



Vesicular herpes zoster eruption following chronic obstructive pulmonary disease treatment in the emergency department: lessons learnt from immunosuppression

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Background: Herpes zoster (HZ) is a reactivation of the varicella-zoster virus (VZV) that can occur in people with weakened immune systems. Chronic obstructive pulmonary disease (COPD) is a chronic lung disease that can also impair the immune system.^{6–8}

Case presentation: The authors present the case of a 65-year-old male with COPD who developed HZ. The patient was initially admitted to the hospital for an acute exacerbation of COPD. After his condition stabilized, he developed vesicular rashes on the medial aspect of his left leg. A skin biopsy confirmed the diagnosis of HZ.

Clinical discussion: This case report provides further evidence that HZ can be induced in patients who are undergoing treatment for COPD. The authors recommend that COPD patients be vaccinated against HZ to prevent this complication.

Conclusion: HZ can develop in COPD patients, mainly using inhaled steroids. Compliance to medication should be monitored, on the other hand zoster vaccination should be provided to prevent it and its foremost complication which includes secondary bacterial infection, post-herpetic neuralgia, scarring, nerve palsy and encephalitis in case with disseminated zoster.

Keywords: COPD, Herpes zoster, Vaccine, covid, emergency medicine, emergency department

Introduction

Herpes zoster, commonly known as shingles, is a viral syndrome caused by the reactivation of the varicella-zoster virus (VZV). This condition manifests as a painful rash that typically affects the chest and abdomen but can occur anywhere on the body, including the face, eyes, and genitals^[1]. The varicella-zoster virus remains dormant in the sensory ganglia of the cranial nerve or the dorsal root ganglia following primary infection with varicella, also known as chickenpox. Herpes zoster primarily affects adults or the elderly, whereas varicella is more commonly observed in children^[1].

The Centers for Disease Control and Prevention (CDC) estimates that approximately one in three individuals will experience shingles at some point in their lives^[2]. The reactivation of the

HIGHLIGHTS

- Chronic obstructive pulmonary disease (COPD) patients are at an increased risk of developing herpes zoster (HZ) due to their weakened immune system, which can be further compromised by inhaled corticosteroids commonly used for COPD treatment.
- The association between COPD and HZ has been supported by various case reports and studies, indicating a higher prevalence of HZ in COPD patients compared to the general population.
- Herpes zoster can lead to complications such as post-herpetic neuralgia, pneumonia, and secondary bacterial infections in COPD patients, emphasizing the need for timely diagnosis and management.
- Vaccination against HZ, such as the zoster vaccine live (ZVL), is recommended for COPD patients to prevent HZ and its complications. However, careful evaluation of the patient's overall health status and potential contraindications should be considered before recommending vaccination.

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Sponsorships or competing interests that may be relevant to content are disclosed at the end of this article

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Annals of Medicine & Surgery (2024) 86:1659–1663

Received 10 July 2023; Accepted 24 December 2023

Published online 11 January 2024

<http://dx.doi.org/10.1097/MS9.0000000000001698>

varicella-zoster virus is influenced by various factors, such as compromised immune status, autoimmune diseases (e.g. rheumatoid arthritis, systemic lupus erythematosus, Crohn's disease), long-term use of corticosteroids, advancing age, underlying conditions like HIV, and malignancy^[3]. Although there are some evidences regarding the association between herpes zoster and these risk factors, it is crucial to identify them to facilitate the timely and appropriate management of this condition. Herpes zoster can lead to numerous complications, including chronic

pain (post-herpetic neuralgia), which significantly impacts an individual's daily life and can be further complicated by anxiety and depression in certain cases^[4].

Chronic obstructive pulmonary disease (COPD) is a lung condition characterized by breathing difficulties and encompasses conditions such as emphysema (damage to the air spaces in the lungs) and chronic bronchitis (long-term inflammation of the airways). Smoking is a major contributor to the development of COPD, but exposure to fumes and dust (e.g. silica dust, coal dust, flour, grain dust, welding fumes) also plays a role^[5]. COPD is a chronic, incurable disease, and recent research has suggested its potential involvement in the eruption of herpes zoster^[5]. The presence of a case demonstrating the incidence of herpes zoster in COPD patients prompted the writing of this case report, aiming to shed light on this association among clinicians. This report adheres to the CARE (CAse REport) guidelines for clinical case reporting^[6].

