☆</sup>



### La excepción que confirma la regla: herpes zoster duplex y multiplex

To the Editor:

Herpes zoster is a relatively common disease worldwide, with a detected lifetime incidence between 10% and 20%. The classic clinical picture is characterized by clusters of papular and vesicular lesions on an erythematous base distributed unilaterally along a single dermatome. This characteristic presentation makes herpes zoster easily recognizable, even by non-dermatologist clinicians of different specialties. Involvement of 2 or more unilateral and contiguous dermatomes is not an uncommon finding in older patients and patients with other risk factors for immunosuppression. However, simultaneous involvement of 2 non-contiguous dermatomes—unilaterally or even bilaterally—is an exceptional finding that can make diagnosis difficult. In the literature, this manifestation has been called herpes zoster duplex.<sup>1</sup> Isolated cases of patients with involvement of more than 2 non-contiguous dermatomes have been called herpes zoster multiplex.<sup>2</sup>

We present 2 cases of herpes zoster duplex and 1 of herpes zoster multiplex diagnosed in our department between 2015 and 2017. The clinical and epidemiological characteristics are shown in [Table 1](#).

The 2 cases of herpes zoster duplex (cases 1 and 2) occurred in immunocompetent patients aged 27 and 66 years, respectively, who consulted for the acute appearance of unilateral or bilateral vesicular lesions with zosteriform distribution. Neither patient experienced pain in the affected dermatomes or presented fever or other extracutaneous symptoms throughout the process. The patient who presented with herpes zoster multiplex (case 3, [Fig. 1](#)), was a male aged 41 years who had already started treatment with famciclovir 72 h earlier, prescribed by his primary care physician. In spite of this treatment, new lesions continued to appear. None of the 3 patients reported any prior episodes of herpes zoster. In all 3 cases, viral culture of the exudate confirmed the diagnosis a posteriori, with detection of the varicella zoster virus in all 3 cases. The results of serologies performed to rule out HIV infection were negative in all 3 patients. With the diagnosis of herpes zoster duplex in cases 1 and 2 and multiplex in case 3, antiviral treatment was prescribed at standard doses complemented by topical care with zinc sulphate and fusidic acid until the lesions were completely healed.

The probability of developing herpes zoster duplex or multiplex is extremely low, with a documented incidence

in the largest series of less than 0.1% of all herpes zoster cases.<sup>3</sup>

In 2015, Zhang and Zhou<sup>4</sup> reviewed all the cases of herpes zoster duplex reported in the literature, affecting in total 36 patients. They highlighted several associated risk factors in that series: Asian origin (over 66%), older age (44.4% were over 50 years of age), female sex (63.9% were women), and immunosuppression (47.2%) associated with a variety of causes (immunosenescence, HIV, hematologic malignancies, solid organ tumors, chemotherapy, and prolonged therapy with corticosteroids or other immunosuppressive drugs). In a review of the literature published in 1999,<sup>2</sup> only 7 cases of herpes zoster multiplex were found, almost all associated with causes of immunosuppression.

Following primary varicella-zoster virus infection, the virus establishes a latent infection in the dorsal and trigeminal root ganglia; this has been demonstrated by viral DNA analysis in autopsies.<sup>5</sup> Reactivation of the virus in the ganglion with the highest latent viral load—mediated by multiple triggers—gives rise to the characteristic herpetic lesions in the affected dermatome. In herpes zoster duplex and multiplex, simultaneous reactivation of the virus in different, non-contiguous dorsal ganglia gives rise to the uncharacteristic clinical presentation and is also facilitated by immunosuppression.<sup>6</sup> However, other factors that have not yet been elucidated must also play a role because most of the cases reported, including our 3 patients, have occurred in immunocompetent patients.<sup>1,3,7-9</sup>

In routine clinical practice, classic herpes zoster is usually diagnosed on the basis of the clinical presentation. When there is doubt, however, or when the presentation is atypical, confirmation of the diagnosis by testing is recommended. In our 3 cases, diagnosis was confirmed by viral culture of two cell lines (MRC-5 human lung fibroblasts and A549 human lung tumor epithelial cells). The cultures were maintained for 3 weeks, during which it was checked for cytopathic effect every 3 to 4 days. The appearance of a cytopathic effect was confirmed by staining with monoclonal antiviral antibodies (Argene<sup>®</sup> Anti Varicella Zoster Virus Ref 11-017), with fluorescence being observed under the microscope in positive cases.

The treatment of patients with herpes zoster duplex and multiplex is the same as that used in classic cases, and involves antiviral coverage, pain control, and topical care. In our patients, follow-up confirmed complete cure without sequelae after the antiviral treatment was completed with the usual dose and treatment duration.

