

Mucormycosis prevalence in diabetic individuals in the northeast of Iran: a 10-year retrospective study

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Abstract

Background and objective: Currently, due to an increase in the number of individuals with immune deficiency, long-term chemotherapy, and underlying diseases, an appropriate situation has been provided for the development of opportunistic infections, including fungal infections. This study was conducted with the aim of evaluating clinical symptoms, laboratory findings, and the treatment outcome of mucormycosis in diabetic individuals.

Methods: In this cross-sectional retrospective study, all recorded cases of mucormycosis in the health centers of Gorgan city, northeast of Iran, in diabetic individuals were extracted during 15 years from 2002 to 2016. All information was extracted from patient-related records and then was analyzed. In the period from 2002 to 2016, 12 diabetic individuals with mucormycosis were referred to health centers.

Results: There were statistically significant differences in the categories of sex, residence, education, taking drug, addiction, diabetes status, methods of diagnosis, involved area with mucormycosis, treatment type of mucormycosis, and treatment outcome of mucormycosis. Furthermore, no statistically significant difference was observed in the categories of age, underlying diseases (other than diabetes), hospitalization, and diagnostic time.

Conclusion: Due to the rareness or lack of an appropriate diagnostic method, and in addition, due to lack of an appropriate treatment, attention should be paid to invasive mucormycosis in individuals with immunodeficiency.

Keywords: Diabetes, Gorgan, Iran, Mucormycosis

Introduction

Currently, due to an increase in the number of individuals with immune deficiency, long-term chemotherapy, and underlying diseases, an appropriate situation has been provided for the development of opportunistic infections, including fungal infections [1]. Mucormycosis, is one of the fungal infections that can cause disease in these individuals. Infection in susceptible people is usually initiated from the nasal cavity or lung alveoli [2]. Moreover, this disease is capable of causing vascular and tissue damages in the invasive form [3]. Based on the conditions of the host's immune system and the organ involved, the disease is divided into five main forms, including rhino-orbito-cerebral, pulmonary, cutaneous, gastrointestinal, and central nervous system, from which the rhino-orbito-cerebral is the most common and serious form [4]. Moreover, invasive rhino-orbito-cerebral and pulmonary mucormycosis are associated with a poor prognosis [5, 6].

Members of the Mucoraceae family cause mucormycosis, and its members include *Mucor* spp., *Rhizopus* spp., and *Absidia* spp. [7, 8]. These organisms are mainly transmitted by air and easily grown and found in nature. Furthermore, their spores are usually not pathogen, and only where predisposing factors are available can cause the disease [9]. The most common predisposing conditions for this disease include diabetes mellitus, metabolic acidosis, taking glucocorticoids, organ transplantation, hematologic malignancies, acquired immune deficiency syndrome (AIDS), and iron accumulation.

Today, type 1 diabetes is one of the common autoimmune diseases so that new cases are increasingly being reported worldwide [10].

Fungal infections after diabetic foot syndrome are the most common problem in diabetic individuals, especially in advanced cases [11-13].

Therefore, due to the high prevalence of diabetes and the high mortality rate of mucormycosis in individuals with underlying diseases, this study was conducted with the aim of evaluating the prevalence rate of mucormycosis in diabetic individuals with emphasis on clinical symptoms, laboratory findings, and the treatment outcome.

Materials and Methods

Ethical considerations

This study was approved by the Ethics Committee of the Golestan University of Medical Sciences, Gorgan, Iran (Ethical Code: 151029). All personal information of the individuals remained confidential.

Study design

In this cross-sectional retrospective study, all reported cases of mucormycosis in diabetic individuals documented at the health centers of Golestan Province, the north of Iran, were evaluated during 15 years from 2002 to 2016. All information was extracted from patient-related records and then was analyzed.

Data analysis

Data was analyzed by IBM-SPSS v16 software (IBM SPSS Inc., Armonk, NY, USA) using statistical tests including two-tailed t-test and chi-square, and the results were considered significant where the statistical difference was < 0.05 .

Results

In the period from 2002 to 2016, 12 diabetic individuals with mucormycosis were referred to the health centers in the north of Iran. Information extracted from the records of

these individuals has been presented in Table 1. Three methods were used for these 12 mucormycosis cases, 9 of which were detected by biopsy method, and this method was more efficient than other ones.

Table 1. The variables and their frequency in diabetic individuals infected with mucormycosis

| Variable | Category | Number (%) | P-value |
|-------------------------------------------|---------------|------------|---------|
| Age | ≤ 60 | 5 (41.66) | > 0.05 |
| | > 60 | 7 (58.33) | |
| Sex | Man | 4 (33.33) | < 0.05 |
| | Woman | 8 (66.67) | |
| Residence | Rural | 4 (33.33) | < 0.05 |
| | Urban | 8 (66.67) | |
| Education | Literate | 2 (16.67) | < 0.05 |
| | Under diploma | 4 (33.33) | |
| | Diploma | 5 (41.66) | |
| | Academic | 1 (8.33) | |
| Underlying diseases (other than diabetes) | HTN | 2 (16.67) | > 0.05 |
| | IHD | 2 (16.67) | |
| | COPD | 1 (8.33) | |
| | HTN/HLP/IHD | 1 (8.33) | |
| | HTN/IHD | 1 (8.33) | |
| | HTN/CKD | 1 (8.33) | |
| | None | 4 (33.33) | |
| Taking drug | Insulin | 5 (41.66) | < 0.05 |
| | Metformin | 5 (41.66) | |
| | Antibiotic | 1 (8.33) | |
| | None | 1 (8.33) | |
| Addiction | Yes | 4 (33.33) | < 0.05 |
| | No | 8 (66.67) | |
| Diabetes status | Controlled | 3 (25) | < 0.05 |

