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Case report

Acute myocardial infarction caused by coronary mucormycotic embolism

Sohei Kitazawa [a,*], Riko Kitazawa [b]

[a] Ehime University, Graduate School of Medicine, Department of Molecular Pathology, Japan
[b] Ehime University Hospital, Division of Diagnostic Pathology, Japan

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ABSTRACT

Described here is a rare cardiac complication attributed to mucormycosis in a 63-year-old woman who developed sudden cardiac arrest and pulmonary insufficiency in the course of being treated for acute monocytic leukemia (acute myelogenous leukemia, AML M5a). At autopsy, fresh thrombi were noted in the left pulmonary artery and the left atrium. Postmortem coronary angiography revealed complete occlusion of the circumflex branch of the left coronary artery, and histological examination showed a mucormycotic embolism in the corresponding portion. Multiple small mucormycotic thrombi were also noted in both coronary and pulmonary arteries with hemorrhagic infarction in the corresponding areas.

Introduction

With the increasing number of elderly patients receiving chemotherapy against malignancies and those undergoing hemodialysis attributed to diabetic nephropathy and declining renal function, hibernating opportunistic infections against immunocompromised hosts have contributed to the direct cause of death [1–3]. Mucormycosis is recognized as one of the three most common causes of deep-seated mycoses (candidiasis, aspergillosis, and mucormycosis) [4]. Although infrequent, once mucormycosis occurs its rapid progression and difficulty in reaching a definitive diagnosis result in its notably low survival rate [5]. Moreover, since its serologic diagnosis is more difficult than that of other fungi, autopsy is often a prerequisite to reaching a definitive diagnosis [4,6]. Clinically, mucormycosis, like aspergillosis, grows vascularly invasive and tends to form thrombi and emboli [7]. As a result, the patients present with a variety of clinical manifestations depending on the organ and site of thrombus/embolus formation [8–11]. We describe a case of acute myelogenous leukemia (AML, M5a) whereby the patient died suddenly due to mucormycosis-induced embolism in the left coronary artery.

Case presentation

A 63-year-old woman was admitted to the hospital presenting with week-long general fatigue, low-grade fever and nasal bleeding. On admission, severe anemia, an oral temperature of 37.5 C, blood pressure of 120/70 mmHg and pulse rate of 80 beats/min were noted. Lymph nodes enlargement and splenomegaly were not observed by physical examinations. Laboratory data revealed hemoglobin 7.8 g/dl, white blood cell count 81.9 $\times$ 10^9/L, monoblasts 85%, monocytes 12%, lymphocytes 3% and neutrophils 0%. The patient diagnosed with acute monocytic leukemia (AML, M5a), was treated with cytarabine plus daunorubicin chemotherapy for AML, M5a. The patient received no antimicrobial prophylaxis. On day 5 after admission, erythrocyte sedimentation rate, monitored daily for inflammatory change, had gradually accreted with dyspnea, and a chest X-ray showed bronchopneumonia and focal collapse of the left lung. Bronchofiberscopic examination revealed narrowing of the left main bronchus due to an edematous polypoid lesion. A biopsied specimen of the lesion revealed non-specific chronic inflammatory change of the bronchial epithelium. Cultured specimens of sputum and blood were sterile. On day 12, the patient complained of severe chest pain and dyspnea. A chest X-ray showed diffuse consolidation of the left lung and an electrocardiograph revealed ST elevation in II, III, aVf. The patient suffered cardiac arrest and died on the following day.

Postmortem findings

The body, in the post-therapeutic state of AML, M5a, was that of an emaciated old woman. The left lung showed hemorrhagic infarction and partial collapse due to a bloody mass in the left main bronchus and left pulmonary artery. Flat fungal embolism formation, 1.2 $\times$ 0.8 cm, was observed in the left atrium. A coronary angiogram at autopsy revealed complete obstruction of the left circumflex artery at its orifice (Fig. 1,

* Corresponding author.
E-mail addresses: kitazawa@m.ehime-u.ac.jp (S. Kitazawa), riko@m.ehimr-u.ac.jp (R. Kitazawa).

