Acta Haematologica Polonica 2024
Number 1, Volume 55, pages 54–57
DOI: 10.5603/ahp.97943
ISSN 0001–5814
e-ISSN 2300–7117

VIA MEDICA

Magnusiomyces clavatus: a rare cause of fungal infections in patients with acute myeloid leukemia

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Introduction

Fungal infections pose a significant threat to immunocompromised patients, with *Candida* and *Cryptococcus* yeast infections being common culprits [1, 2]. However, in some cases, non-pathogenic fungi such as *Magnusiomyces clavatus*, prevalent in warmer climates, can exploit weakened immune systems to cause illness. There have been documented cases in neighboring countries, but none reported in Poland to date [3–6].

Case report

In 2021, a 23-year-old female patient in Luhansk, Ukraine was initially diagnosed with thrombocytopenia, having experienced a deteriorating general condition, weakness, increased fatigue, and periodic bleeding from the gums and nose at her place of residence. At that time, methylprednisolone was included in her treatment. She periodically required blood component transfusion and her condition remained stable. In February 2022, she was infected by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2). In March 2022, she sought refuge in Poland due to the outbreak of armed conflict in Ukraine, and she was further managed at this clinic. At that time, bone marrow examination did not show evidence of malignancy. In July 2022, laboratory tests revealed pancytopenia, and her general condition was deteriorating. Based on the bone marrow examination conducted in July 2022 (cytological, immunophenotypic, and histopathological examinations), a diagnosis of acute myeloid leukemia with maturation features (with blast cells accounting for 87%) was made. The patient was qualified for intensive systemic treatment according to the DAC (daunorubicin, cytarabine and cladribine) protocol (PALG-AML for <60 years old) and complete remission of leukemia was achieved.

In September 2022, the patient underwent the first consolidation remission treatment and received posaconazole (3 × 50 mg/day) as prophylaxis against fungal infections. During the bone marrow reconstitution period, the patient developed fever accompanied by abdominal pain and increased inflammatory markers [procalcitonin, C-reactive protein (CRP), interleukin 6 (IL-6)], as well as elevated liver enzyme activity. In this situation, broad-spectrum antibiotic therapy was initiated (set as first day of treatment, see Table I), and after receiving information about the presence of fungi in blood, liposomal amphotericin B was added at a dose of 0.7 mg/kg per day. After several days, the fungus cultured from the blood was identified as *Magnusiomyces clavatus*. On the 11th day of treatment, a cardiac arrest episode (SCD) was successfully managed, but numerous ventricular rhythm disturbances (*torsades de pointes*) were observed. Despite modifications to compensate for severe electrolyte imbalances, normalization of the cardiac rhythm could not be achieved. Thereafter, a pharmacological coma was induced, after which no more cardiac rhythm disturbances were observed. Abdominal and chest computed tomography (CT) scans (Figures 1A–C) revealed the presence of fluid in the pericardial sac, pleural cavities, and suspected abscess formation in the liver, kidneys, and spleen. Due to recurrent infection symptoms, the antibiotic therapy was modified, and antifungal

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Received: 24.10.2023 Accepted: 11.12.2023 Early publication: 29.01.2024

Table I. Treatment schedule and medication administration log

Date	Day of treatment	Medicine	Doses/day	Type of administration
10 September to 22 September	Prophylaxis	Posaconazole	3 × 5 mg	*p.o.*
23 September* to 24 September*	1–2	Posaconazole	3 × 5 mg	*p.o.*
25 September*	3	Fungizone	30 mg	i.v.
26 September*	4	Fungizone	30 mg	i.v.
27 September* to 30 September	5–8	Fungizone	50 mg	i.v.
1 October	9	Liposomal amphotericin B	100 mg	i.v.
2 October to 3 October**	10–11	Liposomal amphotericin B	200 mg	i.v.
4 October to 5 October	12–13	Liposomal amphotericin B	200 mg	i.v.
		Micafungin	100 mg	
6 October	14	Liposomal amphotericin B	200 mg	i.v.
7 October	15	Liposomal amphotericin B	200 mg	i.v.
		Voriconazole	800 mg	
8 October* to 9 October	16–17	Liposomal amphotericin B	200 mg	i.v.
		Voriconazole	300 mg	
10 October*	18	Liposomal amphotericin B	350 mg	i.v.
		Voriconazole	300 mg	
11 October†	19	Voriconazole	200 mg	i.v.

*Received mycogram: positive for *M. clavatus;* **sudden cardiac death and pharmacological coma induced; †patient passed away; i.v. — intravenous; *p.o.* (*per os*) — oral administration

treatment was escalated, including liposomal amphotericin B, voriconazole, and micafungin. The full treatment schedule and medication administration of the patient is shown in Table I, together with important events. The escalated treatment did not prevent multiorgan failure. Due to prolonged agranulocytosis, granulocyte colony-stimulating factor (G-CSF) was added along with intravenous immunoglobulins. Coagulation disorders were corrected using fresh frozen plasma (FFP). Due to further deterioration of the general condition, the patient was transferred to the intensive care unit (ICU) for further treatment. On the 17th day of treatment, despite forced diuresis, oliguria was observed, accompanied by worsening metabolic acidosis and electrolyte disturbances. Furthermore, progressive circulatory failure manifested as progressive hypotension, rhythm disorders, and treatment-resistant complications. Despite the maximum intensification of treatment, the patient passed away on the 19th day of fungal sepsis treatment.

