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CASE REPORT

Tale of an Atypical Herpes Zoster Mimicking Ecthyma and Perforating Dermatosis in Chronic Kidney Disease

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ABSTRACT

Introduction: Herpes zoster (HZ) is the prototypical cause of zosteriform dermatoses. Additionally, many infectious, inflammatory, and neoplastic conditions may mimic this distribution pattern. Immuno compromised patients, such as those with end-stage renal disease (ESRD), are predisposed to both infectious and reactive skin conditions. In these cases, HZ may present with atypical morphologies, leading to diagnostic challenges. This report presents a case of atypical herpes zoster in a patient with chronic kidney disease (CKD) showing dimorphic ulcerative ecthymatous lesions and crusted umbilicated papulonodules mimicking reactive perforating collagenosis (RPC). This report highlights the importance of histopathology in distinguishing these conditions.

Case Report: A 48-year-old male with stage - VCKD on haemodialysis, presented with acute onset of unilateral, multiple painful papulonodules culminating into ulcers over the right lower back and abdomen. The lesions were diverse ranging from punched out ulcersto umbilicated papules with central keratotic crusting. This evoked the differentials of ecthyma or segmental RPC. None of the past or present lesions were vesicular. Investigations revealed anaemia, deranged sugar levels and renal function parameters. Bacterial cultures showed no growth, while Tzanck smear demonstrated multinucleated giant cells. Skin biopsy revealed viral cytopathic changes and follicular involvement typifying herpes viral infection. The patient responded well to renal-adjusted acyclovir therapy, with significant improvement in symptoms and healing of ulcers.

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Conclusion: Atypical morphologies of herpes zoster, such as ecthymatous and that mirroring RPC, should be considered in immunosuppressed patients. Misdiagnosis as ecthyma or perforating dermatosis can delay appropriate antiviral treatment. Histopathology plays a crucial role in distinguishing HZ from its mimickers. This case underscores the need for heightened clinical suspicion while diagnosing atypical zoster and early intervention to prevent further complications in CKD patients.

KEYWORDS

• Herpes zoster • Zosteriform dermatoses • Ecthyma • Reactive perforating collagenosis

INTRODUCTION

Recognition of pattern or distribution of skin lesions is an indispensable clue in clinical dermatology. The zosteriform pattern is characterized by a unilateral and belt or girdle like portrayal of a dermatosis along the sensory nerve territory of a dermatome.[1] Although Herpes Zoster (HZ) is the prototype of zosteriform dermatoses, a multitude of other infectious, inflammatory, neoplastic and miscellaneous skin diseases may also demonstrate a zosteriform distribution. End stage renal disease (ESRD) is a severe entity which is the most sinister across the gamut of chronic kidney disease (CKD). The secondary immunodeficiency and structural changes in the skin that occur in a patient of CKD, predispose to the development of infections such as herpes zoster and ecthyma on one hand as well as reactive diseases such as perforating dermatoses on the other hand.[2] Herpes zoster may present an array of morphologies and distributions depending upon the immune status of the patient. While the peculiar morphology is typified by grouped vesicles and bullae on erythematous base, the distinct distribution is dermatomal. A dermatologist can face challenges in the diagnosis of HZ, when it presents with atypical morphologies or when the dermatomal distribution is illustrated by other similar looking entities, especially in the immuno compromised scenario.

We report this case of a middle-aged man with CKD, who developed rapidly progressive segmental ulcers and umbilicated lesions reminiscent of ecthyma or segmental acquired perforating dermatosis respectively, who was later diagnosed as a case of atypical herpes zoster showing significant response to acyclovir. This case report highlights the rare and atypical presentation of HZ in a patient with underlying immunosuppression (due to CKD) where histopathology and cytology ruled the roost and helped ascertain the diagnosis.

