Case Report

Herpes zoster: A clinicocytopathological insight

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Abstract

Herpes zoster or shingles is reactivation of the varicella zoster virus that had entered the cutaneous nerve endings during an earlier episode of chicken pox traveled to the dorsal root ganglia and remained in a latent form. This condition is characterized by occurrence of multiple, painful, unilateral vesicles and ulceration which shows a typical single dermatome involvement. In this case report, we present a patient with herpes zoster involving the mandibular division of the trigeminal nerve, with unilateral vesicles over the right side of lower third of face along the trigeminal nerve tract, with intraoral involvement of buccal mucosa, labial mucosa and the tongue of the same side. Cytopathology revealed classic features of herpes infection including inclusion bodies, perinuclear halo and multinucleated cells.

Key Words: Herpes zoster, intranuclear inclusions, multinucleate cells, perinuclear halo

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INTRODUCTION

Varicella zoster virus (VZV) is a ubiquitous DNA virus that belongs to the family of human herpes viruses. The association between varicella and herpes zoster was first made in 1892.[1] Herpes zoster infection (HZI) requires preexposure to the VZV. HZI probably results most often from failure of the immune system to contain latent virus replication.[2]

The most common symptoms of HZI are sensations of burning pain, itching, hyperesthesia (oversensitivity) or paresthesia ("pins and needles," tingling, pricking or numbness) unilaterally. Cytopathology and histopathology are typical for HZI. Here, we present a case of HZI in a 45-year-old female patient which demonstrates all the typical characteristic cytological features that are seen in HZI.

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CASE REPORT

A 45-year-old female reported to our institution with the chief complaint of ulcers in the mouth and eruptions on the face for 3 days. History revealed the presence of pricky type pain 4–5 days ago. Then, she had noticed vesicles, which appeared 3 days ago on the right side of the face and in the oral cavity. Subsequently, the vesicles ruptured to form ulcers which were very painful. Extraoral vesicles were intact. All the vesicles and ulcers were limited to the face and oral cavity of the right side only until the midline.

Medical history and dental history were not contributory except for the fact that the patient had undergone extraction of teeth 6–7 years ago. On examination, the right submandibular lymph nodes were palpable, tender and mobile. Examination of face revealed multiple vesicles extending from the right preauricular area

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to the right corner of the mouth. Encrustation was seen on the right side of the lip, but was not crossing the midline [Figure 1].

Intraorally, multiple shallow ulcerations with erythematous irregular borders and tissue tags were seen on the buccal mucosa, tongue and labial mucosa unilaterally on the right side. These ulcers were painful causing difficulty in eating and mouth opening. There were no other skin lesions accompanying the orofacial lesions. After careful clinical examination, a provisional diagnosis of HZI was made [Figures 2 and 3].

Clinical differential diagnosis included herpes simplex infection (HSV). HSV infection appears in a similar fashion and if mild and localized to one side may be mistaken for HZI; cultures helps to differentiate between the two.

Cytosmear prepared from the labial mucosa revealed epithelial cells. Epithelial cells were arranged in clusters, and few isolated cells were seen. These epithelial cells were showing intranuclear eosinophilic inclusions with margination of chromatin resembling Cowdry A type inclusion [Figure 4]. Multinucleated cells [Figure 5], perinuclear halo [Figure 6] and nuclear fragmentations [Figure 7] were also seen.

Cytological features were suggestive of the herpes infection. Hence, correlating the clinical feature with cytological features, a final diagnosis of HZI was concluded.

DISCUSSION

HZ is more commonly known as shingles, from the Latin cingulum, for "girdle." This is because a common presentation of HZ involves a unilateral rash that can wrap around the waist or torso like a girdle. Similarly, the name zoster is derived from classical Greek, referring to a belt like binding (known as a zoster) used by warriors to secure armor.[2]

Zoster lesions contain high concentrations of VZV that can be spread, presumably by the airborne route. This