In summary, we consider it important to recognize these rare presentations and their potential association with causes of immunosuppression. In the presence of typical herpetic skin lesions with metameric distribution, the involvement of non-contiguous and/or bilateral dermatomes should not lead us to change the generally accepted treatment regimen, although such cases should be monitored closely.

### Conflicts of Interest

The authors declare that they have no conflicts of interest.

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**Table 1** Review of Diagnosed Cases of Herpes Zoster Duplex and Multiplex in the Emergency Department of the Hospital Gregorio Marañón During the Period 2015-2017.

Case	Sex	Age	Dermatome	Immune Status	Comorbid Diseases	Diagnosis	Antiviral Treatment
1	Woman	66	Left S2-S3 Right S1-S2	Immunocompetent	COPD treated with systemic corticosteroid therapy	Viral culture	Aciclovir 800 mg 5 times a day for 7 d
2	Woman	27	Left V1 Left V3	Immunocompetent	–	Viral culture	Valaciclovir 1 g every 8 h for 7 d
3	Man	41	Left D6 Left L5 Right S2	Immunocompetent	Hepatitis C	Viral culture	Famciclovir 500 mg every 8 h for 7 d

Abbreviations: COPD, chronic obstructive pulmonary disease.



**Figure 1** Case 3. Herpes zoster multiplex presenting with clusters of vesicles in a zosteriform distribution affecting the L5 dermatome on the left leg (A and B, tibial crest and plantar arch) as well as D6 (C) on the left side and S2 (D) on the right side.

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## Parotid Fistula After Skin Biopsy: Treatment With Botulinum Toxin<sup>☆</sup>



### Fístula parotídea tras biopsia cutánea: tratamiento con toxina botulínica

To the Editor:

Of the various causes of salivary gland fistula, the most common include accidental trauma and postoperative complications. Salivary gland fistula is characterized by marked discomfort due to drainage of saliva through the fistula, a phenomenon that usually intensifies with chewing. Proteolytic enzymes present in saliva can impair healing, leading to a chronic condition that can be difficult to resolve.<sup>1</sup>

A 76-year-old woman presented with asymptomatic, multinodular, indurated subcutaneous plaques of 2.5 × 3 cm in diameter in both parotid regions that had appeared several months earlier (Fig. 1A). Injection of a filling material 12 years before was the only medical history of interest. The patient reported no symptoms prior to appearance of the plaques, which became evident following significant weight loss. Suspecting foreign body granuloma, a skin biopsy was obtained using a 4-mm punch. The biopsy showed infiltration of the parotid with 4 different filling materials: hyaluronic acid, polylactic acid, calcium hydroxyapatite, and a fourth unidentified material (Fig. 2).<sup>2</sup>

One week later the patient presented with secretion of saliva from the biopsy site, a phenomenon that clearly intensified with chewing. A reinforcing suture was placed in the wound and a compression bandage applied. No

improvement in the patient's clinical signs was observed. Subsequent wound margin debridement and closure of the defect with interrupted sutures at the otorhinolaryngology department failed to achieve symptom control (Fig. 1B).

One week later the patient was seen for enlargement of the fistula. The margins were macerated and irritated, and the amount of saliva secreted had increased. We decided to locally administer botulinum toxin-A (Botox, Allergan Inc., Irvine, CA, USA); 100 U was diluted in 2 mL of physiological saline and 24 U of the solution was injected subcutaneously at 6 sites around the defect (Fig. 1C). While a clear decrease in the size of the defect was observed 2 weeks later the patient's symptoms persisted, and she received a second round of subcutaneous botulinum toxin-A injections (24 U). Four weeks later total closure of the fistula was achieved, with no treatment-related complications observed (Fig. 1D).

Parotid fistula most commonly occurs as a complication of parotid surgery, with incidences as high as 14% reported in some series. Fistulas can be classified according to duration: early fistulas last less than 6 weeks, while permanent fistulas last longer.<sup>3</sup> This distinction is important. While both forms pose therapeutic challenges, the former tend to respond to conservative treatment with a compression bandage, whereas permanent fistulas tend to respond poorly and often require surgical intervention.

Injection of botulinum toxin-A is one form of treatment that has shown good results in recent years.<sup>4,5</sup> The toxin temporarily blocks the release of parasympathetic cholinergic neurotransmitters, thereby reducing secretion by the salivary gland and facilitating closure of the fistula. Although the effect is temporary, this approach is minimally invasive, is associated with few complications, and is well tolerated.

Doses of botulinum toxin usually range from 10 U to 40 U, administered 2 to 4 weeks apart.<sup>6,7</sup> A reduction in saliva secretion is observed after a few days. However, it is important to remind the patient that the maximum effect may not be observed for several

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