CASE REPORT

A 48-year-old male patient with stage V-chronic kidney disease (CKD) on treatment with hemodialysis, was referred from nephrology department, in view of multiple raw areas associated with burning sensation, over his right side of back and abdomen, since last 2 weeks. The lesions started as red-raised pea-sized lesions which later ruptured to form raw areas. There was history of on and off watery discharge from few of the ulcers. The patient did not have history of fever or fluid filled lesions prior to the onset of raw areas. There was no associated itching, bleeding or extrusion of whitish material. There was no history of similar episode in the past. There was no history of prior dermatological disease at the same site. Patient denied history of trauma, insect bite or irritant application. The patient had a past history of varicella in childhood. His medical comorbidities included uncontrolled type 2 diabetes mellitus, hypertension, hyperlipidemia, CKD with prior history of uremic encephalopathy and atherosclerotic peripheral vascular disease. His treatment history included, in addition to salt and fluid-restricted diet, bi-weekly hemodialysis, injection insulin, tablet amlodipine and tablet torsemide. On cutaneous examination, multiple dusky erythematous, brownish and grayish colored papules and nodules with central umbilication covered with scale-crust, ranging in diameter from 0.5 centimeter (cm) to 1.5 cm, were present over right lower back and right lower abdomen in dermatomal pattern. (*Figure 1a*) Multiple round-oval punched out

ulcers covered with yellowish slough and keratotic inflamed border, ranging in size from 0.5 cm to 3 cm in largest diameter, were present over the same region. (*Figure 1b*) Few varioliform atrophic brownish scars ranging in size from 0.5 cm-1 cm in greatest diameter, were present, admixed with the above lesions. Based on these findings, clinical differentials of ecthyma, zosteriform (segmental) perforating dermatosis and herpes zoster (with ecthymatous presentation) were considered. Gram stain showed polymorphonuclear cells without any organisms and bacterial culture sensitivity reports showed no growth. Tzanck smear cytology portrayed rounded acantholytic cells with multinucleate giant cells. His hemogram displayed low hemoglobin (7.4 grams/ deciliter [g/dL], normal leucocyte and platelet count. His renal parameters were deranged with serum creatinine value of 7.12 milligram/ dL (mg/dL) {reference range- 0.4-1.4 mg/dL}, blood urea value of 91.96 mg/dL (reference range - 15-45 mg/dL) and high sodium value of 148.04 millimole /liter (mmol/L) {reference range - 132-146 mmol/L) with low serum calcium (8.56 mg/dL) {reference range - 8.8-10.3 mg/dL). His blood sugar profile was deranged with random blood sugar value of 350 mg/dL). His virological markers for human immunodeficiency virus (HIV), hepatitis B virus and hepatitis C virus were negative. With the aforementioned clinical differentials, skin punch biopsy was done from two sites: one from the edge of the ulcer and the other from a papular lesion. The hematoxylin and eosin (H & E) stained section of the biopsy from an ulcer edge revealed presence of multinucleated epidermal giant cells along with a superficial and mid-dermal dense perivascular mononuclear cell infiltrate (*Figure 2a*). The biopsy from a papular lesion revealed, follicular involvement in the form spongiosis, acantholysis, margination of chromatin of keratinocytes along with mononuclear inflammatory cell infiltrate within follicular lumen (*Figure 2b*). These features were suggestive of herpes virus induced histopathological changes. Upon clinical correlation, a diagnosis of ecthymatous herpes zoster was made. The patient was treated with intravenous (IV) acyclovir in a dose of 5 mg/kilogram (mg/kg) of body weight per day in two divided doses for 3 days, followed by 200 mg twice a day orally for 5 days (renal corrected dose). Mupirocin 2% ointment was prescribed for topical application with a frequency of twice daily application. On the 10th post-treatment follow-up day, the patient depicted clinical improvement in his symptoms (burning and oozing) with significant healing of ulcers. The patients' renal and neurological functions were monitored during this treatment course to pick-up the signs of acyclovir induced nephrotoxicity or neurotoxicity.

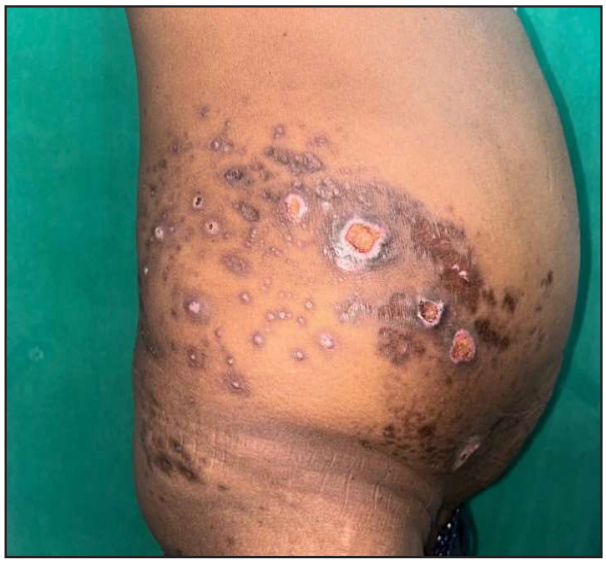

Figure 1 a: Multiple dusky erythematous, brownish and grayish colored papules and nodules with central umbilication covered with scale-crust present over right lower back and right lower abdomen in dermatomal pattern

