CASE REPORT

Palmar-Plantar Erythrodysesthesia in a young infant: a case report

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ABSTRACT

The Hand-Foot Syndrome or Palmar-Plantar Erythrodysesthesia (Palmoplantar Erythrodysesthesia) or Acral Erythema or chemotherapy-induced acral erythema or Burgdorf's reaction is a dermatological toxic reaction following chemotherary or biological therapies in patients (children or adults) with cancer. It is characterized by painful erythema of both palms and soles with symmetrically well-defined borders, which may progress to bullae formation and desquamation. In the literature, there is only one other case, concerning an adult patient who was treated with vancomycin. We report a case of an infant, aged 36 days old, with a Burgdorf reaction following administration of vancomycin. The clinical manifestations and the usual drugs involved in the aetiology of the syndrome are also described. The pathophysiology, histological findings, prognosis and treatment are discussed.

Keywords: Hand-Foot Syndrome, Palmar-Plantar Erythrodysesthesia (Palmoplantar Erythrodysesthesia), Acral Erythema, Burgdorf's reaction, vancomycin

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INTRODUCTION

The Hand-Foot Syndrome (HFS) or Palmar - Plantar Erythrodysesthesia (Palmoplantar Erythrodysesthesia) or Acral Erythema or chemotherapy-induced acral erythema or Burgdorf's reaction is a dermatological toxic reaction which can present initially as erythema, dysesthesias, and swelling of palms and soles, and can further progress to the stage of blisters formation and rarely ulceration [1,2]. This sequence of events can limit daily functions and may affect the patients' quality of life [2]. Vancomycin – HFS induced is extremely rare, with only one case report in literature [1].

CASE REPORT

A 36-day-old male infant presented to the hospital emergency room with fever (body temperature of 38.5°C). The parents reported him to have had irritability for the past 5 hours. From the clinical examination, the infant was

looking sick with mottled skin. From the laboratory test: WBC:7080/mm3 (Neutrocytes: 54%, Lymphocytes: 24%, Monocytes: 22%), PLT:316000/mm^3, CRP:7mg/l, biochemical pannel within normal limits. Cerebrospinal fluid analysis was negative for Central Nervous System infection. Blood cultures, urine culture (suprapubic aspiration) and cerebrospinal fluid culture were sterile. Chest X-ray was normal. Due to the young age of the patient and the severity of the clinical picture, indicating bacteremia, the infant was initially treated empirically with intravenous administration of cefotaxime (150mg/kg/day) and amikacin (15mg/kg/day). In the 30th hour of hospitalization, due to worsening of clinical status (critically ill patient, grunting, irritability, cold extremities, mottled skin, high fever, Capillary Refill Time (CRT)>3sec, hypotension (60/40mmHg) the initial treatment changed to intravenous administration of cefotaxime (200mg/kg/day) and vancomycin (40mg/kg/day) and amikacine was discontinued. Twenty-four hours after the onset of vancomycin administration, the young patient showed significant clinical improvement with no more grunting, hypotension or mottled skin. However, he demonstrated a peripheral edema on hands and legs [Figure 1], progressively worsening. A few hours later, there was a high degree of edema and erythema on his palms and soles. Fourty-eight hours after the onset of vancomycin, the patient had no more fever and his vital signs (blood pressure, heart rate, CRT) were normal but the edema and erythema of his palms and soles got worse. Both parents and doctors reported an increase in redness during the

