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Disseminated invasive aspergillosis in patients with severe influenza infection

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ABSTRACT

A female 66 year-old patient, not immunocompromised, was admitted in ICU for severe influenza complicated by severe acute respiratory distress syndrome (ARDS) leading to extra-corporeal membrane oxygenation (ECMO). During ICU hospitalization, she developed a disseminated invasive aspergillosis with cerebral access and coronary occlusion which lead to cardiac arrest. Despite a successful revascularization procedure, the patient died of refractory shock.

A female 66 year-old patient, not immunocompromised, was admitted in ICU for severe influenza complicated by severe ARDS leading to extra-corporeal membrane oxygenation (ECMO). Given respiratory disease severity, bronchoalveolar lavage (BAL) was not performed during this period, but iterative searches for aspergillosis using serum galactomannan test and cultures on tracheal aspirates were performed. Because delayed recovery of awakening, cerebral computed tomographic scan and subsequent magnetic resonance imaging showed a non-specific right fronto-temporal collection (Fig. 1). CSF revealed meningitis with predominance of lymphoid-cells, and PCR for HHV6 was positive in the cerebrospinal fluid, in serum and in the bone marrow aspirate examination, probably reflecting an immunocompromised state induced by severe influenzae, and leading to initiation of Ganciclovir. Subsequently, she had transient cardiac arrest with ST-segment elevation myocardial infarction, and coronarography revealed acute occlusion of the anterior interventricular artery. Despite a successful revascularization procedure, the patient died of refractory shock. Given the uncertainty of diagnosis, a clinical autopsy was performed. Histological examination found disseminated mycelial filaments in the form of abscesses in the lungs and the brain, but also disseminated in the kidney, colon, spleen and heart, strongly suggesting aspergillosis. Coronary artery occlusion was directly due to angio-invasive mycelial filaments (Fig. 2). *Aspergillosis fumigatus* PCR was performed twice but paraffin inclusion seems to be responsible for the failure. Our last culture for aspergillosis on tracheal aspirate was performed more than one week before death and we cannot know whether negative culture was due to rapid progression of aspergillosis over the last week or due to low sensitivity of culture.

Recent literature has reported cases of invasive aspergillosis in the non-immunocompromised host with severe influenza infection [1,2]. Indeed invasive pulmonary aspergillosis was diagnosed early in the course of severe influenza aspergillosis (3 days after ICU admission in median) [2]. Therefore, BAL would probably help to diagnose these patients and should be discussed, even in patients with severe ARDS. However, according to usual algorithms for aspergillosis diagnosis [3,4], more than one-third of patients were not classifiable because they had a positive galactomannan test but negative culture on BAL. A recent study found high sensitivity to detect aspergillosis by combining galactomannan test and PCR aspergillosis on BAL [5]. The authors reported that a combination of galactomannan test and PCR aspergillosis on BAL with 1-3-beta-d-glucan on serum resulted in 100% sensitivity.

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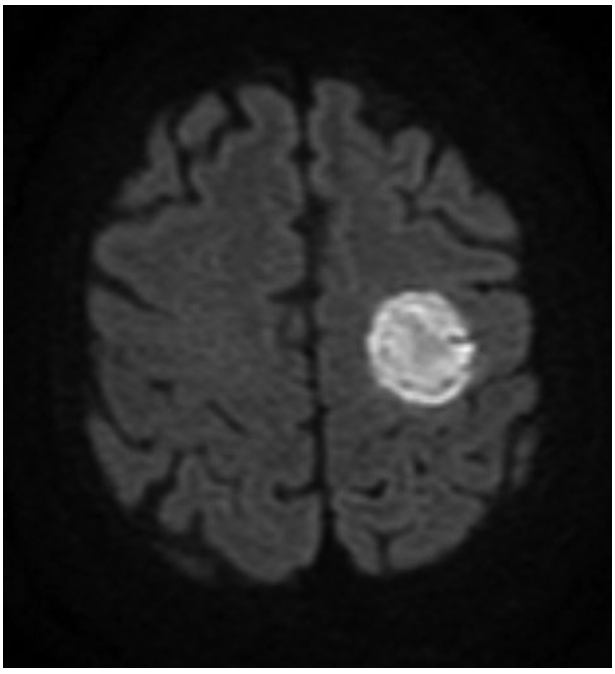

Fig. 1. Cerebral MRI diffusion sequence: right frontal-temporal collection (arrow).

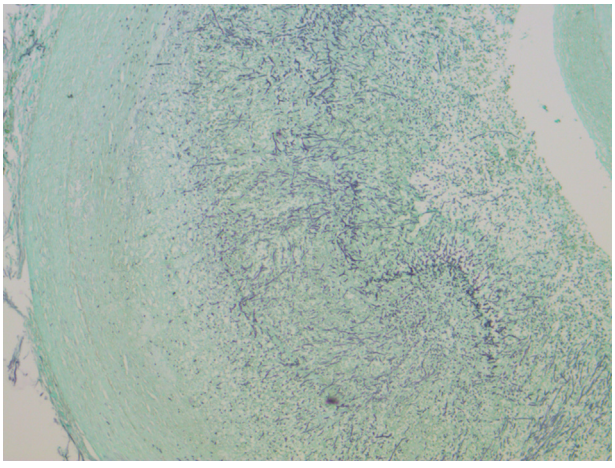

Fig. 2. Coronary vessel ×10, Grocott coloration: coronary vessel with endoluminal occlusion by mycelian filament (arrow).

In conclusion, aspergillosis may occur in severe influenza and BAL should be performed whenever possible for diagnosis, using culture, galactomannan and PCR on BAL, even in the most severe acute respiratory failure.

Author contribution

G.M., M.W. and A.W.T. wrote the majority of the manuscript; M. F., K.B., F.R., D.M., F.B., D.C., A.V., J.P.F. and R.R. participated in writing the manuscript and approved its final version; G.M., K.B. and M.F. realized the pictures

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Declaration of Competing Interest

None.

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Glossary

ARDS: acute respiratory distress syndrome
BAL: bronchoalveolar lavage
ECMOe: xtra-corporeal membrane oxygenation
HHV6: human herpes virus 6
ICU: intensive care units
PCR: polymerase chain reaction