Case Report

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Case Series of Herpes Zoster in Children; Ultraviolet as a Trigger?

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ABSTRACT

Background: *The condition of immunosuppression is a known condition that triggers reactivation of varicella zoster virus, to its manifestation as herpes zoster. Excessive exposure to ultraviolet is shown to decrease the immune system, even the effects can be systemic. Children often experience excessive UV exposure during play. Is excessive UV exposure a precursor to HZ in children?*

Case Report: *We observed five cases of HZ in children aged 3-14 years; three of them are HZ ophthalmic, one HZ thoracic and one HZ brachialis. All had never received vaccine immunization and no history of intrauterine infection. Only one of them has suffered from varicella. There was no pathologic immunosuppression (HIV infection, organ transplant, immunosuppressant therapy, systemic disease) in these five children, but all children experienced intense UV exposure 3-5 days before the cutaneous lesions appeared. After treatment according to the HZ protocol, all recover without complications.*

Discussion: *Various experimental models prove that UV exposure can suppress the immune system in some conditions: after vaccination, infection and provocation of allergic contact dermatitis in skin exposed directly or indirectly. This condition is in accordance with the state of immunosuppression that can trigger the reactivation of VVZ to HZ. The incidence of HZ is also reported to increase in the summer. All the patients we observed had intense UV exposure a few days before the emergence of HZ cutaneous lesions. Although only one patient clearly showed a history of varicella, subclinical VVZ infection may explain the reactivation of VVZ in all four cases. Based on the various evidence mentioned above, we conclude that intense UV exposure is very likely the main precipitating factor of HZ reactivation in children.*

Keywords

Immunosuppression, Rreactivation, Ultraviolet, Zoster.

Introduction

Herpes zoster (HZ) is caused by reactivation of varicella zoster virus (VVZ), it can occur at any age but is rare in children and adolescents, although recent studies have shown an increasing incidence in children [1-3]. In children usually without prodromal symptoms, skin lesions are lighter, shorter duration and less post-herpetic neuralgia. The incidence of HZ in children is reported to be about 42-238,5 per 100,000 people per year [3]. In children aged less than 10 years of 0.25-1.15 per 1000 and 0.43-1.60 per 1000 HZ in adolescents. Impaired immunity such as a history of primary intrauterine infection, immunocompromised, and infected first-year varicella of childhood is a risk factor for HZ in children [2-6]. The virus replicates in the sensory dorsal nerve ganglion and when a person's cellular immunity decreases, the activated VZV travels through the sensory nerve to the skin [7].

Ultraviolet (UV) exposure, especially UVB waves, can suppress the immune system in several ways. UVB inhibits antigen presentation, inducing the release of immunosuppressive cytokines and causing leukocyte apoptosis. However, UVB does not cause general immunosuppression but inhibits immune reactions through

specific antigens. Application of contact allergens on UV exposed skin does not cause sensitization but induces specific antigen tolerance because such individuals cannot be sensitized to the same allergen in the future. This specific immunosuppression is mediated by a specific antigen suppressor/ regulatory T cell. UVB DNA damage is a major molecular trigger for immunosuppression. Presentation of antigens by Langerhans cells that have been damaged by UV in lymph nodes appears to be one of the essential requirements for the formation of regulatory T cells [7-9].

Case Report

There were reported five cases of HZ in children. All the cases we observed had never received vaccine immunization and no history of intrauterine infection. Only one of them has suffered from varicella. No immunosuppressed condition (HIV infection, organ transplant, immunosuppressant therapy, or systemic disease) was observed in five children.

Case 1

Boy, aged 3 years, according to his mother appeared a rash of multiple clusters on arms, fingers III-IV and part of the palm of the right hand suddenly since 2 days ago without fever and pain. On physical examination found vesicles clustered in the region brachialis, ulnar and medianus. History of UV exposure while swimming in the pool four days before the cutaneous lesions appear and has suffered from varicella at 2.4 years of age.

Case 2

Girl, aged 7 years, 3-day history that occurs in reddened skin on the left eyelid, forehead and nose, burns without fever, no headache and no sore eyes. On physical examination vesicular eruptions were found in groups in the left ophthalmic region. History of UV exposure while playing on the beach three days before the cutaneous lesions appear.

Case 3

Boy, aged 7 years, 5-day history unnoticed appeared rash filled liquids clustered, then broked and dried on the forehead, eyelids and nose; pain without fever, burning and headaches. On physical examination found erosion, crusting in the right ophthalmic region. History of UV exposure when swimming on the beach four days before the cutaneous lesions appear.

Case 4

A 12-year-old boy, said 3 days ago experience pain fluid filled lession clustered in the left chest distribute to the left arm. On physical examination found vesicles clustered in the thoracic region (dermatomes T4-T5). History of UV exposure when follow fun-bike five days before cutaneous lesions appear.

Case 5

A 14-year-old boy, a 5-day history of right side right headache and 4 day appeared a rash of multiple clusters liquids on the eyelid and right side of the forehead is mild and swollen. On examination found vesicular and crustal eruptions in the ophtalmic region. History of UV exposure when working on the field five days before skin lesions appear.