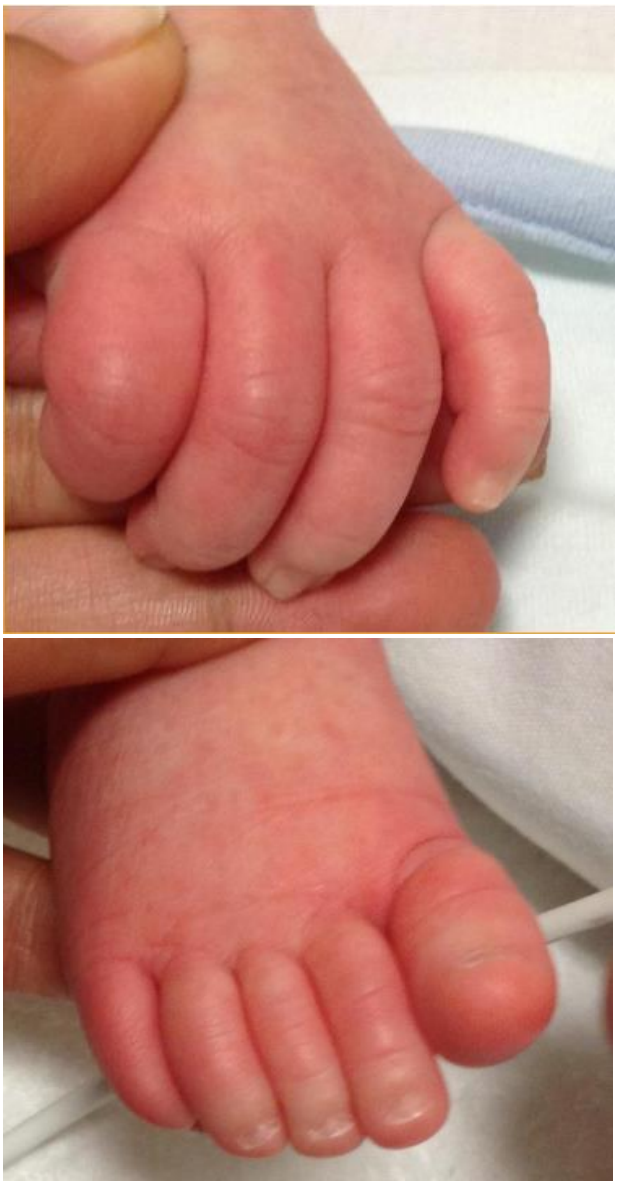

Figure 1. Peripheral edema on hands and legs.

infusion of vancomycin. As no systemic manifestations such as generalized erythema, rash, or hypotension were reported, we excluded the red man syndrome diagnosis and the Burgdorf reaction was considered as the most likely cause of edema and redness of the palms-feet. Consequently, vancomycin was discontinued. Cefotaxime was not interrupted and continued for 7 days. Following discontinuation of vancomycin, edema and

erythema gradually improved over the next 4 days without specific treatment.

DISCUSSION

Burgdorf's reaction was first decribed by Lokich and Moore in 1984 in a patient treated with 5-fluorouracil [3]. It is typically observed in patients with malignancies who are treated with chemotherapeutic or biological agents [2]. The most commonly responsible drugs are capecitabine, 5-fluorouracil, doxorubicin, doxorubicin liposomal and interleukin-2 [4]. Only one case of a patient on hemodialysis has been reported in the literature, in whom vancomycin was considered to be the inducing agent [5].

The initial manifestations are palmar-plantar dysesthesia and tingling sensation [2]. These can progress to painful symmetrical erythema, edema, bubbles, blisters, erosions and ulcers [2]. Exfoliation, often, is the most important point of the syndrome [2]. Most commonly, it is localized on the palms and soles although in severe cases, the dorsal surface of the hands and feet may be recruited, as well as the areas of pressure applied with clothing [2]. Lesions are usually symmetrical, but a case of unilateral HPS in a patient with hemiparesis has been reported [4]. In general, lesions occur within a few days, but may also occur after 2-4 weeks of the initiation of treatment [6].

According to the National Cancer Institute (NCI) there are three grades of Burgdorf's reaction:

- Grade 1: Minimal skin changes or dermatitis (e.g., erythema, edema, or hyperkeratosis) without pain.
- Grade 2: Skin changes (e.g., peeling, blisters, bleeding, edema, or hyperkeratosis) with pain, limiting instrumental ADL (activities of daily living).
- Grade 3: Severe skin changes (e.g. peeling, blisters, bleeding, edema, or hyperkeratosis) with pain, limiting self-care ADL [7].