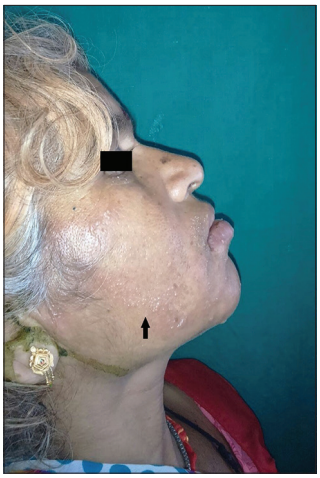

Figure 1: Clinical image shows extraoral vesicles at the right side of the face

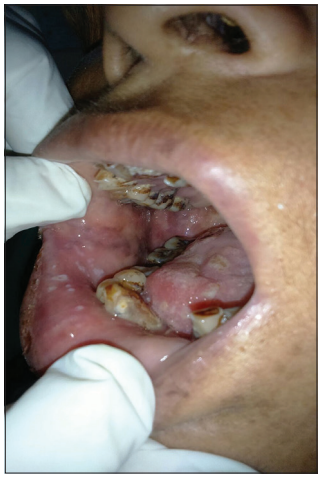

Figure 2: Clinical image shows intraoral vesicles on the right side of the buccal and labial mucosa

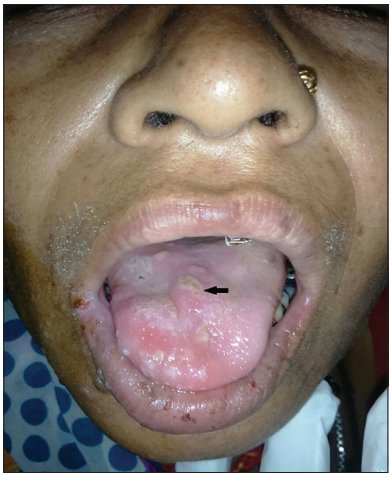

Figure 3: Clinical image shows intraoral vesicles at dorsum surface of tongue, not crossing the midline

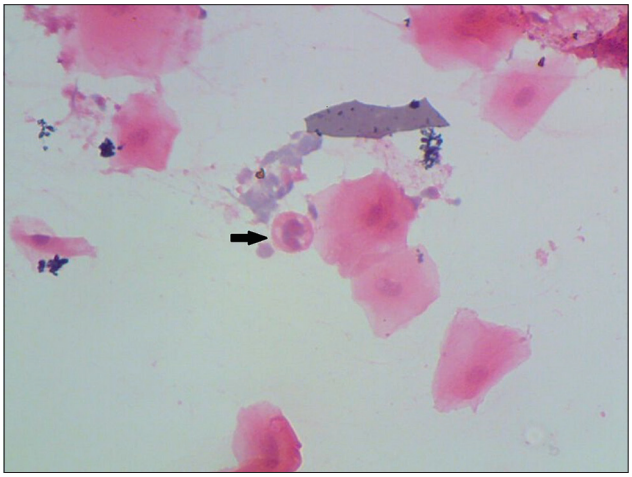

Figure 4: Cytosmear shows nuclear inclusion (H&E stain, ×400)

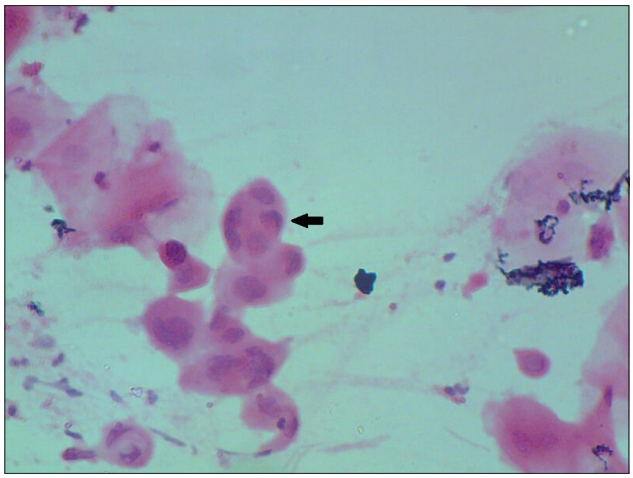

Figure 5: Cytosmear shows multinucleated cell (H&E stain, ×400)

