CASE REPORT

Disseminated herpes zoster in immunocompetent patients: Two cases report

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INTRODUCTION

Disseminated herpes zoster (DHZ) is a recurrent infection of the Varicella Zoster Virus (VZV) on the skin, characterized by the appearance of vesicles in certain skin dermatomes with more than 20 lesions, or vesicles lesions in more than 2 dermatomes. Prevalence of the DHZ varied in number and clinical manifestations.1-5 There are 41 patient of DHZ reported in hospitals of Argentina, between 2010-2015, with 70.73% classic DHZ and 29.27% atypical DHZ that manifest in purulent, hemorrhage and necrosis vesicles.4 There is classic DHZ in 6 years old boy after vaccination, atypical DHZ in immunocompromised patient, classic DHZ with hypertension, or ophthalmic DHZ with seconder infection.1,3,5 There is complication in 56.1% DHZ patients.4 DHZ occurs more frequently in immunocompromised than immunocompetent patient. In addition, DHZ is more likely to occur in aging and psychological stress patients.4 There is 58.54% DHZ patient with immunosuppressive, more than 66% of patients with this disease are aged > 50 years and stress factor find in the 39.02% patient.4 Almost all article reports that DHZ found in the older patients with more than 60 years old.3,4,6,7 In this report we present 2 cases with age less than or equal to 60 years old and they are immunocompetent, which are rare cases.

CASES

Case 1

A 60-year-old man, a carpenter, came to the dermatology clinic with the main complaint of facial blisters and headache. The patient had a history of fever for 3 days and pain in the left face and scalp. A day later, blisters appeared on his face and gradually increased in number and swollen eyes. The lesions spread to his torso, arms, and thighs. The patient had no history of diabetes, decrease of body weight or taking other medications. Patient also denial psychological stress. The vital sign examination within normal limits. The dermatological examination showed edema, vesicles, and bullae with an erythematous base, and erosions on the left ophthalmic dermatome (Figure 1). There are erythematous papules and vesicles on his trunk and both thighs. The patient was diagnosed with DHZ. The patient was treated with acyclovir tablet 5x800 mg for 7 days, diclofenac potassium 2x50 mg, amitriptyline 1x25 mg, and topical gentamicin cream for the erosion. Three days later, the patient came to the clinic because of decreased vision. The patient consulted an ophthalmologist and was diagnosed as ophthalmic neuritis. The ophthalmic complaint was addressed with methyl prednisolone 2x16 mg for 5 days and chloramphenicol eye drops 4 times a day. Seven days later, patient have improvement lesion, with crusted lesion, without edema, pain, or visual impairment. The patient denied side effect of acyclovir or diclofenac, like stomach upset or nausea, diarrhea, constipation, gas, headache, drowsiness, or dizziness.

Case 2

A 45-year-old man, a carpenter, came to the dermatology clinic with the main complaint of pain in the left side of the body. The patient had a history of fever for 7 days, body aches with nausea and vomiting. Two days later, a wound appeared on his left body and it gradually increased in number and size, but the temperature dropped. The patient went to the doctor and received antibiotics,
gas, headache, drowsiness, or dizziness. The potassium diclofenac 2x50 mg and topical gentamycin cream 2 times a day are continued for 7 days to prevent the postherpetic neuralgia.

