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Pulmonary Nocardiosis Following Chemotherapy

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Abstract

Case History/Exploration: A 75-year-old patient was admitted to hospital one month after diagnosis of a glioblastoma. Shortly after receiving her first course of chemotherapy (temozolomide/dexamethasone), she had collapsed at home. Clinically there were signs of pneumonia.

The chest x-ray showed extended shadows, consistent with inflammatory infiltrates, which also resembled metastases. During bronchoscopy creamy pus discharged through the ostium S3. Microbiologic cultures grew Nocardia pseudobrasiliensis.

Therapy/Development: First calculated antibiotic therapy with piperacillin/tazobactam plus amikacin was started. After the antibiogram was available, trimethoprim/sulfamethoxazole was administered orally. In response to the treatment, symptoms and radiologic findings improved substantially. Eventually the patient could be dismissed to further palliative treatment at home.

Conclusion: Nocardiosis is a rare cause of pulmonary abscesses and pneumonia and therefore should be considered when treating immunocompromised patients.

Keywords: Nocardiosis; Immunosuppression; Pneumonia; Abscess

Introduction

Pneumonia is the most common infectious cause of death in Europe. Community-acquired bacterial pneumonia in immunocompetent patients is most commonly caused by streptococcus pneumoniae, atypical pathogens (Mycoplasma pneumoniae, Legionella pneumophila, Coxiella burnetii, Chlamydophila pneumoniae) or Haemophilus influenzae.[1] In contrast, the spectrum of pathogens found in hospital-acquired pneumonia (nosocomial pneumonia) is more diverse and pathogens with multiple antibiotic resistances (e.g. MRSA, Pseudomonas aeruginosa, Enterobacterales, Acinetobacter baumannii, Stenotrophomonas maltophilia) have to be expected.[2] Under (additional) immunosuppression, the spectrum expands further to include fungi (Candida spp., Cryptococcus neoformans, Aspergillus spp., Pneumocystis jirovecii), slow-growing bacteria

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(Mycobacterium spp., aerobic actinomycetes), and various viruses.[3] In order to avoid an ineffective therapy, the (cultural) detection of microorganisms is crucial in these patients. Species that are difficult or impossible to cultivate must also be considered and require special diagnostic conditions. Here we report a case of pulmonary nocardiosis in a patient undergoing chemotherapy.

Case Report

A 75-year-old patient was admitted to the emergency department after collapsing at home. Before admission, the blood sugar was significantly elevated at 300 mg/dl and the patient complained of nausea and vomiting. About a month earlier, a left thalamic glioblastoma WHO grade IV had been diagnosed. Immediately after diagnosis, treatment with dexamethasone was initiated. The patient had completed the first cycle of palliative chemotherapy with temozolomide two days before admission.

Findings

On admission, the patient was in a reduced general condition, tachycardic and slightly febrile (38°C). Blood gas analysis showed hypoxaemia (pO_2 45 mmHg) and the oxygen saturation was 83%. Bilateral pneumonic rales were heard on auscultation. With massively increased CRP (412 mg/l), PCT (6.57 ng/ml) and leukocytosis (15300/µl), clinical suspicion of pneumonia arose. The X-ray of the thorax showed extensive densifications on both sides, compatible with inflammatory infiltrates (Figure 1). However, there was also the aspect of metastases. The initially obtained blood cultures (three pairs) remained without bacterial growth until the end of the incubation period of 7 days. Initially, no other material (e.g. sputum) was examined microbiologically. Legionella antigen in the urine was negative.