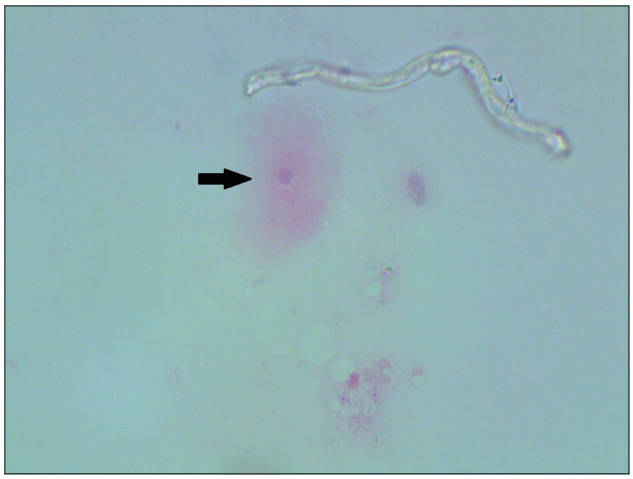

Figure 6: Cytosmear shows perinuclear halo (H&E stain, ×400)

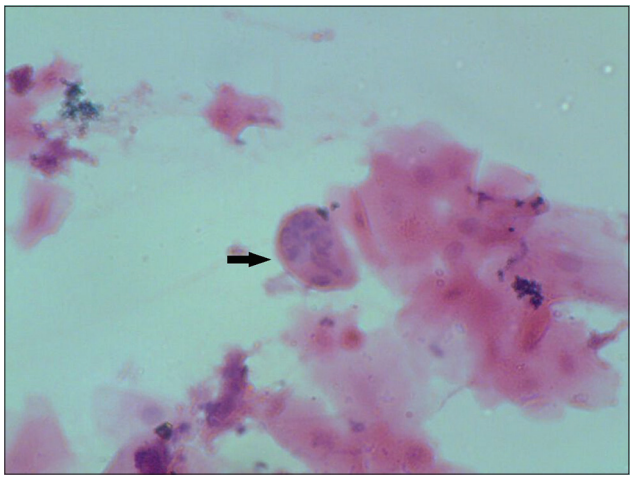

Figure 7: Cytosmear shows fragmented nucleus (H&E stain, ×400)

causes primary varicella infection in exposed susceptible persons. Localized zoster is only contagious after the rash erupts and until the lesions crust.[2-5]

Herpes zoster progresses as a cluster of small bumps which turns into blisters; the blisters further fill with lymph and break open. Then, crust formation occurs over the blister; finally, it disappears. Postherpetic neuralgia can sometimes occur due to nerve damage.[2]

Most people are infected with this virus as children and suffer from an episode of chickenpox. The immune system eventually eliminates the virus from most locations, but it remains dormant (or latent) in the ganglia adjacent to the spinal cord (called the dorsal root ganglion) or the ganglion semilunar (ganglion *Gasseri*) in the base of the skull. Repeated attacks of herpes zoster are rare.[2,6-8]

The clinical features of HZI can be grouped into three phases: (1) prodromal, (2) acute and (3) chronic. Initially, the adult patient exhibits fever, general malaise and pain and tenderness along the course of the involved sensory nerves, usually unilaterally. Often the trunk is affected. Within a few days, the patient has a linear papular or vesicular eruption of the skin or mucosa supplied by the affected nerves. It is typically unilateral and dermatome in distribution. After rupture of the vesicles, healing commences, although secondary infection may intervene and slow the process considerably. Approximately 10% of affected individuals will exhibit no prodromal pain. Conversely, on occasion, there may be recurrence in the absence of vesiculation of the skin or mucosa. This pattern is called zoster sine herpete (zoster without rash) and affected patients have severe pain of abrupt onset and hyperesthesia over a specific dermatome. Fever, headache, myalgia and lymphadenopathy may or may not accompany the recurrence.[9]