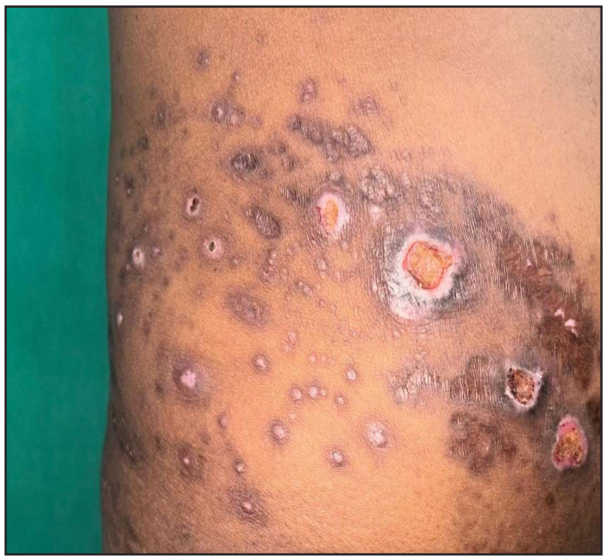

Figure 1 b: Multiple round-oval punched out ulcers covered with yellowish slough and keratotic inflamed border, ranging in size from 0.5 cm to 3 cm in largest diameter, present over right lower abdomen and lower back

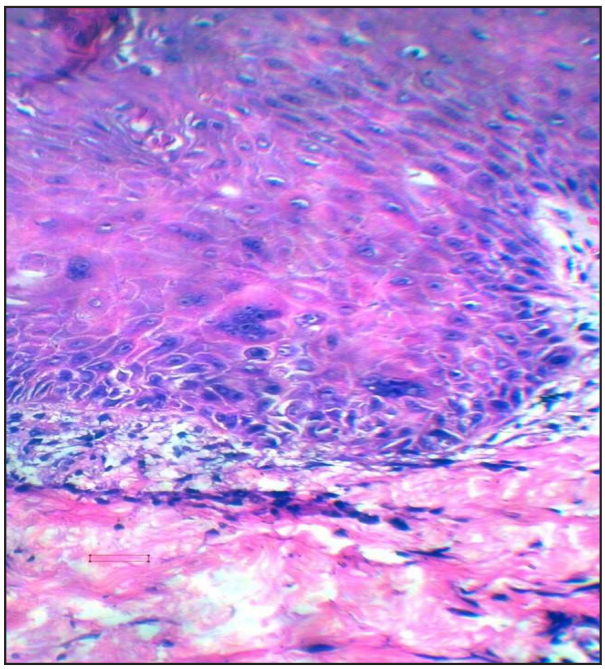

Figure 2 a: The hematoxylin and eosin (H & E) stained section of the biopsy from an ulcer edge showing, multinucleated epidermal giant cells along with a superficial and mid-dermal dense perivascular mononuclear cell infiltrate

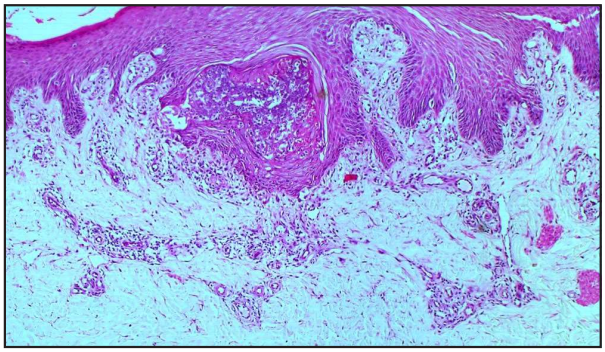

Figure 2 b: The biopsy from a papular lesion showing, follicular involvement in the form spongiosis, acantholysis, margination of chromatin of keratinocytes along with mononuclear inflammatory cell infiltrate within follicular lumen

