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Acute middle ear *Aspergillus niger* infection in a patient with Stevens–Johnson syndrome: a case report

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ABSTRACT

Rationale: Stevens-Johnson syndrome is a disorder mostly attributed to drug use, which can cause different skin problems.

Patient concerns: A 31-year-old woman presented with severe pain and pounding in the left ear.

Diagnosis: Fluconazole-induced Stevens-Johnson syndrome with fungal infection in ear.

Intervention: Surgical and systemic antibiotic therapy.

Outcomes: The patient recovered and resumed her normal life.

Lessons: The prescription of fluconazole for patients with underlying conditions should be done with caution.

1. Introduction

Stevens-Johnson syndrome (SJS), which is a rare disorder across different societies, is usually a medical emergency[1]. This lesion develops following the use of particular types of drugs[2]. Antibiotics, especially, like fluoroquinolones, anti-epileptic drugs, and non-steroidal anti-inflammatory drugs are among the most important medications inducing this syndrome[3]. Besides, genetic predisposition, such as polymorphism of the human leukocyte antigens, can also be involved in SJS[4]. Investigation of this condition usually takes several weeks to months, which depends on the intensity of the lesion. The annual mortality rate of SJS is as high as 34%[5]. In a study on 59 patients with toxic epidermal necrolysis and SJS, 55 (93%) cases were SJS cases notably, over 80% of these

cases had a history of medication use. Most patients (76%) had generalized lesions while the rest suffered the lesions limited to the head, neck, and upper limbs[6]. In a review study on 257 patients with SJS, there were no statistically significant differences between males and females (128 males and 129 females). These patients had a mean age of (56.6 ± 21.8) years, and 47.5% of them suffered different types of infectious diseases. It was concluded that patients with multiple infections had greater intensities of skin and eye diseases[7]. In a study investigating the ear, nose, and throat (ENT) problems among 49 individuals, 26 subjects (53%) had various problems, including purulent discharge and pain in the ear; however, the major problem was related to the oral mucosa. As infection is

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the main cause of death in these individuals, constant assessment of these lesions can be helpful[8]. Given the lack of report on aggressive ear infection in patients with SJS in Iran, in this investigation, the clinical signs and symptoms were described, and the course of diagnosis and treatment was examined in a patient with otomycosis caused by the use of fluconazole.

2. Case report

This research was approved by the Ethics Committee of Babol University of Medical Sciences (IR.MUBABOL.HRI.REC.1396.201). The informed consent was obtained from the patient.

A 31-year-old woman referred to an ENT specialist in Babol City, Iran on 5th September 2018 for severe pain and pounding (10 on visual analogue scale) and ear infection. According to her history, she had been suffering severe blisters in different parts of her body since nine years ago (2009), and even her mouth suffered from blisters after less than one day following taking two fluconazole pills, so she was treated with 150 mg daily dose of oral fluconazole for the treatment of oral candidiasis. She underwent a one-month hospitalization in Rouhani Hospital in Babol. After receiving the primary treatment, the patient suffered bilateral ear pain and hearing loss; afterward, she was examined four times by an ENT specialist. The problem in the right ear was resolved through ear cleaning and suction following the diagnosis of cerumen. Nevertheless, considering the persistence of the problem in the left ear which was in pain and itching for three months, she referred to the current specialist. In the microscopic examination, the ear cavity showed ulcers and discharge. With the deterioration of the lesions, bony coverage was involved, and the necrosed bone was visible. In the audiometry, a 35 dB gap was observed and recorded. The patient underwent general anesthesia (due to local anesthesia intolerance) on the 10th September 2018, whereby the necrosed tissue and granulation tissue were removed, and the patient was discharged the next day after recovery and a short rest. A part of the sample was sent to the laboratory for histopathology. In the direct examination test, fungal mycelia were observed. For precise identification of the fungal species, a part of the sample was cultured on Sabouraud Dextrose Agar medium (Merck, Germany) containing chloramphenicol, where the growth of *Aspergillus niger* was observed. This isolate was identified definitely by the PCR-RFLP method[9]. After the operation, pharmacotherapy using with ciprofloxacin tablets (500 mg/BID), acetaminophen-codeine, and topical miconazole were initiated.

Two months after the surgery, the pain was completely resolved (visual analogue scale=0-1), and the pus and the swelling were completely removed; however, the tympanic membrane was repaired after graft by temporalis fascia; and temporal bone, external auditory canal bone was good covered by using skin graft. After controlling the fungal infection of the patient with topical antifungal drugs, she was a candidate for tympanomastoidectomy and canaloplasty. The



Figure 1. Recovery of the ear canal in case of fungal infection with Stevens-Johnson syndrome after three months of surgery.

patient condition was stabilized three weeks after the surgical and systemic antibiotic therapy, and following three months after the surgery, the previous hearing loss was resolved. The skin of the ear canal was restored, and the reconstructed tympanic membrane (eardrum) was visible after the graft (Figure 1). At the moment, the patient had no problem in her ears and resumed her normal life.

3. Discussion

SJS is an important disorder which is associated with various skin lesions across the body[8]. Although this disease is rare, due to its severe complications, the ear canal could be affected alongside other skin problems. The present case report dealt with Stevens-Johnson disorder which occurred in the ear following the use of fluconazole tablets and caused extensive skin damage and loss of a significant portion of the tympanic membrane. Typically, the skin lesions caused by this disease are manifested after a short period of time. Skin blisters was the first complication after the patient taking fluconazole tablets. However, ear problems emerged approximately two months later. In this case, although these symptoms were improved, to some extent, with the right ear following symptomatic treatments (cleaning and suction), the left ear failed to respond to the treatment. The main stimulating factors of these lesions are drugs[2,3]. Besides, antibiotics, especially anti-tuberculosis fluoroquinolones, penicillin drugs, and anti-epileptic drugs are important factors that can cause SJS. Some previous studies also reported the development of Stevens-Johnson lesions caused by fluconazole[10,11]. Nevertheless, SJS can be caused by different types of drugs[3,10]. A study reported a 25-year-old woman with HIV developed this disease following the initiation of antiviral therapy[12]. In another study on 49 patients, it was found that 53% of those with ear infections were female. In a review study, male to female ratio of patients with SJS was 1:1.3, while in another study, 52.5% of the affected patients were male[5]. In a study by Bequignon *et al.* on 49 patients, the mean age was 37 years (17-89) years[10]. In a review study by Patel *et al.* (2017) on 352 patients, the age of participants varied from 30 to 78 years[3]. Rahmati *et al.*[6] also indicated that 73% of the afflicted patients were adult. In the present report, the patient had also suffered from the symptoms since 22 year-old, The underlying factors of SJS include cancer, HIV, and kidney problems[10]; nevertheless, no

underlying factor was observed in the present case. The common ENT problem in patients with Stevens-Johnson lesions, which was also reported in the present case, as well as in many other studies. In an investigation, it was reported to be around 29% in severe forms^[10]. The patient under scrutiny in the present study presented degenerating symptom in the ear following a long time after the initial lesion; likewise, another study also stated that the duration of this lesions depends on its severity and may last from several weeks to months^[10]. As a study has indicated that infection can be a risk factor for severe Stevens-Johnson lesions^[7], the extensive infection of the tympanic membrane in the present study can be attributed to this problem. Fungi have been mentioned in limited cases as the factors developing an infection in individuals with SJS^[13]. In the present study, *Aspergillus niger* was also isolated from the culture of the ear tissue of the patient.

Conflict of interest statement

The authors report no conflict of interest.

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