

# Severe atypical herpes zoster as an initial symptom of fatal myelodysplastic syndrome with refractory anemia and blast excess (RAEB II)

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**Abstract:** Herpes zoster is a common disease caused due to varicella zoster virus (VZV) infection with increasing incidence by age. If the patient has a severe, extended, or treatment-recalcitrant course of herpes zoster, this must be a red flag to search for underlying pathologies. Here, we report about a 64-year-old male patient with diabetes, who came to our emergency department because of general malaise, fever, chills, and a pronounced nuchal and facial swelling on the left side. Based on herpetiform-grouped vesicles and yellowish crusts, an impetiginized facial herpes zoster was diagnosed, and combined antiviral and antibiotic treatment was initiated. He was HIV negative. Despite intensified treatment, his situation worsened. We observed blasts in peripheral blood, but bone marrow biopsy was initially denied. Some days later after deterioration of his disease, he accepted further diagnostics. A myelodysplastic syndrome with blast excess (refractory anemia and blast excess II, RAEB II) could be confirmed. The following translocations were detected: t(2;12)(p13; q13) and t(6;9)(p22;q34). REAB II has an unfortunate prognosis. Cytoreductive treatment was initiated by the hemato-oncologist. Unfortunately, the patient deceased due to septic shock.

**Keywords:** herpes zoster, varicella zoster virus, myelodysplastic syndrome, sepsis, emergency

## Introduction

Herpes zoster is caused by varicella zoster virus (VZV). After a short prodromal stage, a dermatomal eruption of herpetiform-grouped vesicles develops due to reactivation of VZV within ganglia and their anterograde transport into axons innervating the skin. Common symptoms are pain, dysesthesia, and paresthesia.<sup>1</sup>

Severe zoster subtypes are characterized by ulcerations, necrosis, or dissemination, with or without vasculitis, paresis, central nervous system involvement, or involvement of other internal organs.<sup>1</sup> Facial edema is another possible symptom<sup>2</sup> (Table 1). Severe zoster infections are a red flag for serious underlying disorders such as infections, immunodeficiency, and malignancies.

## Case report

A 64-year-old male was admitted to our department as an emergency. He suffered from general malaise, fever, chills, and a pronounced nuchal and facial swelling on the left side. Since birth, he suffered from left-sided microtia with complete absence of meatus acusticus. His medical history was positive for diabetes mellitus type 2 treated by diet and an arterial hypertension controlled by 160 mg valsartan 160 mg/d.

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**Table 1** Differential diagnosis of facial swelling

Disorders	Remarks
Acute hemorrhagic edema	Children, after infections, vaccination or drug-induced
Allergic contact dermatitis	Due to aeroallergen or hair dyes
Angioedema	Acquired type (mast cell-related or bradykinin-induced); hereditary type with absolute or functional deficiency of C1 esterase inhibitor
Brachiocephalic venous compression, vena cava superior syndrome	Due to multinodal gout, after venous puncture, and due to tumors
Cushing syndrome, Mb. Cushing	Steroid-induced (syndrome) ACTH overproduction, buffalo hump
Drug induced	Eg by folic acid antagonist pemetrexed or dipeptidyl peptidase 4 inhibitor vildagliptin, periorbital
Erysipelas	Fever, erythema, hyperthermia
Lepra	Facies leontina
Lymphedema	Secondary after surgery and/or irradiation of head-and-neck cancer
Mb. Morbihan	Solid facial erythema with rosacea (Glabella, cheeks, lids)
Strangulation	Strangulation marks
Subcutaneous emphysema	After trauma, skin crackling
Lymphomas	Fever, hepato-splenomegaly, fatigue
Posttraumatic/postsurgery	Medical history
Zygomycosis	Rhino-cerebral type, hyposmia, nasal secretions

**Abbreviation:** ACTH, adrenocorticotrophic hormone.

**Figure 1** Initial presentation of the patient with temporal herpes zoster.

On examination, we observed a left-sided head-and-neck edema with herpetiform-grouped vesicles around the left ear and on the nose and yellowish crusts and formation of bullae in the perioral region (Figures 1 and 2). Laboratory findings were remarkable for leukocytosis with a white blood cell count of 25.7 (normal range: 3.8–11.0), thrombocytopenia of 64 Gpt/L (120–340), lowered hematocrit of 0.245 L/L (0.40–0.54), hemoglobin of 5.1 mmol/L (8.6–12.1), erythrocyte count of 2.5 Tpt/L (4.6–6.2), neutrophilia

**Figure 2** Perioral bullous impetigo, herpetiform vesicles on the nose.

of 13.8 Gpt/L (1.8–7.6), lymphopenia of 11% (20–45), increased number of large unstained cells with 2 Gpt/L (0–0.40), and C-reactive protein (CRP) of 333 mg/L (<5). HIV tests were negative.