The diagnosis of COPD is based on the Global Initiative for Chronic Obstructive Lung Disease (GOLD) criteria such as^[15]:

Stage I: mild, FEV1/FVC < 70%, FEV1 ≥ 80% predicted (post-bronchodilator test).

Stage II: moderate, FEV1/FVC < 70%, 50% < FEV1 < 80% predicted (post-bronchodilator test).

Stage III: severe, FEV1/FVC < 70%, 30% < FEV1 ≤ 50% predicted (post-bronchodilator test).

Stage IV: very severe, FEV1/FVC < 70%, FEV1 ≤ 30% predicted (post-bronchodilator test).

Airway inflammation in COPD is an amplified immune response resulting from prolonged exposure to irritants like cigarette smoke. Case control study by Fachri and colleagues revealed significantly higher levels of ADAM33 mRNA and soluble ADAM33 in COPD patients compared to non-COPD individuals. These findings suggest ADAM33's potential as a biomarker and therapeutic target for COPD-related inflammation^[16].

COPD is associated with an increased risk of developing shingles. This is because COPD patients often have weakened immune systems or due to inhaled corticosteroids, which makes it more likely that the VZV virus will reactivate^[2]. The reactivation of the VZV virus can cause a painful rash that typically appears on one side of the body. The rash can be accompanied by fever, headache, and other symptoms. In COPD patients, shingles can be a serious illness. This is because the rash can spread to the lungs, causing pneumonia. Shingles can also lead to post-herpetic neuralgia, a chronic pain condition that can last for months or even years^[7–9].

The relationship between herpes zoster (HZV) and COPD has been explored in several case reports and case series. For example Thomsen *et al.*^[7] conducted a case series of 10 COPD patients with HZV, finding that the patients were all older adults with a long history of COPD, and that the rash was more likely to occur on the chest or back. Wang *et al.*^[8] published a case report of a COPD patient with HZV who developed pneumonia, likely caused by the HZV rash spreading to the lungs. Safonova *et al.*^[9] described a case of a COPD patient with HZV who developed post-herpetic neuralgia, a severe and long-lasting pain condition. Moreover, Yawn *et al.*^[10] conducted a retrospective study of COPD patients with HZV, finding that the patients were more likely to have a severe course of HZV than the general population. The CDC states that the risk of HZV is 2–3 times higher in COPD patients than in the general population^[2].

In this case report, we present a distinctive case of herpes zoster in a 65-year-old male patient with COPD, contributing to the growing body of evidence regarding the association between these two conditions. By exploring the pathophysiology and potential risk factors, we aim to enhance the understanding of herpes zoster in COPD patients among clinicians, leading to improved management strategies and prevention of complications.

Case report

Case presentation

A 65-year-old male presented to the emergency department with a chief complaint of cough with sputum production for the past 15 years, shortness of breath for 7 years, and swelling of lower limbs for 3 months. The patient had a history of chronic smoking for ~30 years, consuming an average of 20 cigarettes per day, and occasional alcohol consumption. He followed a non-vegetarian diet.

The cough was insidious in onset, on and off in nature, and progressively worsened over time. It was associated with the production of copious amounts of mucoid sputum, ~2 cups full per day, which was non-foul smelling and non-blood mixed. The cough episodes lasted for about 3–4 months once they started. Shortness of breath developed 7 years ago, initially occurring only during strenuous activities (Grade 1 according to MMRC), but gradually progressed to the point where breathlessness was experienced even during ordinary daily activities, such as leaving the house or dressing/undressing (Grade 4 according to MMRC) in the past 15 days. Rest provided relief, while exertion aggravated the symptoms. There was no history of orthopnea or paroxysmal nocturnal dyspnoea.

The patient also reported swelling of both lower limbs for the past 3 months. The swelling appeared insidiously, was painless, worsened on assuming an upright posture for a long time, and partially improved on lying down. One week prior to presentation, the patient experienced mild intermittent fever, which was not documented and was not associated with chills or rigour. There was no history of chest pain, noisy breathing, or weight loss. The patient denied any significant past medical history of tuberculosis, diabetes mellitus, hypertension, asthma, or neurological disorders.

On examination, the patient appeared ill-looking and cachectic. Vital signs were stable, with a respiratory rate of 27/min, regular, and abdomino-thoracic. There were no signs of pallor, icterus, lymphadenopathy, clubbing, cyanosis, or dehydration. Pitting type oedema was present in the lower limbs, and the jugular venous pressure was elevated at 10 cm of H₂O.