DISCUSSION
This is report of two cases of DHZ in immunocompetent patient. The diagnose of DHZ based on the clinical manifestation that characterized by lesions in certain skin dermatomes with more than 20 lesions outside the affected dermatomes. The dermatomal lesions are sometimes hemorrhagic or gangrenous. The diagnose of the herpes zoster can based on the clinical examination, with prodromal symptom such as pain and paresthesia on the related dermatome, followed by skin eruption. The prodromal symptom can be accompanied by fever, malaise, cephalgia or flu like syndrome. The skin lesion starting with erythematous macular papules that develop to grouped vesicles and edema, unilateral location and dermatomal in according to innervation.8 The outlying vesicles or bullae, which are usually not grouped, similar with varicella lesions and are often umbilicated or may be hemorrhagic.9 The diagnose of DHZ in these cases based on clinical manifestation that appear vesicles and bullae on the dermatome. The outlying lesions in these cases were erythematous papules and vesicles and more than 20 lesions that spread over the face, trunk, and extremities. This diagnosis was carried out because of the same clinical manifestation of the disease as DHZ.5 However, the clinical condition of the patients may be atypical as reported in a case study where each of the 2 patients developed an unusual presentation of atypical, generalized Herpes Zoster. In this clinical variant, the lesion develops along a single dermatome, then a diffuse vesicular eruption then develops without dermatomal localization.2 The DHZ occurs chiefly in older and debilitated or immunocompromised individuals.1,9 The incidence of DHZ in elderly correlated with immunosenescence.4 The reactivation of Varicella-Zoster Virus, or zoster, takes place in 10- 20% of subjects who contracted the natural infection, with a
likelihood of developing zoster increasing proportionally with age, especially after 50 years of age. As mentioned in the case report of DHZ in a 72-year-old man with congestive heart failure, chronic obstructive pulmonary disease, and chronic kidney disease. He has symptoms of skin lesions that develop into scattered vesicles on an erythematous base that spreads to the trunk and extremities. A similar case was also reported in a case study in which a 67-year-old woman with a past medical history of controlled hypertension and diabetes mellitus presented with disseminated VZV infection, at least four discrete dermatomes were found to be involved. Although in an immunocompromised state the patient experienced several complications during the treatment period.

Several studies have shown that the cellular immune response by lymphocytes stimulated in vitro through exposure to VZV is diminished with age. The lymphocyte that responsible for VZV infection are CD4+ and CD8+ effector T cell. In the older, there was lower and slower VZV-specific CD4+ and CD8+ effector T cell responses to a VZV challenge compared with young adults. This is may be responsible for the increased risk and morbidity of herpes zoster (HZ) in the older adults including DHZ. The study showed that VZV-specific cell-mediated immunity, quantified as numbers interferon-gamma, among subjects aged 70-79 was on average 10.30 points significantly lower than that among subjects aged 60-69. This study support that the low level of serum antibody against VZV also has a highly significant risk factor in predicting dissemination of disease.

The incidence of DHZ more occur in immunocompromised patient, but in this case the patients have no history or evidence debilitated immune. The patient was a carpenter who included workers with heavy physical activity, especially in the second case who had a history of working overtime in the last 2 weeks before being sick. Nakata study showed that Amount of overtime worker was inversely associated sick. Nakata study showed that Amount of overtime in the last 2 weeks before being the second case who had a history of working overtime was increased associated with natural killer cell (NK) (CD3-CD56+) cell counts. The other study explain that herpes zoster patient displays reduced interferon-gamma secretion from NK cells. These studies showed that overtime worker may have reduced NK cell and interferon-gamma which is normal immune system against viral infection. In addition, the large cross-sectional study shows that overtime work appears to influence stress response indirectly through other stress factors such as self-assessed amount of work, mental workload and sleeping time. Meanwhile, the study also showed that general fatigue score was positively correlated with white blood cell (WBC) and neutrophil counts, but not significantly correlated with lymphocyte counts. The overtime worker could be related with WBC and neutrophil number but not related with CD8 lymphocyte that responsible for herpes zoster infection.

These cases report that DHZ can occur in immunocompetent patients especially with decreased immune response to viral infections. Immunocompetent patients with overtime work associated with decreased interferon-gamma secretion and NK counts, which are responsible for viral infections. Severe VZV infection in an immunocompetent patient has also been reported in a case study of a 16-year-old boy with concurrent HZ-oticus, HZ-ophtalmicus, and disseminated cutaneous HZ. In further investigation no immunosuppressed condition was found, and within three months the rest of the lesions disappeared.

The limitation in this case is that there is no additional examination such as the Tzanck test to support the diagnosis. Polymerase chain reaction examination was also not carried out because it was not available at the hospital.

CONCLUSION

This case report two carpenter with DHZ. In immunocompromised patient clinicians have been able to predict severe VZV infection. However, they should be aware that it can also occur in immunocompetent patients. The disseminated lesion can be happened in the immunocompetent patient especially with reduce immune response for the viral infection, such as in elderly. The immunocompetent patient with overtime work related with reduce the interferon-gamma secretion and NK number, that responsible for viral infection. In other words, patients with a history of VZV infection are expected to be able to maintain their immune system so that there is no recurrence of severe disease in the future.

