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CASE REPORT

Consolato Sergi · Jürgen Weitz · Walter J. Hofmann
Peter Sinn · Andrea Eckart · Gerd Otto
Philipp A. Schnabel · Herwart F. Otto

Aspergillus endocarditis, myocarditis and pericarditis complicating necrotizing fasciitis

Case report and subject review

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Abstract A patient with *Aspergillus* endocarditis, myocarditis and pericarditis is described. A 55-year-old man developed necrotizing fasciitis of the lower abdominal wall, pelvis and right thigh. Despite aggressive surgical débridement and antibiotic coverage, the patient died of multisystem organ failure. Autopsy revealed *Aspergillus* thromboulcerative endocarditis, myocarditis and pericarditis, acute necrotizing fungal bronchopneumonia and mycotic dissemination to brain, kidney and thyroid gland. A review of the literature showed that in the absence of open-heart surgery *Aspergillus* endocarditis and myocarditis are very uncommon.

Key words Necrotizing fasciitis · Endocarditis · Myocarditis · Epicarditis · *Aspergillus*

Introduction

Necrotizing fasciitis is a relatively rare life-threatening soft tissue infection, frequently caused by a combination of multiple aerobic and anaerobic bacteria and characterized by rapidly spreading neutrophilic and lymphomonocytic cell inflammation, necrosis of the superficial fascia and subcutaneous tissue, and fibrinous necrosis of arterial and venous walls [32]. The release of exotoxins and endogenous cytokines by microorganisms trigger systemic effects, including renal, heart, and respiratory failure [29, 36]. In this milieu, patients with necrotizing fasciitis may be at elevated risk for overwhelming fungal infections.

Here we describe the postmortem findings of a patient affected with necrotizing fasciitis who presented with *Aspergillus* endo- , myo- and pericarditis, acute necrotizing fungal bronchopneumonia and mycotic dissemination to brain, kidney and thyroid gland.

Dedicated to Prof. Dr. G. Seifert, emeritus Director of the Institute of Pathology, University of Hamburg, on the occasion of his 75th birthday

C. Sergi · W.J. Hofmann · P. Sinn · P.A. Schnabel
H. F. Otto (✉)
Institute of Pathology, University of Heidelberg,
D-69120 Heidelberg, Germany
Tel.: (49) 6221-56 26 00, Fax: (49) 6221-56 52 51

J. Weitz · G. Otto
Department of Surgery, University of Heidelberg, Heidelberg, Germany

A. Eckart
Institute of Neuropathology, University of Heidelberg, Heidelberg, Germany

Clinical history

A 55-year-old man, who was non-diabetic and negative for human immunodeficiency virus (HIV), was admitted to a local hospital for treatment of a perianal abscess. Surgical drainage was performed on the same day and a first-generation cephalosporin therapy was commenced. On the 2nd postoperative day the patient developed fever, and cultures of débrided tissue revealed *Staphylococcus aureus* and *Escherichia coli*, but without pulmonary manifestation by chest X-ray. On the 5th postoperative day the patient became hypotensive and was transferred to the Department of Surgery at Heidelberg University Hospital. Physical examination and computed tomography scanning showed necrotizing fasciitis of the lower abdominal wall, pelvis, perineum, retroperitoneum and proximal internal regions of the right thigh. Débridement, drainage and a sigmoidostomy were performed. Tissue cultures disclosed *Escherichia coli* and *Enterococci,* and necrotizing fasciitis was confirmed by histological investigation. Third-generation cephalosporins and aminoglycosid were started, and three consecutive sugical revisions with extensive débridement were performed. Despite maximum supportive therapy the patient developed bradyarrhythmia on the 19th postoperative day and died of multisytem organ failure. No serum precipitating antibodies to antigens of *Aspergillus* species were found on the 7th and 12th postoperative days.

Pathological findings

At autopsy, there was an extensive, phlegmonous necrotizing soft tissue inflammation with its main focus in the pelvic wall, spreading to the lower abdominal wall, retroperitoneum and perineum and to proximal regions of the right thigh. Microscopically, no bacterial or fungal