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arrows). Formalin-fixed slices of the heart ventricles revealed a hemorrhagic lesion on the posterolateral wall of the left ventricle (Fig. 2a). Histological examination of the corresponding lesion disclosed hemorrhagic infarction (Fig. 2b), and the coronary artery showed massive mucormycosis thrombus (Fig. 2c and d). Since the left circumflex branch is dominant in this patient, occlusion at left circumflex artery can explain the inferior myocardial infarction discovered at autopsy. Mucormycosis was constrictively confined to the lungs and the heart. No other remarkable pathological findings were observed, except for small remnants of leukemic cells in bone marrow. The polypoid lesion in the left main bronchus observed in the biopsy specimen was retrospectively assumed to indicate submucosal invasion by mucormycosis.

Discussion

Mucormycosis is a serious infection caused by a group of molds called mucormycetes [12]. While these fungi are widely present in soil, fruit, food, laboratories, and even in healthy skin, they are rarely pathogenic to healthy individuals [5]. Risk factors for mucormycosis include diabetes mellitus, severe burns, hematologic malignancies, steroid therapy, liver cirrhosis, chronic renal failure, and administration of deferoxamine (DFO) [13–15]. Two factors, namely immunocompromised condition, especially reduced neutrophilic cell number or function, and iron overload are thought to increase the risk of mucormycosis [15]. Indeed, in the present case, hematological malignancy itself, or associated with severely reduced neutrophilic cell number, and supplementary intake of an iron preparation for anemia before admission may all have been risk factors for mucormycosis. The major routes and modes of infection are rhinocerebral that begin in the sinuses and spread to the orbit and the brain; the pulmonary that involve necrotic foci and emboli in the lungs; the gastrointestinal that spread orally to the digestive tract; the cutaneous that originate from trauma sites; and the disseminated that spread to the entire body [16]. The rhinocerebral and the pulmonary forms are usually rapidly progressive [16]. Since mucormycosis is tissue- and vascular-invasive [9], the ensuing lesions often induce hemorrhagic infarctions and necrosis. In the present case, systemic examination at autopsy showed that the mucor was confined to the lungs and heart. It is therefore assumed that the disease started as pulmonary mucormycosis and that the mucoromycetes components then migrated hematogenously from the lungs to the left atrium, from there to the left ventricle, and then to the aorta, thus forming emboli in the coronary arteries just as the disease had begun to develop into a systemic form of mucormycosis.

Once mucormycosis develops, it is often fatal due to its rapid progression [5]. Early diagnosis and treatment are therefore crucial [17]. Definitive diagnosis by invasive techniques is, however, often difficult in patients with hematologic disorders because of the high hemorrhaging tendency [7]. Also, pulmonary mucormycosis is often difficult to differentiate from pulmonary aspergillosis because imaging findings and clinical picture are very similar [18]. While measurement of β-D-glucan, a major component of the cell wall of the majority of the fungi, is clinically useful in the diagnosis and follow-up of deep-seated mycosis, it is inutile in mucoromycetes composed of chitosan instead of β-D-glucan [4]. It is also difficult to isolate mucormycosis in routine fugal culture [5]. Indeed in the present case, not only did the biopsy sample fail to identify mucoromycetes, but routine laboratory culture from the biopsied specimen also gave negative results. Since autopsy is often the only method of reaching a final diagnosis, mucormycosis could be overlooked or underestimated in facilities with low autopsy rates. Recently a global guideline for the diagnosis and management of mucormycosis is proposed to early diagnosis to rescue the patients by prompt surgical intervention and appropriate anti-fungal drugs [19].