DISCLOSURE

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Conflict of interest
There is no conflict of interest.

Ethical statement
Written informed consent was obtained from the patients and a copy of which had been sent to be reviewed by the editorial team.

Author Contribution
Literature search, manuscript preparation and editing, SATSE. All authors contributed to the conceptualization, design, definition of intellectual content, data acquisition, and manuscript review. All authors serve as guarantors for the current study.

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REFERENCES

1. Rueda JM, Feito-Rodríguez M, Nieto D, Lucas-Laguna R de. Disseminated Herpes Zoster After Varicella Vaccination in a Healthy Boy. Actas Dermosifiliogr. 2017;108(6):587–8.
2. Lewis DJ, Schlichte MJ, Dao H. Atypical disseminated herpes zoster: management guidelines in immunocompromised patients. Cutis. 2017;100(5).
3. Chiriac A, Chiriac AE, Podoleanu C, Stolnicu S. Disseminated cutaneous herpes zoster-A frequently misdiagnosed entity. Int Wound J. 2020;17(4):1089–91.
4. Bollea-Garlatti ML, Bollea-Garlatti LA, Vacas AS, Torre AC, Kowalczyk AM, Galimberti RL, et al. Clinical Characteristics and Outcomes in a Population With Disseminated Herpes Zoster: A Retrospective Cohort Study. Actas Dermosifiliogr. 2017;108(2):145–52.
5. Vittarina P, Tumbelaka AR. Herpes Zoster Oftalmikus Sinistra Diseminata dengan Infeksi Sekunder pada Anak. Sari Pediatr. 2016;6(4):125.
6. Dubey V, MacFadden D. Disseminated varicella zoster virus infection after vaccination with a live attenuated vaccine. CMAJ. 2019;191(37):1025–7.
7. Jethwa T, Bertasi RAO, Kieneker L, Pattanaik S, Pujalte G. Bullous Disseminated Herpes Zoster: An Atypical Presentation. Cureus. 2020;12(7).
8. Widaty S, Soebono H, Nilasari H, Listiawan MY, Siswati AS, Triwahyudi D, et al. Panduan Praktek Klinis bagi Dokter Spesialis Kulit dan Kelamin Indonesia. Jakarta: PERDOSKI; 2017.
9. James W, Elston D, Berger T. Andrews' Diseases of the skin: clinical dermatology. Philadelphia: Elsevier; 2016. 965 p.
10. Freer G, Pistello M. Varicella-zoster virus infection: natural history, clinical manifestations, immunity and current and future vaccination strategies. New Microbiol. 2018;41(2):95–105.
11. Petrun B, Williams V, Brice S. Disseminated varicella-zoster virus in an immunocompetent adult. Dermatol Online J. 2015;21(3).
12. Drone E, Ganti L. A Case of Disseminated Zoster in an Immunocompetent Patient. Cureus. 2019;11(12).
13. Weinberg A, Canniff J, Rouphael N, Mehta A, Mulligan M, Whitaker JA, et al. Varicella-Zoster Virus-Specific Cellular Immune Responses to the Live Attenuated Zoster Vaccine in Young and Older Adults. J Immunol. 2017;199(2):604–12.
14. Nakata A, Takahashi M, Irie M. Association of overtime work with cellular immune markers among healthy daytime white-collar employees. Scand J Work Env Heal. 2012;38(1):56–64.
15. Kim CK, Choi YM, Bae E, Jue MS, So HS, Hwang E-S. Reduced NK cell IFN-γ secretion and psychological stress are independently associated with herpes zoster. PLoS One. 2018;13(2).
16. Sato Y, Miyake H, Thériault G. Overtime work and stress response in a group of Japanese workers. Occup Med (Chic Ill). 2009;59(1):14–9.
17. Nishitani N, Sakakibara H. Association of Psychological Stress Response of Fatigue with White Blood Cell Count in Male Daytime Workers. Ind Heal. 2014;52(6):531–4.
18. Rissardo JP, Caprara ALF. Herpes Zoster Oticus, Ophthalmicus, and Cutaneous Disseminated: Case Report and Literature Review. Neuroophthalmology. 2018;43(6):407–10.