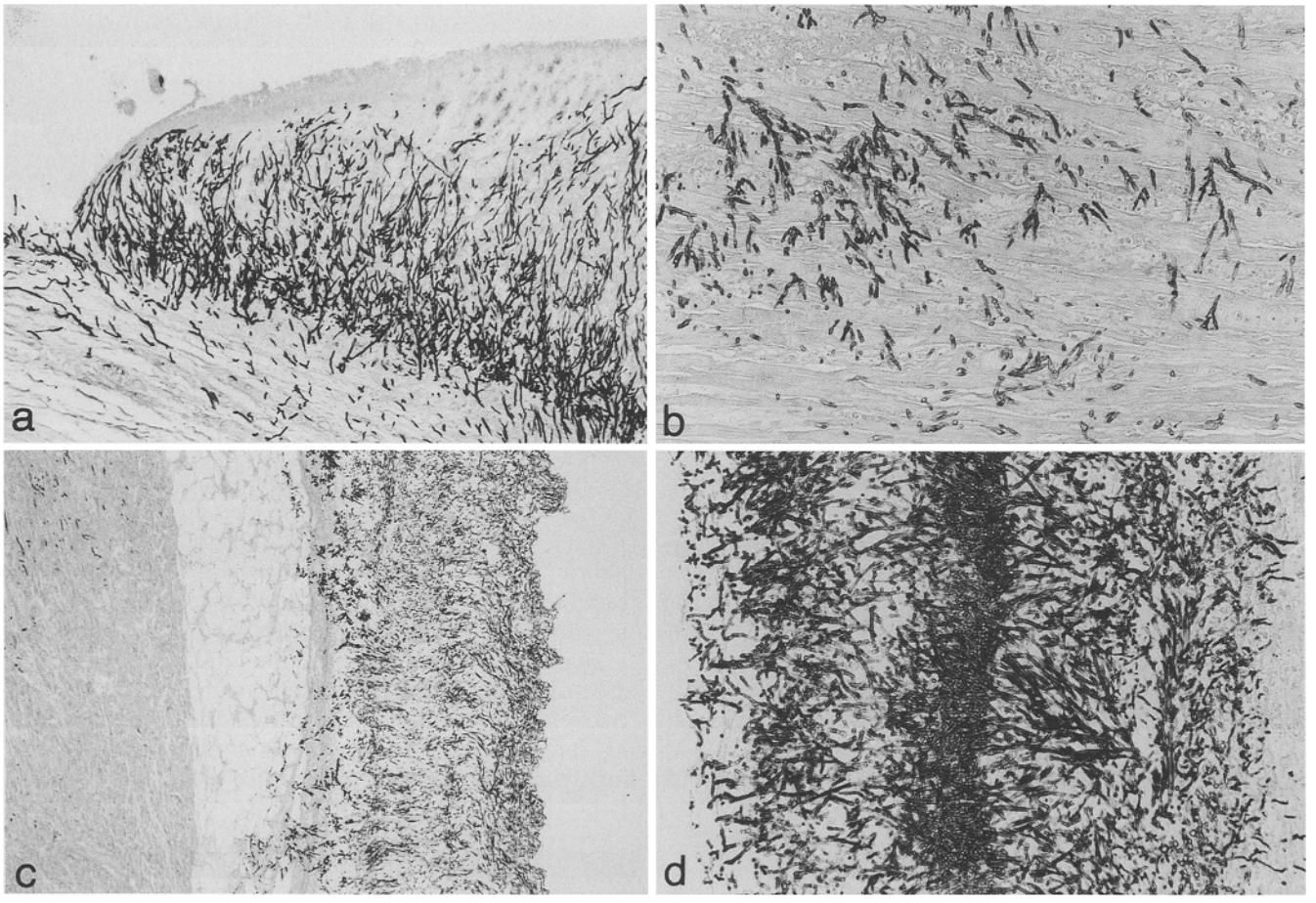

Fig. 1 **a** Section at the level of the transition zone between the left ventricular parietal endocardium and the aortic valve endocardium of the left coronary leaflet, showing an ulcerating and polypoid vegetation with bouquets of 45° angle dichotomous branching septate hyphae, characteristic for *Aspergillus* typus. This invades the underlying myocardium and is disseminating in the bloodstream. GMS, ×50. **b** Myocardium of the posterior wall of the left ventricle, demonstrating infected thromboemboli in the muscular tissue. GMS, ×80. **c** *Aspergillus* spores on the surface of the epicardium. H & E, ×30. **d** Fungal colonies in layers in a bronchial wall. GMS, ×100

colonies were identified. The heart showed fibrinous epicarditis and marked dilatation of all chambers. A area of small ulcerating and polypoid vegetation was seen at the level of the transition zone from the left ventricular parietal endocardium to the aortic valve endocardium of the left coronary leaflet. The mitral, tricuspid and pulmonary valves were unremarkable. The anterior and posterior walls of both ventricles were mottled by multiple haemorrhagic lesions and small foci of fibrosis. Histologically, at all cardiac levels bouquets of 45° angle dichotomous branching septate hyphae were detected. These were characteristic for *Aspergillus* spp.and gave a positive reaction with PAS and GMS stains but a negative one with the Gram stain (Fig. 1a–c). Numerous infected thromboemboli were seen in the intramural coronary arteries, with coagulation necrosis of the adjacent myocardium in all chambers, in the interventricular septum and in the anterior papillary muscle. Both lungs had evidence of acute necrotizing fungal bronchopneumonia (Fig. 1d), but no *Aspergillus* spores were localized in the mediastinum. Mucosa-associated lymphatic tissue in the lung was markedly reduced. Numerous accumulations of branching fungi of the *Aspergillus* were also seen in the thyroid gland, in the left kidney, where a fungal thrombus obliterated an intralobular artery with subsequent infarction of the parenchyma supplied, and in the brain, which displayed a multifocal subacute fungal vasculitis. Micronodular cirrhosis and a splenic tumour were also found.