We have failed to find a description of a previous infection with *M. clavatus* occurring in Poland, although there have been numerous reports (usually case descriptions) from other, particularly southern European, countries [1, 7]. In countries with a warmer climate, this fungus is relatively common in the environment [8]. However, in Poland, conditions for its survival seem to be less favorable. Climate change may suggest that pathogens typically associated with warmer climates, such as *M. clavatus*, will become more often diagnosed in Poland. Nevertheless, *M. clavatus* infections are in fact also rare in southern Europe, and many of the reported cases have had a similar outcome to that of our patient, resulting in death from the disease [1]. Only a few patients have survived, particularly those who initially received combined antifungal treatment including liposomal amphotericin B, voriconazole, and in some cases fluorocytosine [1–3, 5–7, 9].

It is important to emphasize that instituting such treatment in our case neither slowed down the infection, nor resulted in negative blood cultures. There are currently no European Conference on Infections in Leukemia (ECIL) guidelines for the treatment of *M. clavatus* infection, but standard ECIL-suggested antifungal prophylaxis i.e. posaconazole was used in our patient. However, the infection developed while the patient was on this prophylaxis. Another unusual aspect was that the patient, still in complete remission of acute leukemia, was admitted for standard remission consolidation treatment. Therefore, this was not an end-of-life phenomenon.

Summary

Our aim in describing this case was to raise awareness about the potential occurrence of similar events, and recommend the immediate institution of combined anti-fungal

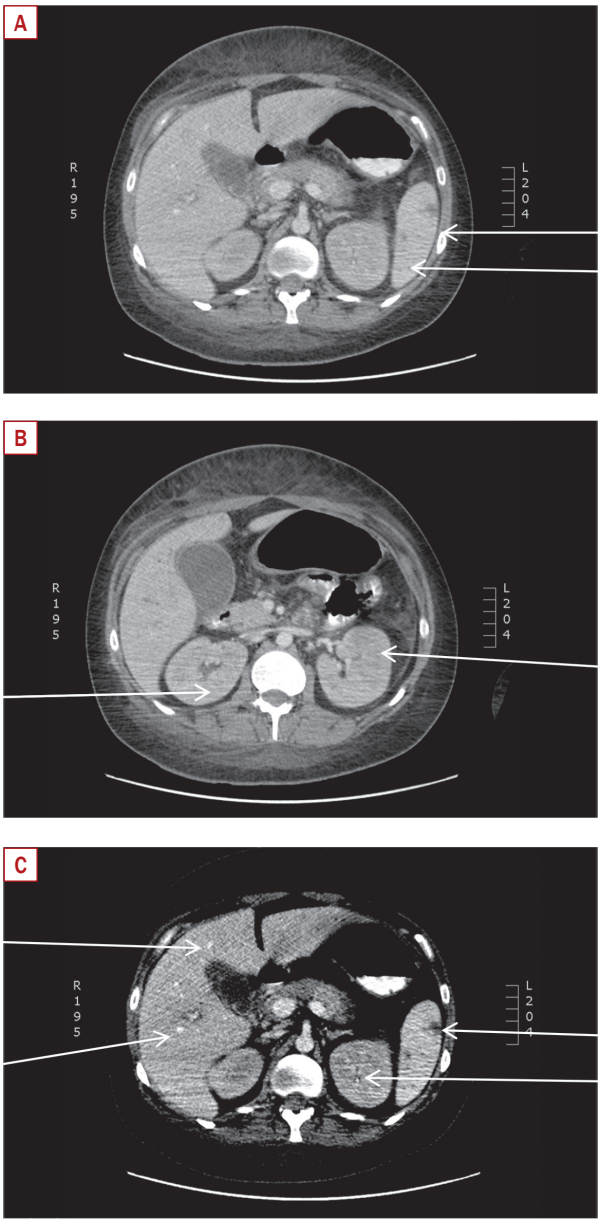

Figure 1A. Computer tomography image taken on day 7 of infection, showing microabscesses detected in spleen; **B.** Computer tomography image taken on day 7 of infection, showing microabscesses detected in kidneys; **C.** Computer tomography image taken on day 10 of infection

treatment as the only possible means of controlling the disease. The apparent resistance of *M. clavatus* to such treatment in our case suggests the ongoing necessity of developing new antifungal agents.

Article information and declarations

Acknowledgments

Not applicable.

Author contributions

IV, WWJ made substantial contributions to design, acquisition of data and interpretation of data. TO, TvW, PP drafted manuscript and revised it critically for important intellectual content. KB-J devised concept and gave final approval of version published.

Conflict of interests

All authors certify that they have no affiliations with or involvement in any organization or entity with any financial interest (such as honoraria; educational grants; participation in speakers' bureaus; membership, employment, consultancies, stock ownership, or other equity interest; and expert testimony or patent-licensing arrangements), or non-financial interest (such as personal or professional relationships, affiliations, knowledge or beliefs) in the subject matter or materials discussed in this manuscript.

Ethics statement

Written informed consent was obtained from the patients' relative for her anonymized information to be published in this article.

Funding

None.

Supplementary material

None.

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