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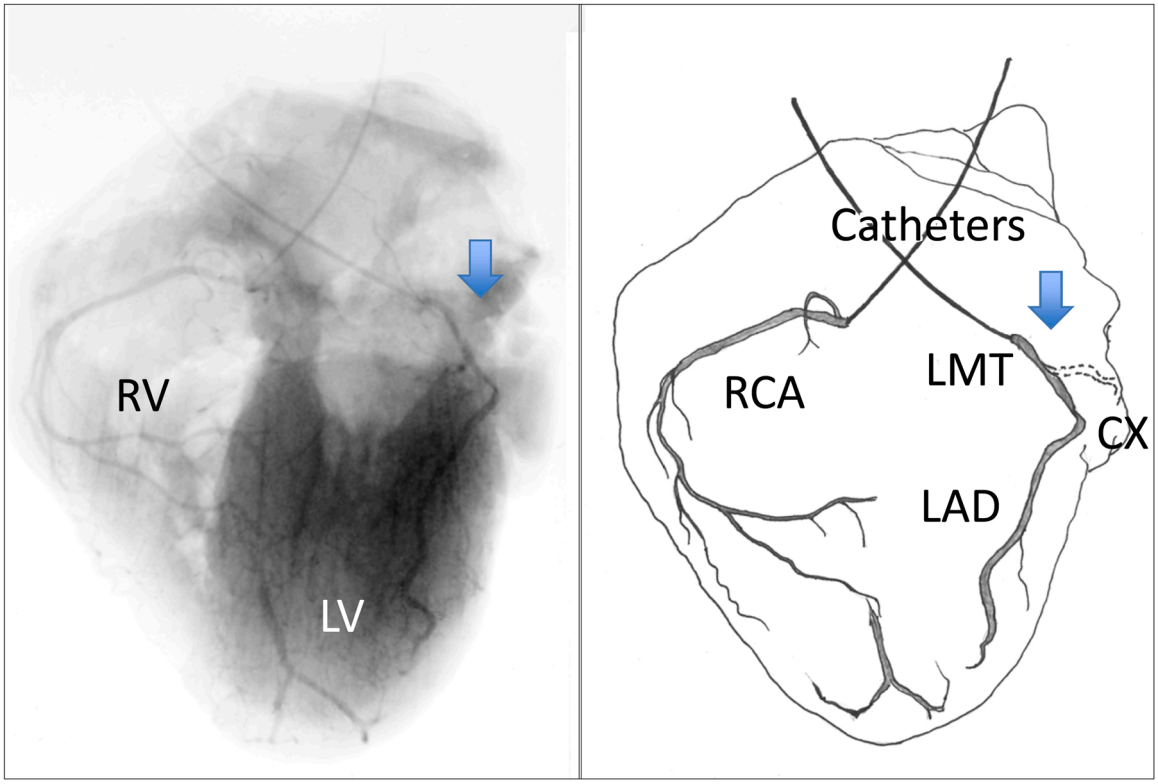

Fig. 1. Postmortem imaging of the coronary arteries by right anterior oblique position during both left main and right coronary artery (RCA) cannulation. Coronary angiograph at autopsy reveals the circumflex branch of the left coronary artery (CX) as totally occluded (arrows), while the left main trunk (LMT), the left anterior descending (LAD) branch and the right coronary artery (RCA) remain intact. RV: right ventricle; LV: left ventricle.