Discussion

The incidence of *Aspergillus* endocarditis has increased notably over the past few decades in step with the greater frequency of cardiovascular surgery [33]. In contrast, *Aspergillus* endocarditis in patients who have not had cardiac surgery is extremely rare. Woods et al. collected only 28 cases described in the literature and added 1 of their own [42]. Our computer-assisted review of the literature revealed 10 additional cases of *Aspergillus* endocarditis without open-heart surgery [1, 3, 7, 8, 12, 14, 18, 19, 28, 35]. To the best of our knowledge only 1 other case of mycotic dissemination by *Aspergillus* endocarditis has been reported in a patient affected with necrotizing fasci-

Table 1 Diseases that may be complicated by Aspergillus endocarditis in 40 patients with no history of cardiac surgery (*IVDA* intravenous drug abuse)

Primary disease	No. of cases	References
Haematological malignancy	13	[4, 14, 16, 18, 23, 25, 27, 28, 30, 35, 40, 41]
Other malignancies	2	[31, 40]
HIV infection and/or IVDA	5	[8, 12, 13, 19, 24]
Organ transplantation[a]	3	[15, 40, 42]
Chronic alcoholism	2	[5, 11]
Tuberculosis[b]	2	[22, 38]
Necrotizing fasciitis	1	Present case
Other[c]	6	[6, 17, 20, 40, 43]
None	6	[1, 3, 7, 10, 37, 39]

[a] Includes 2 kidney transplant recipients [15, 40] and 1 liver transplant recipient [42]
[b] Includes 1 patient with miliary tuberculosis [22] and 1 with silicotuberculosis [38]
[c] Includes 1 patient each with prematurity and "nonsterile" exchange transfusion [20], uveitis [17], mediastinal fibrosis [6], fulminant hepatitis [40], rheumatic heart disease [43], and polytrauma [43]

itis [9]. In that report the authors described the clinical findings without necroscopic evidence of a 60-year-old woman afflicted with diabetes mellitus and chronic renal failure requiring haemodialysis, who developed a fatal *Aspergillus* infection following débridement for necrotizing fasciitis.

Table 1 shows the primary diseases that may be complicated by *Aspergillus* endocarditis in patients without a history of cardiac surgery. The micronodular cirrhosis present in our patient suggests chronic alcohol intake, and alcoholic subjects are considered to have a greater predisposition to infectious diseases than other people. It is probable that in our patient alcohol abuse was the most important predisposing condition, a necessary but not sufficient factor for the development of *Aspergillus* endocarditis. Zimmerman attributed the dissemination of fungus in the body to a combination of three factors, all of which were present in this case. These are a general lowering of resistance by a debilitating disease, a local point of entry for the fungus, and the use of antibiotics, causing suppression of the normal bacterial flora and inflammatory response [43, 44]. Subsequent studies have supported this and emphasized the role of steroids in the suppression of inflammatory response [21, 33].

Aspergillus spp. are airborne organisms that are ubiquitous in the environment. It therefore seems probable that in our patient the route of entry could have been the respiratory tract, with subsequent spread. An attempt at cinical detection of the fungus was unsuccessful, but this is not surprising since blood cultures fail to reveal *Aspergillus* or are positive in less than 11% of patients with cardiac aspergillosis, broncho-alveolar lavage with culture discloses only approximately 50% of those with pulmonary aspergillosis, and *Aspergillus* antibody tests have limited value in immunocompromised patients [2, 21, 33, 42].

With regard to the course of the necrotizing fasciitis, it is difficult to say whether the outcome would have been any different if the diagnosis had been made rapidly. Upon arrival at the hospital, the patient was already extremely ill from the systemic manifestations of the disease. The best outcome in patients with necrotizing fasciitis has been associated with extensive operative procedures in the first 24–48 h after onset of the illness [26]. This patient was already at an advanced state of the illness at the time of presentation. Although the soft tissue infection and the mediators of systemic illness were removed, a complete reversal of the multiorgan failure was not possible, because disseminated aspergillosis dominated the postoperative course.

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