Systemic examination revealed a normal upper respiratory tract. Chest examination showed bilaterally symmetrical chest movement, but diminished bilaterally. The patient demonstrated increased depth of the supraclavicular fossa and suprasternal notch bilaterally. Use of accessory muscles of respiration, particularly the sternocleidomastoid, was noted. The patient had a respiratory rate of 27/min, regular, thoracic-abdominal type. There were no visible scar marks, pulsations, or venous prominence. Palpation revealed no local rise of temperature or tenderness. The anteroposterior and transverse diameters of the chest were 22 and 27 cm, respectively (AP < transverse). There was decreased chest expansion bilaterally (<1 cm) with a

centrally placed trachea. Tactile vocal fremitus was normal. Percussion of the lungs yielded a resonant note in all areas. Auscultation revealed decreased breath sounds bilaterally with prolonged expiration.

Cardiovascular examination showed an apex beat shifted outward, ~1 cm lateral to the midclavicular line in the fifth intercostal space, along with the presence of epigastric pulsation and left parasternal heave. Auscultation revealed normal heart sounds (S1S2) with no murmurs. Abdominal examination was unremarkable. Percussion of the abdomen indicated liver dullness starting at the fifth intercostal space. The central nervous system examination was intact.

Investigations and diagnosis

Investigations such as routine blood investigations, chest X-rays, arterial blood gases (ABG), and electrocardiograms (ECG) were performed and found to be within normal limits. The patient was managed in the emergency department with supportive oxygen therapy at a rate of 2 l/min via nasal prongs. Nebulization with salbutamol, ipratropium bromide, and normal saline cocktail (1:1:2) was administered. The patient received a stat dose of hydrocortisone 100 mg, followed by twice-daily doses. The diagnosis of an acute exacerbation of COPD was made based on GOLD criteria, and the patient was admitted to the medical ward for further observation and management.

Management

Two days after admission, the patient developed vesicular rashes over the medial aspect of his left leg near the knee joint (L4 dermatome) (see Fig. 1). The rash was associated with pain, tingling, and itching sensations. The patient was diagnosed with herpes zoster and prescribed acyclovir 800 mg four times daily for 7 days, levocetirizine 5 mg at bedtime for 7 days, topical calamine lotion twice daily for 7 days, and paracetamol 1000 mg as needed after consulting with senior medical staff. The patient was discharged with these medications and advised to follow-up in a week. However, the patient did not appear for the scheduled follow-up, and further management and outcomes could not be assessed. Figure 2 shows the clinical course of the patient.

Discussion

COPD is a preventable and treatable disease characterized by progressive airflow limitation and an abnormal inflammatory response of the lungs to noxious particles or gases, primarily caused by cigarette smoking^[11]. It is a chronic condition that significantly impacts respiratory function and quality of life. In recent years, studies have indicated a potential association between COPD and the reactivation of HZ or shingles. We previously conducted a comprehensive literature review on the association of asthma and herpes zoster and the role of vaccination^[12].

Several studies have highlighted the increased risk of HZ in individuals with COPD^[10-13]. A study conducted in the United States involving 735 respondents found that 26.1% of them reported previous episodes of HZ, with 25.5% reporting increased COPD symptoms during HZ episodes^[10]. Another study in Taiwan, involving 8,486 COPD patients and 33 944 matched control patients, demonstrated that patients with COPD



Figure 1. Image of our patient showing herpes zoster rash the medial aspect of his left leg near the knee joint (Lumbar 4-L4 dermatomal distribution).

had a higher risk of developing HZ compared to those without COPD. The study also found that herpes zoster was slightly greater for patients with COPD using oral steroids than inhaled steroids, possibly due to immunosuppression^[8]. These findings suggest a potential link between COPD and the development of HZ.

The precise mechanisms underlying the association between COPD and HZ reactivation are not yet fully understood. However, it is believed that the chronic inflammation and immune dysregulation associated with COPD may contribute to the reactivation of the varicella-zoster virus (VZV) responsible for HZ. Additionally, the use of inhaled corticosteroids, commonly prescribed for COPD management, has been proposed as a potential triggering factor for HZ eruption and exacerbation^[9].