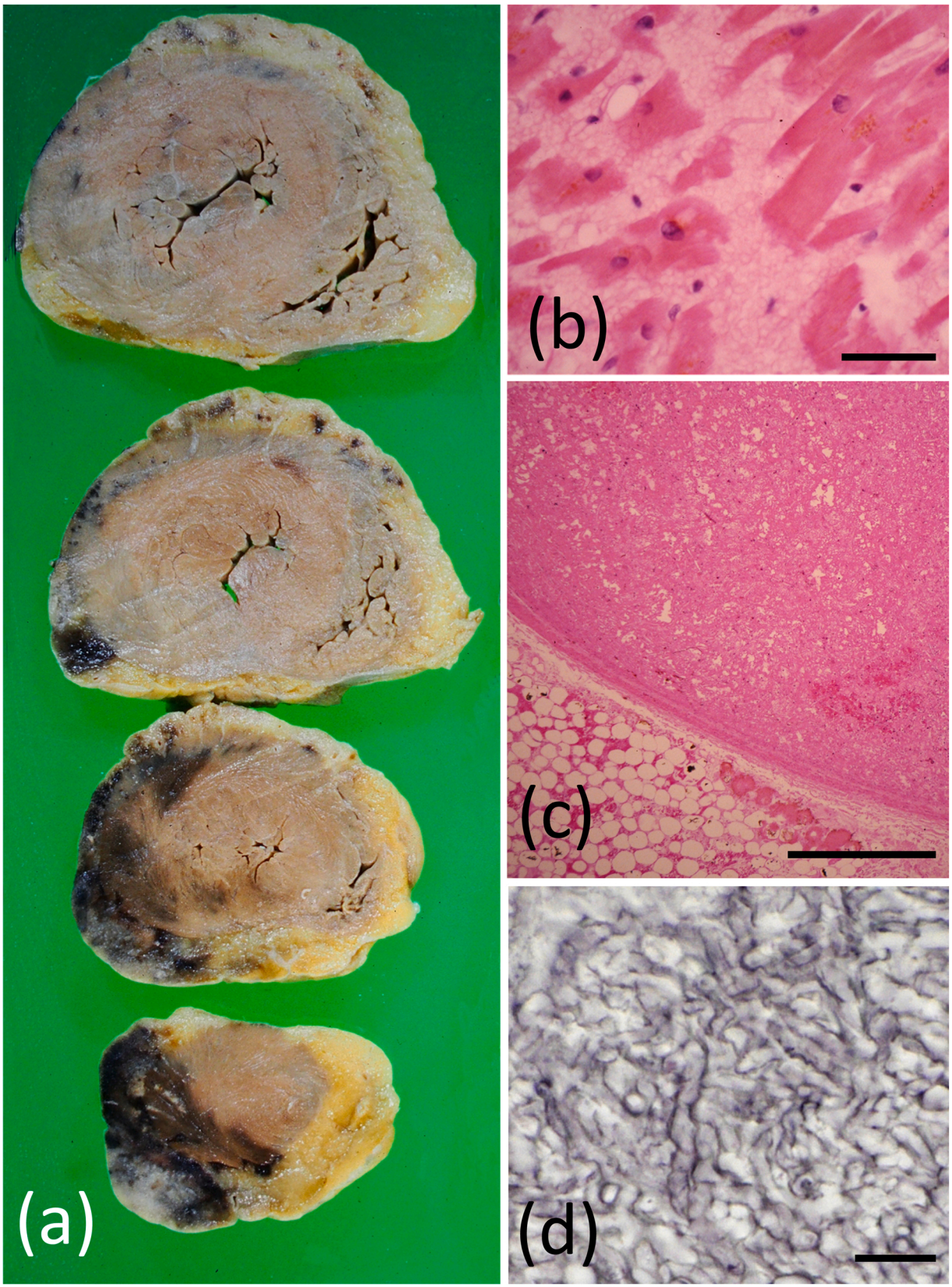

Fig. 2. Macroscopic and microscopic findings. After fixation, serial slices of the heart ventricles reveal a hemorrhagic lesion in the posterolateral wall of the left ventricle (a). Histological examination of the corresponding lesion shows hemorrhagic infarction (b, H.E., x400), and the corresponding circumflex coronary artery demonstrates massive mucormycosis thrombus (c, H.E., x40 and d, Grocott stain x400).

agencies, commercial, or non-profit sectors.

CRediT authorship contribution statement

Sohei Kitazawa, MD, PhD – Conceptualization, Writing, Autopsy and Histopathological analysis. Riko Kitazawa, MD, PhD - Conceptualization, and Histopathological studies.

Ethical approval

Not applicable.

Consent

Written consent was obtained from the patient's next-of-kin and included in the patient's medical record. This study as a case report did not require approval by an ethics committee.

Conflict of interest statement

The authors have no conflicts of interest to disclose.

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