Before submission, antibiotic treatment with sultamicillin was started and continued after submission at a dosage of 3 × 3 g/d intravenously (iv). The facial swelling, however, worsened. Therefore, the patient was referred to our Ear Nose Throat-department for diagnostics. Diagnostic ultrasound and thoracic computerized tomography (CT) were performed to exclude a bacterial or mycotic abscess formation.

With the diagnosis of impetiginized herpes zoster, antibiotic treatment was changed to 3 × 800 mg clindamycin/d plus aciclovir 3 × 500 mg/d. Pain management was realized using metamizole sodium 3 × 30 gtt/d. During the following days, only a minor clinical improvement was seen. In the peripheral blood, 11% blasts were noted. A bone marrow biopsy was suggested, but the patient refused.

The further course was characterized by malodorous oozing, formation of bullae, and increasing edema. On the left chin and left submandibular region, firm infiltrates were noted, and skin biopsies were taken to exclude specific infiltrates of a malignancy. Histopathology, however, was nonspecific, demonstrating only a putrid inflammation. Vesicles showed dissemination suggesting zoster generalisatus (Figures 3 and 4). Accordingly, we increased the dosage of aciclovir to 10 mg/kg (3 × 1000 mg/d) iv. The pain sensations become worse, and pregabalin was started in increasing doses. Certoparin sodium 3000 I.E. anti-Xa/d was injected subcutaneously for thrombosis prophylaxis.

Nevertheless, the situation did not improve. CRP increased to >400 mg/L, leukocytosis of 28.4 Gpt/L developed, and procalcitonin increased to 3.65 ng/mL (normal range: 0–0.5).



**Figure 3** Increased facial edema and necrotic herpes zoster lesions.



**Figure 4** Generalization of herpes zoster vesicles.

Under the suspicion of septicemia, we transferred the patient to the intensive care unit. Central venous access was realized by a subclavian catheter. The patient was treated by 4.5 g piperacillin, 500 mg levofloxacin, 1000 mg acyclovir every 8 hours, and initially 100 mg prednisolone. During the treatment course, he developed doughy stool; therefore, the antibiotics was changed to vancomycin 4 × 500 mg per os. Stool samples for *Clostridium difficile* remained negative. Clinical improvement was accompanied by reduction of vesiculation and edema.

After patient consent, CT and bone marrow biopsy were performed. Bone marrow analysis disclosed atypical myelopoiesis, reduced atypical erythropoiesis, and micromegakaryocytic megakaryopoiesis with 10% of bone marrow blasts confirming a myelodysplastic syndrome (MDS) refractory anemia and blast excess II (RAEB II). Chromosomal analysis and cytogenetics revealed a karyotype 46/XY and translocations t(2;12)(p13; q13) and t(6;9)(p22;q34). Due to anemia, erythrocyte concentrates were required.

Two weeks after admission, the patient suffered from pain in his right arm. The skin surrounding the subclavian catheter became erythematous. Therefore, the catheter was removed, but microbial cultures of the tip remained negative. Venous duplex sonography disclosed vena subclavia thrombosis and soft tissue hematoma.

In the following days, oozing of the scalp and the ear helix was observed. Microbial swabs identified *Pseudomonas aeruginosa*.

We intensified diuresis because of a progressive edema. Hemato-oncologist initiated cytoreductive treatment with azacitidine. Anemia and thrombocytopenia required erythrocyte and thrombocyte concentrates. Herpes zoster persisted. During intravenous infusion of varicella immunoglobulin, the patient developed an anaphylactic shock, which could be managed by intensive care. Six days later, the patient died due to a septic shock.

Written informed consent has been obtained from the patient before his tragic outcome to have the case details and any accompanying images published.

## Discussion

In most cases, the diagnosis of herpes zoster can be confirmed clinically by the presence of herpetiform-grouped vesicles and unilateral localization within a dermatome, in combination with pain and paresthesia.<sup>3</sup> In the present case, a severe zoster with delayed and minimal response to treatment was the red flag for a serious underlying disorder in a patient previously healthy and capable. Antiviral drug therapy was modified accordingly during the course.<sup>4</sup>

Further diagnostics were initially delayed due to patient refusal for bone marrow biopsy. But afterward, the diagnosis of MDS was confirmed.

MDS is accompanied by an increased risk of zoster infection. A recent study using data of Surveillance, Epidemiology and End Result (SEER)-Medicare data base calculated an odds ratio of 1.31.<sup>5</sup>

MDS with RAEB is characterized by an increased mortality. RAEB I is defined as a peripheral blast excess <5% and bone marrow blasts <10%, without Auer rods. RAEB II shows peripheral blasts >5% and bone marrow blasts >10%, and Auer rods may occur.<sup>6</sup> Mean survival of patients with MDS REAB-II is ~16 months.<sup>7,8</sup> Translocation t(6;9)(p22;q34) worsens the prognosis with a mean survival of 12 months.<sup>9</sup>

Severe atypical zoster is a red flag. Patients need a workup for serious underlying diseases. Unfortunately, improvement of individual prognosis is not always possible.

## Disclosure

The authors report no conflicts of interest in this work.

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