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Esophageal Aspergillosis in Acute Leukemia Remitted by the Combination of Amphotericin B and Flucytosine

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= 국문초록 =

Amphotericin B와 Flucytosine로 치유된 급성 백혈병 환자에서의 식도 국균증

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아스페르길루스 감염증은 주로 백혈병과 같이 면역 기능이 저하된 환자에서 호발하며 주로 폐나 부비동 등에 호발하며 식도에만 단독으로 발생하는 경우는 매우 드물다. 저자들은 관해 유도를 받은 급성 골수성 백혈병 환자에서 합병된 식도 아스페르길루스 감염증을 경험하였다. 아스페르길루스는 식도 내시경 및 생검 조직 소견으로 확진하였고 amphotericin B와 flucytosine을 병합 투여하여 성공적으로 치유되었다. 저자들은 국내 최초로 식도 아스페르길루스증 1예를 보고하는 바이다.

Key Words: Aspergillosis, Esophagus, Leukemia

Introduction

Invasive aspergillosis is one of the important infectious complications in leukemic patients[1-3]. Unless early diagnosis and treatment are instituted, it can ultimately lead to irreversible and fatal outcome[4-6]. There are a number of reports about invasive aspergillosis mainly involving respiratory tract or paranasal sinus, etc., but those of esophageal involvement are very rare[7-10]. We report a case of esophageal aspergillosis complicating in a patient with acute leukemia which was successfully eradicated by medical therapy.

Case Report

A 50-year old man was admitted to our hospital with acute myelogenous leukemia, FAB-M2. Physical examination on admission revealed no remarkable findings. The white blood cell count was 15,800/mm^3 with a differential of 19 mature neutrophils, 17 monocytes, 17 lymphocytes, and 47 blast cells. The hemoglobin was 11.6g/dl and the hematocrit was 36.2percent. The platelet count was 392,000/mm^3. The blood chemistry

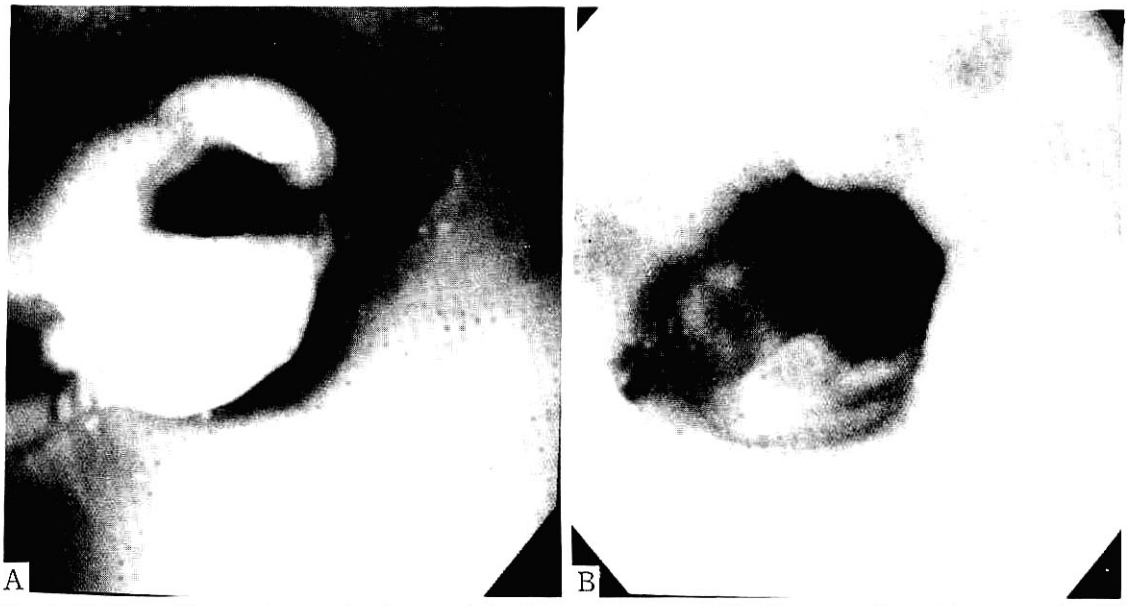

Fig. 1. (A) Gastrofiberscopic examination revaled a large mass surrounding lower esophageal lumen on day 30 after chemotherapy.
(B) One month after intensive antifungal therapy, the mass was eradicated.