The aetiology and pathogenesis are unknown, although several theories have been proposed. As lesions occur primarily at the extremities, many theories focus on vascular anatomy, cell differences (rapid cell division), eccrine glands and temperature gradients of these areas. The main hypotheses claim persistent microinjuries of the capillaries into palms and soles by mechanical stress due to daily activities, with subsequent extravasation of the drug and damage to the surrounding tissues. The essential role of that daily stress of the affected areas in the pathogenesis of this specific skin reaction is supported by the unilateral appearance of this reaction in a person with hemiparesis [4]. Burgdorf's reaction occurs when, due to damage of the cells or capillaries of these areas, the administered drug is extravasated and damages the surrounding tissues. Another possible mechanism is the higher concentration of the drug or its active metabolites in the palms and soles and its excretion in the sweat from the eccrine sweat glands in these areas (allegedly occurring with capecitabine and its active metabolite, 5 – fluorouracil) [5].

Histopathological examination is not specific. Necrotic and dyskeratotic keratinocytes and vacuolar degeneration of the basic layer are usually present. Histological findings depend on the degree of clinical severity [7].

HFS must be differentiated from other conditions, such as the graft- versus- host disease, erythema multiform and toxic epidermal necrolysis [7].

It is not considered an emergency condition and the prognosis is guarded. Overall, a severe grade of Burgdorf's reaction can have a significant influence on a patient's quality of life [7].

Early diagnosis is essential in order to apply the appropriate treatment on the patients. Our main handling is the discontinuation of the inducing pharmacologic agent in order to avoid the transition from the initial stages (I and II) to stage III, which could potentially cause permanent damage or death of the affected individuals. The patients respond positively to cold compresses, steroids and pyridoxine. The causative pharmacologic agent may be cautiously reintroduced in the future in a lower dose [8].

In conclusion, the most well-known reaction after vancomycin administration is Red Man Syndrome (or Red – Neck Syndrome). It is characterized by pruritus, erythema of the face, neck and upper torso and in severe cases, angioedema and cardiovascular collapse. It can be relieved by antihistaminic medication [8].

Burgdorf's reaction attributed to vancomycin administration has been reported in only one case: a 65-year-old patient in hemodialysis with fever and positive blood culture for methicillin-resistant staphylococci (MRSA) [5].

In our knowledge, after reviewing the available literature, our infant patient is the only case of pediatric population reported with Burgdorf's reaction after vancomycin administration.

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ΠΑΡΟΥΣΙΑΣΗ ΠΕΡΙΣΤΑΤΙΚΟΥ

Βρέφος με παλαμο-πελματιαία ερυθροδυσαισθησία: παρουσίαση περιστατικού

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ΠΕΡΙΛΗΨΗ

Το Σύνδρομο Χεριών-Ποδιών ή Παλαμο-πελματιαία Ερυθροδυσαισθησία ή Ερύθημα Άκρων ή Επαγόμενο από Χημειοθεραπεία Ερύθημα Άκρων ή Αντίδραση Burgdorf είναι μια τοξική δερματική αντίδραση που συχνά έπεται της χημειοθεραπείας ή της θεραπείας με βιολογικούς παράγοντες σε ασθενείς με καρκίνο. Χαρακτηρίζεται από επώδυνο ερύθημα των παλαμών και των πελμάτων, σαφώς καθορισμένο, το οποίο μπορεί να εξελιχθεί σε σχηματισμό φυσαλίδων και απολέπιση. Στη βιβλιογραφία υπάρχει καταγεγραμμένη μόνο άλλη μια περίπτωση ενήλικου ασθενούς που εμφάνισε το Σύνδρομο μετά από χρήση βανκομυκίνης. Περιγράφουμε την περίπτωση βρέφους ηλικίας 36 ημερών, που παρουσίασε την αντίδραση Burgdorf κατά τη διάρκεια θεραπείας με βανκομυκίνη. Περιγράφουμε επίσης τα κλινικά χαρακτηριστικά, τους συνήθεις φαρμακευτικούς αιτιολογικούς παράγοντες και την αιτιολογία του Συνδρόμου και αναλύουμε την παθοφυσιολογία, τα ιστολογικά ευρήματα, την πρόγνωση και τη θεραπεία του.

Λέξεις-ευρετηρίου: Σύνδρομο χεριών-ποδιών, παλαμοπελματιαία ερυθροδυσαισθησία, ερύθημα άκρων, αντίδραση Burgdorf, βανκομυκίνη

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