Case	Sex	Age (year)	Side	Regio/ Dermatom	Symptom	Vaccine varicella	has suffered from varicella age/ year	UV exposure before cutaneous appear	UV exposure
1	M	3	Right	Brachialic C5-T1	-	-	2,4 Years old	4 days	Swimming on the pool
2	F	7	Left	Ophtalmic	Burns	-	-	3 days	Playing on the beach
3	M	7	Right	Ophtalmic	-	-	-	4 days	Swimming on the beach
4	M	12	Left	Thoracic T4-T5	Pain burns	-	-	5 days	Fun bike event
5	M	14	Right	Ophtalmic	Swollen mild pain	-	-	5 days	Working on the field

Table 1: Conclusion of five cases of herpes zoster in children.

Discussion

Diagnosis of HZ is primarily clinical but can also be done with Tzank smear examination and to distinguish with herpes simplex can be done direct fluorescent monoclonal antibody test [2-5,10]. The case of HZ brakhialis that we observed was supported by Tzank smear examination and found multinucleated giant cells. The other four cases were diagnosed only clinically. All children treated with acyclovir 20 mg/ KgBB, four times daily for five days and symptomatic therapy for itching and pain [1-3].

The reactivation mechanism of VZV is not fully understood. It is believed that reactivation is the result of reduced cellular immunity specific to VZV, and periodic exposure to people with varicella or herpes zoster will enhance cell-specific immunity against VZV characterized by periodic subclinical reactivation. Many studies have shown no pattern of herpes zoster season, while other studies suggest a higher incidence in summer in the middle of the year, as a consequence of increased exposure to ultraviolet light [5,6]. The results of Wu et al. study found an increase in HZ incidence very strongly associated with UV. Recent research has reported an increase in the incidence of HZ in summer in countries with several different seasons of the year, this pattern is associated with UV peak summer exposure and possibly a HZ trigger [5-7,10,11]. All the children we reported experienced intense UV exposure 3-5 days before the cutaneous lesions appeared, so we concluded that UV exposure was the initiator of VZV reactivation. Although it is not argued that UV exposure can suppress immunity, it is clear that the way it works is very complex with the possibility of various pathways involved in local UV immunosuppression; an antigen is applied to the irradiated area, apparently local suppression due to contact hypersensitivity. This corresponds to the three

cases of ophthalmic HZ we observed. Whereas under systemic UV immunosuppression conditions, the antigen is applied to an unexposed area but no alteration in function or antigen presenting cells amount in the lymph node adjacent to the contact site with the antigen. Thus, there may be other types of cells or the release of mediators from the exposed area. Various mediators are produced in areas exposed from keratinocytes to other cells. The first possibility is a platelet activation factor that can bind to receptors in monocytes, mast cells and the release of keratinocytes and the release of prostaglandins. This is followed by the release of various cytokines, including interleukin (IL)-4 and IL-10, both of which are immunosuppressive. Other molecules are also found locally, such as histamine, progtaglandin, TNF-α, IL-1β, neuropeptides and neurohormones, which can have systemic effects [8,9,11,12]. The allegations above may explain the effects of immunosuppression in one patient observed which suffered from HZ thoracic, but UV exposure did not occur directly in the area of the rash due to a closed rash. Complementary systems are also involved. UV-activated C3 is important for skin infiltration by monocytes/ macrophages (CD11b + cells), which contribute to immunosuppression [9,11].

All of the above components have significant effects on the migration and function of some immune cells, some of which are involved in antigen presentation. Some Langerhans cells, the main antigen presenting cells in the epidermis, migrate into the lymph nodes by passing the exposed area, or if the UV dose is high, then it may experience apoptosis in situ. Dermis dendritic cells also migrate to the drainning of the lymph nodes. Specific monocyte / macrophage populations capable of producing IL-10, migrate into the skin and then to lymph node drainage when stimulated with antigen. The end result is thought to be an abnormal change of antigen presentation in the epidermis, dermis and lymph node drain. In the latter case, there is a decrease in the production of IL-12 and IL-23, a key cytokine that normally promotes the activation of immune cells including T cells and which is capable of reducing DNA damage due to UV exposure. Simultaneously, the T helper (Th1) cytokine level was reduced, and a group of regulatory T cells (Treg) were stimulated, specific to antigens found at exposure to UV. These cells have CD4 +, CD25 +, Foxp3 + and CTLA4 + phenotypes. They are cytotoxic for antigen presenting cells, producing IL-10 at activation and may suppress activation, cytokine production and the proliferation of other immunostimulatory T cells. There is also little evidence of the involvement of natural killer cells (NK), which secrete IL-4 during activation. These cells represent a unique collection of lymphocytes that express NK cell markers plus T cell receptors [9,12].

Although the number of infections in humans affected by UV radiation exposure is quite limited, the most interesting in the field of UV infection and radiation is the question of whether UV exposure can adversely affect the immune response to vaccination. Four animal models have indicated that UV radiation exposure has the ability to alter the efficacy of vaccination in such a way that the response/ memory response produced by the vaccine is significantly reduced. There is little research on human vaccination and little data is available today regarding infection protection [8].

Only one of the cases we observed had varicella at 2.4 years and on the C5-T1 dermatome. A study concluded that children younger than 2 years with varicella infections have the highest and most rapid risk of HZ. Other studies suggest that immune status at the time of primary infection is important in determining the presence of HZ in childhood. Low lymphocyte levels, NK cells and cytokines are found in infants, along with viral-specific immunoglobulins. All of these can cause an inability to keep VZV latency so that zoster arises early in children [3].

This serial case observation proves that UV exposure as one of the precipitating factors for HZ reactivation in immunocompetent children determines the education that should be given to the public regarding their exposure to UV to prevent HZ in children. Further observation in larger populations is still needed.

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