| | Not controlled | 9 (75) | |
|------------------------------------------|----------------------------------|-----------|--------|
| Hospitalization | ≤ 30 | 5 (41.66) | > 0.05 |
| | > 30 | 7 (58.33) | |
| Diagnostic time^a | ≤ 7 days | 6 (50) | > 0.05 |
| | > 7 days | 6 (50) | |
| Methods of diagnosis | Smear/culture | 2 (16.67) | < 0.05 |
| | Biopsy | 9 (75) | |
| | Biopsy and CT ^b scan | 1 (8.33) | |
| Involved region with mucormycosis | Mouth | 1 (8.33) | < 0.05 |
| | Nose | 1 (8.33) | |
| | Paranasal sinus | 2 (16.67) | |
| | Orbit | 2 (16.67) | |
| | Lung | 5 (41.66) | |
| | Skin | 1 (8.33) | |
| Treatment of mucormycosis | Amphotericin B | 4 (33.33) | < 0.05 |
| | Amphotericin B/surgery | 7 (58.33) | |
| | AmphotericinB/Surgery/Antibiotic | 1(8.33) | |
| Treatment outcome of mucormycosis | Improved and discharged | 9 (75) | < 0.05 |
| | Transferred to other center | 1 (8.33) | |
| | Expired | 2 (16.67) | |

Discussion

In many developing countries, the problem of increasing drug resistance in fungi to standard medicines on the one hand, and the lack of facilities for a definitive diagnosis on the other hand, makes it difficult to assess early detection of invasive fungal diseases while the number of individuals with immunodeficiency is increasingly being reported. After candidiasis and aspergillosis, mucormycosis is the third most common cause of invasive fungal infection. Spores from this group of fungi enter in the nasal and

lung cavities through inhalation, and in subjects with immunodeficiency or a neutrophil functional disorder such as those with diabetes, tissue invasion may be observed. In this matter, the most frequently reported genus is *Rhizopus* spp. [14]. Clinical manifestations may be often observed in the form of rhino-orbito-cerebral or rhino

cerebral, but they can invade the lung, gastrointestinal tract, and rarely other organs, and can even be manifested as systemic infection [6, 15]. Effective chemoprophylaxis has not yet been known for mucormycosis and, in fact, the use of prophylactic regimens,

including fluconazole and voriconazole, increases the risk of this disease. Apart from Amphotericin B, Posaconazole is the only new antifungal agent against this disease. The total mortality rate of mucormycosis is 49%, while in the local forms the mortality rate is 41.9% and individuals with disseminated infection usually die [6, 16].

One of the reasons why mucormycosis is likely to be increased in people with diabetes is the presence of excess sugar in the body, providing conditions for these fungi to grow and replicate easily in the diabetic individuals' body. On the other hand, uncontrolled diabetes due to the presence of acidic substances in the blood provides appropriate growth conditions for these fungi, especially the genus *Rhizopus* spp. [17].

In a study on 22 diabetic individuals with mucormycosis, one quarter of the cases were found with immunodeficiency. Only 20% of the cases were identified by culture and the diagnosis was mainly based on biopsy [18], like what has been reported in the present study. It seems that in diabetic individuals with mucormycosis, early diagnosis, early surgery and necrotic tissue removal, appropriate antifungal therapy, and control of risk factors such as diabetes are the main parameters for successful management of this infectious disease [19]. It appears that the mortality rate of individuals with pulmonary mucormycosis is about 76% [20], while researchers in a study found that a lower mortality rate occur in individuals with only bronchial involvement due to the limited extent of the disease to the bronchial area [21].

Diagnosis of this disease is difficult because these fungi are not properly stained by routine laboratory stains and does not grow easily in

the culture medium. The reliable diagnostic method for this fungus is microscopic examination [20]. The average time for diagnosis from the onset of the disease is about 16.2 days [22]. In the current study, this time was not different in two examined groups of ≤ 7 days and > 7 days.

conclusion

In conclusion, one of the most important issues in the treatment of individuals with mucormycosis is the timely diagnosis of the disease, which is often delayed due to the rareness or lack of an appropriate diagnostic method, and in addition, due to lack of appropriate treatment, the prognosis is often poor. In spite of this, the treatment outcome is related to several risk factors and should be remarkedly considered. Finally, attention should be paid to fatal diseases with low prevalence in individuals with immunodeficiency such as invasive mucormycosis.

Conflict of interest

The authors declare that they have no conflict of interest.

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