Fig. 2. Esophagogram showed stenosis of lower esophagus.(arrow heads)

was normal. An electrocardiography and a chest roentgenogram were normal. Induction chemotherapy including idarubicin (12mg/m^2 for 3 days), cytosine arabinoside(200mg/m^2 for 7 days), and 6-thioguanine (100mg/m^2 for 7 days) was done. Bone marrow biopsy on day 7 after initiation of induction chemotherapy revealed incomplete remission. Augmentation chemotherapy (cytosine arabinoside 200mg/m^2 for 3days) was followed. Follow-up bone marrow biopsy showed Mo marrow on day 21. The patient was well until he complained odynophagia on postchemotherapy day 30. The granulocyte count was still below 1,000/mm^3 at that time. Endoscopic evaluation showed gastric ulcer and huge mass surrounding cardiac junction 36 cm from incisor teeth(Fig. 1A). Esophagogram showed signigicant stenosis of esophagus(Fig. 2). Plain chest film showed no remarkable abnormalities at that time. Endoscopic biopsy of esophageal mass revealed finding of dichotomously brancing septate hyphae which strongly suggested aspergillosis(Fig. 3). *In situ* hybridization for cytomegalovirus and herpes simplex virus in order to scrutinize the other possible causes of esophagitis turned out to be negative(data not shown). Amphotericin B(1mg/kg per day) and flucytosine (50mg/kg three times a

Fig. 3. Biopsy of esophageal mass revealed dichotomously branching septate hyphae with acute angle(silver methenamine stain×400).

day) were immediately administered and the odynophagia was improved thereafter. Serial endoscopic follow-up with one week's interval showed progressive reduction of esophageal mass size. One month after, the mass was cleared up on endoscopy(Fig. 1B), and follow-up biopsy showed clearing of aspergillosis.

Discussion

Aspergillus species is one of the most life-threatening fungal pathogen complicating leukemic patients[1-4]. Respiratory tract involvement is the main feature, but gastrointestinal tract especially esophagus is the extremely rare site of invasion.

There are only a few reports of esophageal aspergillosis which were not isolated esophageal involvement but coexistent with pulmonary aspergillosis[7,10]. The rarity of esophageal involvement might be due to: (1) the development of chemotherapeutical modalities followed by qualitative improvement of supportive care and of surveillance, (2) more empiricalavailability of antifungal agents such as amphotericin B and/or flucytosine.

The reason why this patient was presented as isolated esophageal aspergillosis without pulmonary involvement is unknown. The mucosal damage by acidic reflux or mucositis induced by cytotoxic chemotherapeutical agents could be a cause of mucosal barrier destruction which might have resulted in colonization of Aspergillus species. Prolonged neutropenia before the onset of aspergillosis might contribute to this process as well. The negative results of *in situ* hybridization could rule out another possible causes of co-infection, such as herpes simplex virus, cytomegalovirus, etc.

Despite of no remarkable symptoms and signs except odynophagia, the total 2g dose of amphotericin B was given systematically early because: (1) amphotericin B is the mainstay of antifungal agent against aspergillosis until now, (2) surgical removal could be impossible and risky, (3) relief of patient's symptoms such as swallowing difficulty and odynophagia by reducing the size of obstructing mass were necessary, (4) it can lead to fatal outcome such as tracheo-esophageal fistula[9] or aorto-esophageal fistula[10] unless early treatment is initiated. In addition, we also used flucytosine in expectation of achieving a synergistic antifungal effect. Fortunately, the patient were tolerable to the agents and did not suffer from any toxicities. He showed excellent

response to medical treatment, and the mass was cleared up within a month, which was confirmed by the follow-up gastrofiberoptic evaluation.

Although there are a few reports about esophageal aspergillosis, this case, to our knowledge, may be the first record which was successfully treated by medical therapy.

Even though candida species or herpesviruses can be regarded as the main cause of esophagitis, we should not underscore the possibility of aspergillus infection. Whenever the granulocytopenic patient complains esophagitis symptoms, such as substernal discomfort, or odynophagia, or dysphagia, etc., endoscopic evaluation must be performed as soon as possible in order to institute the early treatment, if necessary, and to prevent possible fatal outcome.

Summary

We report a case of esophageal aspergillosis in a patient with acute myelogenous leukemia, M_2. To our knowledge, this is the first case of esophageal aspergillosis which was successfully treated by medical therapy.

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