Herpes zoster may have additional symptoms, depending on the dermatome involved. Herpes zoster ophthalmicus involves the orbit of the eye and occurs in approximately 10–25% of cases. It is caused by the virus reactivating in the ophthalmic division of the trigeminal nerve. In a few patients, symptoms may include conjunctivitis, keratitis, uveitis and optic nerve palsies that can sometimes cause chronic ocular inflammation, loss of vision and debilitating pain. Zoster oticus, also known as Ramsay Hunt syndrome type II, involves the ear. It is thought to result from the virus spreading from the facial nerve to the vestibulocochlear nerve. Symptoms include hearing loss and vertigo (rotational dizziness).[2,10,11]

Oral lesions occur with trigeminal nerve involvement and may be present on the movable or bound mucosa. The lesions often extend to the midline and frequently are present in conjunction with the involvement of the skin overlying the affected quadrant. Like varicella, the individual lesions manifest as 1–4 mm, white, opaque vesicles that rupture to form shallow

ulcerations. Involvement of the maxilla may be associated with devitalization of the teeth in the affected area.[9]

The cytological presentation includes binucleated, syncytial multinucleated giant cells along with the ballooning of cytoplasm and cowdry type A intranuclear eosinophilic inclusions with partial or complete loss of chromatin; these inclusions were separated from the thick nuclear membrane by a clear zone or halo. The cells also showed enlarged degenerated nuclei with smudged and homogenized ground glass or slat gray appearance (cowdry B type nuclei). These infections do not show intracytoplasmic inclusions; however, subtle shading within the nucleus may be mistaken for inclusions.[12]

Histopathology revealed that virus exerts its main effects on the epithelial cells. Infected epithelial cells exhibit acantholysis, nuclear clearing and nuclear enlargement, which have been termed ballooning degeneration. The acantholytic epithelial cells are termed Tzanck cells (not specific for herpes; refers to a free-floating epithelial cell in any intraepithelial vesicle). Nucleolar fragmentation occurs with condensation of chromatin around the periphery of the nucleus. Multinucleated, infected epithelial cells are formed when fusion occurs between adjacent cells. Intercellular edema develops and leads to the formation of an intraepithelial vesicle. Mucosal vesicles rupture rapidly; demonstrate a surface fibrinopurulent membrane.[9]

Zoster diagnosis might not be possible in the absence of rash (e.g., before rash or in cases of zoster sine herpete).[13] In its classical manifestation, the signs and symptoms of zoster are usually distinctive enough to make an accurate clinical diagnosis once the rash has appeared.[14,15] The accuracy of diagnosis is lower for children and younger adults in whom the incidence of zoster is lower and its symptoms are less often classic.[7,16]

In some cases, particularly in immunosuppressed persons, the location of rash might be atypical, or a neurologic complication might occur well after the resolution of the rash. In these instances, laboratory testing might clarify the diagnosis.[8,17] Tzanck smears are inexpensive and can be used at the bedside to detect multinucleated giant cells in lesional specimens, but they do not distinguish between infections with VZV and HSV. Direct fluorescent antibody (DFA) staining of VZV-infected cells in a scraping of cells from the base of the lesion is rapid and sensitive. DFA and other antigen detection methods also can be used on biopsy material, and eosinophilic nuclear inclusions (Cowdry type A) can be observed on histopathology.

Polymerase chain reaction techniques performed in an experienced laboratory also can be used to detect VZV DNA rapidly and sensitively in properly-collected lesion material. In immunocompromised persons, even when VZV is detected by laboratory methods in lesional specimens, distinguishing chickenpox from disseminated zoster might not be possible by physical examination or serologically. In these instances, a history of VZV exposure, a history that the rash began with a dermatomal pattern and the results of VZV antibody testing at or before the time of rash onset might help guide the diagnosis.[18,19]

CONCLUSION

Herpes zoster is a painful blistering infectious disease, characterized by numerous cytological changes. When these cytological changes are demonstrated in an ideal smear prepared from the blisters, identification of the condition becomes simple, without warranting a biopsy.

Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent forms. In the form the patient(s) has/have given his/her/their consent for his/her/their images and other clinical information to be reported in the journal. The patients understand that their names and initials will not be published and due efforts will be made to conceal their identity, but anonymity cannot be guaranteed.

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Conflicts of interest

There are no conflicts of interest.

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