Herpes zoster vaccines have been developed to prevent HZ and its complications. The first licensed vaccine, zoster vaccine live (ZVL), was approved for use in the USA in 2006 by FDA. Studies have shown the effectiveness of ZVL in preventing

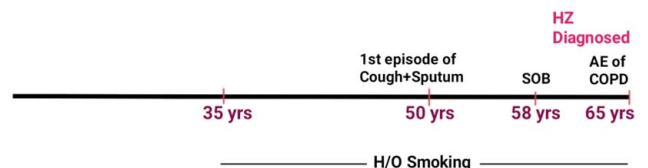


Figure 2. Clinical course of the patient; AE, indicate Acute Exacerbation; COPD, chronic obstructive pulmonary disease; HZ, herpes zoster; SOB, Shortness of Breath.

hospitalization due to HZ and post-herpetic neuralgia (PHN) in adults^[14]. A study conducted in New Zealand on indigenous people found that ZVL reduced the risk of hospitalization due to HZ and PHN in both immunocompetent and immunocompromised adults^[14]. Since the FDA approval the vaccine is licensed in almost 90 countries. Initially, it was approved for older than or equal to 60 years of age but in July 2021 it was updated to be given to adults 18 years and older who are at risk of HZ^[9].

Despite the potential benefits of HZ vaccination, the specific management of HZV in individuals with COPD requires careful consideration. Patients with COPD may have unique challenges and considerations when receiving vaccinations due to their compromised respiratory function and potential medication interactions. Therefore, it is crucial for healthcare professionals to assess the individual's overall health status, vaccination history, and potential contraindications before recommending HZ vaccination.

The management of HZ in individuals with COPD should also address the acute symptoms and complications associated with HZ, such as pain, post-herpetic neuralgia, and secondary bacterial infections. Antiviral therapy, such as acyclovir, is the mainstay of treatment for HZ and should be initiated within 72 h of symptom onset to reduce the duration and severity of the disease. Pain management with analgesics, such as acetaminophen or nonsteroidal anti-inflammatory drugs (NSAIDs), can help alleviate discomfort. In some cases, the use of opioids may be necessary for severe pain control^[7–11].

Furthermore, comprehensive patient care should include strategies to manage COPD exacerbations and optimize respiratory function. This may involve the use of bronchodilators, corticosteroids, oxygen therapy, and pulmonary rehabilitation programs. Regular follow-up visits are essential to monitor the patient's respiratory status, provide ongoing support, and adjust treatment as needed with special attention for HZ eruption in risk groups in both inpatients and outpatients follow-up.

Finally, there is growing evidence of an association between COPD and the reactivation of herpes zoster. Individuals with COPD may be at an increased risk of developing HZ, and the use of inhaled corticosteroids for COPD management may contribute to HZ eruption, likely due to immunosuppression. Vaccination against HZ can be an effective preventive measure, but careful consideration of individual health status and potential contraindications is necessary. Management of HZ in COPD should focus on antiviral therapy, pain management, and comprehensive COPD care to optimize respiratory function and improve patient outcomes.

Conclusion

In conclusion, this case highlights the association between chronic obstructive pulmonary disease (COPD) and the development of herpes zoster (HZ) in older individuals. The patient's history of long-term smoking and occasional alcohol use, along with the use of inhalant bronchodilators and corticosteroids, may have contributed to the development of COPD and subsequent HZ reactivation and eruption, perhaps because of immunosuppression. The management involved supportive care, bronchodilator therapy, corticosteroids, and specific treatment for HZ with antiviral medication. The patient's subsequent development of HZ-related dermatomal rash underscores the need for

comprehensive care and awareness of potential complications in individuals with COPD. Further research is warranted to explore preventive strategies, including proper public health awareness and vaccination, especially in this population.

Ethical approval

Ethics approval is not required for case reports at our institution. (M Abdur Rahim Medical College, Dinajpur, Bangladesh).

Consent

June, 2023 I certify that, since the case report is not disclosing any patient data (his/her name, identifiable image etc.), they do not need to obtain any consent form for publishing it. So, the need for patient consent is waived.

Sources of funding

Not required as it is a case report.

Author contribution

All authors contributed equally.

Conflicts of interest disclosure

We have no conflicts of interest.

Research registration unique identifying number (UIN)

Not required as it is a case report.

Guarantor

Abhigan Shrestha.

Data availability statement

Data sharing is not applicable to this article as it is a case report.

Provenance and peer review

Not commissioned, externally peer-reviewed.

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