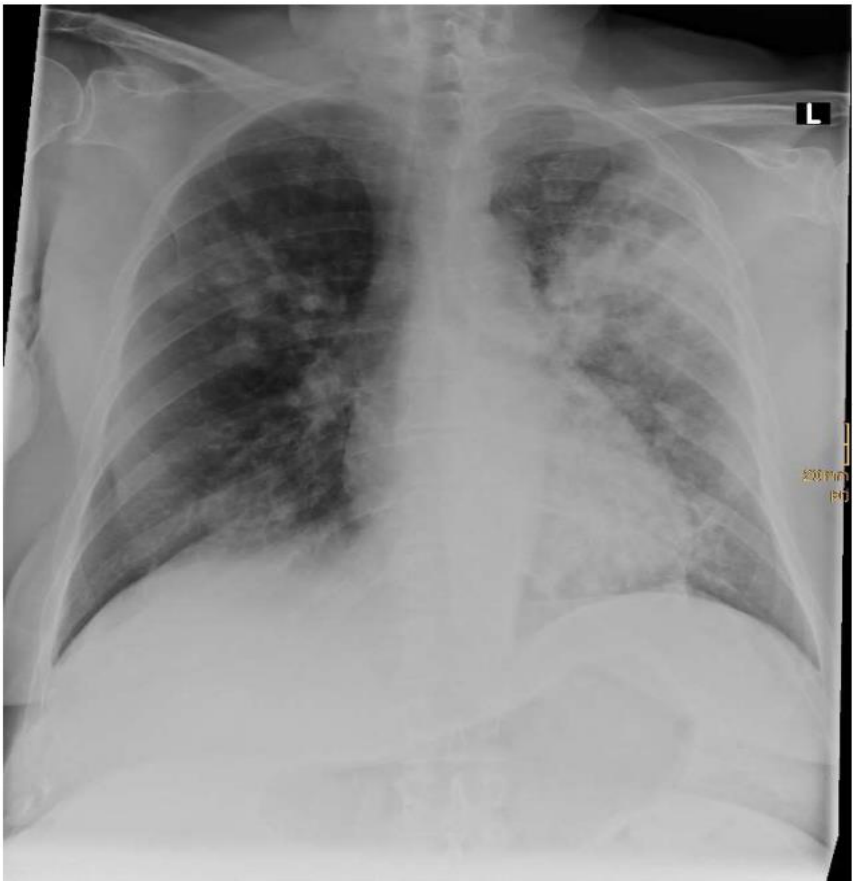

Figure 1: Chest X-ray a.p. on the day of admission

Treatment with piperacillin/tazobactam (3 g × 4.5 g) improved clinical signs and findings only slightly. Because extensive pneumonic infiltrates were still visible in both lungs after five days, further diagnostics measures were initiated. One week after admission, mycobacterial diagnostics of sputum and urine were conducted, but remained negative until the end of the incubation period. In the CT of the thorax, the changes presented as atypical pneumonic infiltrates with extensive abscesses (Figure 2). A tumorous genesis was regarded as rather improbable.

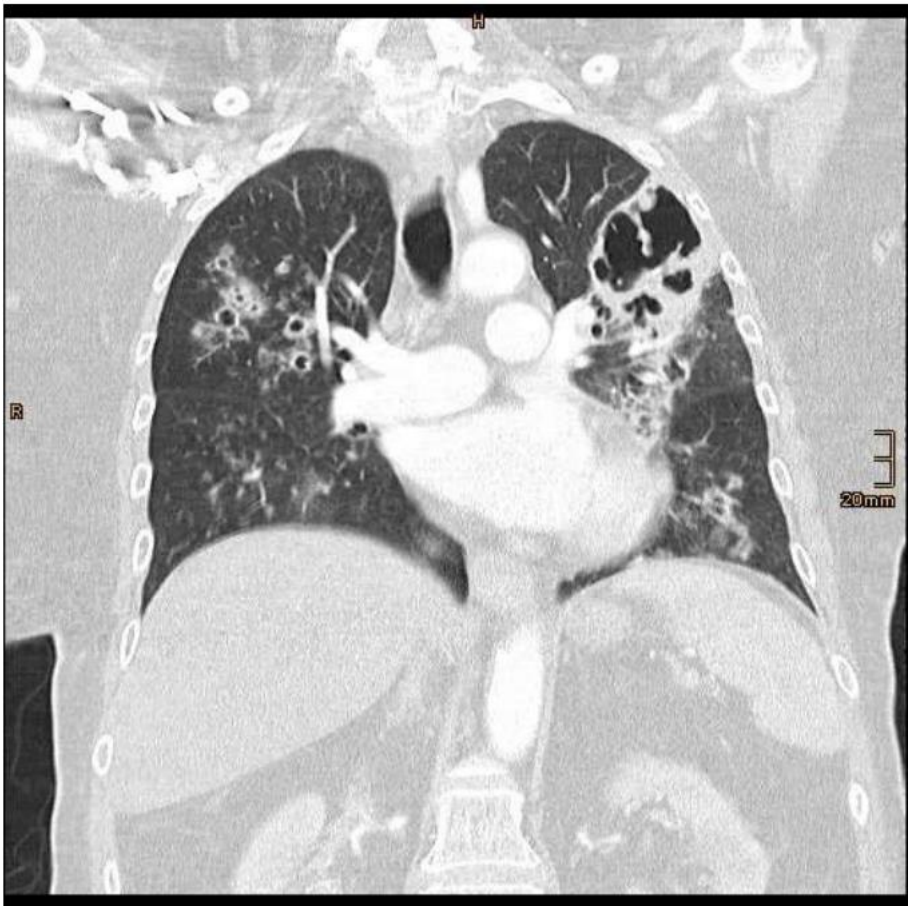

Figure 2: Chest CT ap., 8 days after admission.

Bronchoscopically, creamy pus could be obtained, which grew Nocardia spp. after four days of incubation. By mass spectrometry (MALDI-TOF) the colonies were identified as N. pseudobrasiliensis. Analysis of genetic sequence following 16S-rRNA-PCR could reliably differentiate the strain at genus level only (Nocardia).