DISCUSSION

Zosteriform dermatoses encompass a variety of dermatological conditions that manifest with a dermatomal distribution, with herpes zoster (HZ) being the most well-recognized entity. However, other infectious, inflammatory, neoplastic, and miscellaneous conditions may also exhibit a similar distribution, making clinical differentiation a challenge. Our case presents an atypical manifestation of herpes zoster with an ecthymatous morphology in a patient with chronic kidney disease (CKD), necessitating a thorough discussion on its distinction from other dermatomal conditions such as segmental reactive perforating collagenosis (RPC) and ecthyma/ecthyma gangrenosum (EG)[1].

Aplethora of conditions mimicking herpes zoster in distribution, but with different aetiologies and pathogenesis have been recognised. The neural pathway[3] involving an interplay of neurotropism and nerve cell-surface receptor interaction is implicated in HZ and neurotropic malignancies such as zosteriform metastatic breast cancer and squamous cell carcinoma. The blaschkoid pathway gives rise to dermatoses that follow embryonic cell-migration lines and account for a multitude of pigmentary, nevoid as well as mosaic conditions[1]. The isotopic response[4] is characterized by local neuro-immune dysregulation and altered responses or delayed hypersensitivity to varicella zoster virus that results in the dermatoses occurring at the site of previous HZ, the most common being granulomatous diseases. Some of the notable zosteriform dermatoses include inflammatory, granulomatous and autoimmune conditions like lichen planus, morphea, lichen aureus, granuloma annulare and sarcoidosis, infective conditions such as dermatophytosis (isotopic) and cutaneous leishmaniasis[5], diseases with a genetic predisposition such as Darier's disease andporokeratosis, neoplasms such as leukaemia, cutaneous lymphoma, metastatic breast cancer, melanoma and reactive diseases associated with metabolic comorbidities such as reactive perforating collagenosis (RPC)[1].

Our patient demonstrated dimorphic zosteriform lesions including umbilicated or crateriform papulonodular lesions with central crusting reminiscent of RPC and punched out ulcerated lesions with a rim of erythema, typical of ecthyma.

Segmental RPC is a rare variant of acquired RPC[6] frequently seen in patients with diabetes mellitus, CKD and chronic liver disease. It is characterized by umbilicated, keratotic papules resulting from transepidermal elimination of altered dermal collagen. Collagen alteration can result from microangiopathy and inflammation. Dermatomal distribution of RPC mimicking HZ, may stem from localized alteration of collagen turnover, probably as a result of nerve mediated factors or isotopic

phenomenon at the site of previous zoster[7]. This clinically raises the possibility of RPC being mistaken for a chronic or resolving phase of herpes zoster, further complicating clinical evaluation[8].

In our patient with stage V-CKD, few lesions which clinically resembled segmental RPC, but he was in turn diagnosed to have HZ. Unlike zoster, RPC lesions persist chronically (cf. our patient had acute onset and short duration of lesions), are associated with mild trauma and/ or itching (cf. our patient had burning sensation) and do not show viral cytopathic changes on histology (as described in our case)[8] Histopathological examination, as subsequently discussed differentiates RPC from HZ by demonstrating trans epidermal elimination of altered collagen, rather than showing viral cytopathic effects typical of herpetic infection[9].

In addition to the above-described lesions, our patient also had oval, punched out ulcers redolent of ecthyma, without prior vesicular lesions. He also denied history of prior zoster at the same site. Ecthyma, commonly caused by *Streptococcus pyogenes*, presents as ulcerative lesions covered with necrotic crusts. A more severe variant, Ecthyma Gangrenosum (EG), is classically associated with *Pseudomonas aeruginosa* bacteraemia and occurs predominantly in immunocompromised patients, such as those undergoing chemotherapy, organ transplant recipients or CKD[10].

Although our patient did not have a history of typical grouped vesicles on erythematous base, evocative of zoster, clinical soft cues such as dermatomal distribution of ulcers helped differentiate our case from ecthyma, wherein the lesions wouldhave been randomly scattered[10]Additional points of distinction between ecthyma and zoster include presence of eitherstreptococci or Gram-negative (pseudomonas) bacilli in smears orbacterial cultures in the former, and Tzanck cellsalong with multinucleated giant cells in the latter (as found in our patient)[11]. Moreover, from treatment point of view, ecthyma and EG respond to systemic antibiotics, while antivirals such as acyclovir or valacyclovir are required to treat HZ.

Gilson *et al* reported ecthymatous herpes zoster as an uncommon presentation of HZ, predominantly encountered in immunosuppressed individuals, including those with CKD and HIV[12]. Other atypical forms include disseminated herpes zoster and long-standing ulcerative lesions, primarily reported in advanced HIV cases where the immune suppression is profound. These presentations often lack the typical vesicular morphology, mimicking ecthyma, chronic ulcers, deep fungal infections or even neoplastic conditions[13,12]compared to previously reported cases of HZ in HIV positive individuals[14], our patient, although immunosuppressed due to CKD, did not exhibit disseminated disease and had a well-defined dermatomal distribution, suggesting a role of localized immune dysregulation.

Histopathology played a key role in confirming the diagnosis in our case. One of the skin biopsies of our patient exhibited acantholysis and chromatin margination involving follicular keratinocytes. Studies by Walsh *et al*[15] have shown that follicular involvement is more commonly seen with varicella zoster virus than with herpes simplex virus. The other biopsy demonstrated presence of multinucleated epidermal giant cells. The above changes helped us clinch the diagnosis of herpes zoster, upon clinical correlation. Diverse histological changes described in zoster include-dense perivascular (as seen in our case) and sparse interstitial infiltrates of lymphocytes and at times focal lichenoid infiltrates, deeper infiltrates involving subcutaneous tissue, lymphocytic folliculitis (cf. follicular involvement in our case) and perifolliculitis, lymphocytes within sebaceous or eccrine glands, perineural lymphocytic infiltrate, lymphocytic exocytosis into the lower epidermis, spongiosis with or without vacuolar alteration, necrotic keratinocytes within follicular lumen (cf. acantholytic cells, intra-follicular infiltrate seen in our patient), papillary dermal oedema with dilated blood vessels, red blood cell extravasation, some admixed neutrophils within the infiltrate and few atypical lymphocytes.[9] Contrary to above findings, histology of EG shows bacterial colonies and vascular necrosis (EG article), while that of RPC shows cup shaved invagination of epidermis, epidermal perforation, trans-epidermal elimination of altered collagen with focal basophilic staining character and irregular epidermal acanthosis.[2]

Although polymerase chain reaction (PCR) performed on lesional samples as well as on

paraffin blocks, serology for varicella zoster virus (VZV) and immunostaining for VZV seem lucrative diagnostic modalities[9], these tests have limited utility in resource-poor settings (as in our case).

In our case, diagnosis was confirmed based on a combination of clinical dermatomal distribution, histopathological findings, and Tzanck smear positivity for multinucleated giant cells. Unlike previously reported cases relying solely on clinical diagnosis, our case highlights the critical role of histopathology in ruling out mimickers like EG and segmental RPC. Misdiagnosis in such cases may lead to inappropriate treatment; for example, antibiotics alone would be ineffective in herpes zoster, while delayed antiviral therapy may prolong the disease course and increase complications. In our case, prompt administration of acyclovir led to significant improvement, underscoring the importance of timely intervention.

Another critical aspect is the immunosuppressive state of CKD patients, which may contribute to both the atypical morphology and increased susceptibility to herpes zoster. As a corollary, the authors emphasize the rolevaccination in CKD patients to reduce the risk of herpes zoster reactivation. Additionally, CKD patients often have altered pharmacokinetics, necessitating dose adjustments of antiviral therapy to prevent toxicity. In our case with stage - VCKD, renal adjusted acyclovir dosing was employed.[16]

CONCLUSION

This case underscores the necessity of considering atypical herpes zoster presentations in immunosuppressed patients, particularly those with CKD. The distinction from segmental RPC and ecthyma/ EG is crucial due to differing therapeutic implications. Histopathological examination remains a cornerstone for accurate diagnosis, especially when clinical morphology deviates from the classic vesiculobullous presentation. This report highlights the need for awareness of ecthymatous herpes zoster as an entity and reinforces the importance of early recognition and appropriate antiviral treatment in immuno compromised individuals.

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