Course

The therapy was supplemented with amikacin (1000 mg once a day) on day 17 as a result of the microbiological findings, which slowly improved the clinical picture. The inflammation values were regressive, but sub-febrile temperatures were still present. The atypical pneumonic infiltrates were also slowly declining on CT.

After the antibiogram was available (Table 1), antibiotic therapy was switched to sulfamethoxazole /trimethoprim (3 mg × 960 mg), which can also be administered orally. Nocardiosis should be treated very long-term (usually 6-12 months).[4,5] In this case, however, due to the palliative treatment situation, a balance had to be found between immunosuppression and infection control. A few days after switching therapy to sulfamethoxazole/trimethoprim and clinical improvement, chemotherapy with temozolomide could be restarted. Dexamethasone as an additional immunosuppression was not administered. Approximately 6 weeks after

admission, the patient was discharged with significantly improved lung findings for further palliative therapy (Figure 3). She died a few weeks later due to the glioblastoma.

Table 1: Antibiogram (transmitted on day 26), determined MIC values (E-test method) of relevant agents and interpretation according to CLSI, M24-A2 (MIC: minimal inhibitory concentration; R: resistant; S: susceptible).[6]

Antibiotic agent	MIC	Interpretation
Piperacillin/tazobactam	>256 mg/l	R
Cefotaxime	>32 mg/l	R
Imipenem	>32 mg/l	R
Ciprofloxacin	0.064 mg/l	S
Linezolid	0.5 mg/l	S
Tigecycline	0.5 mg/l	S
Amikacin	1 mg/l	S
Sulfamethoxazole/trimethoprim	0.016 mg/l	S

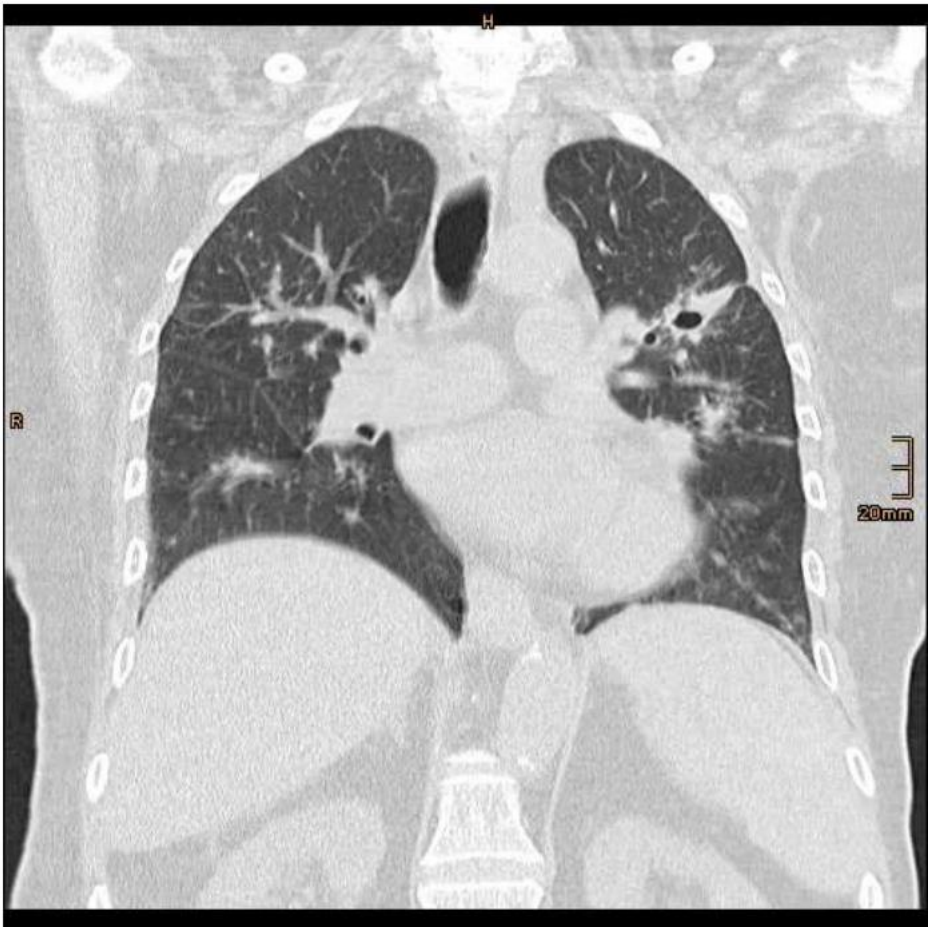

Figure 3: Chest CT a.p. before discharge.

Discussion

We describe here the rare case of nocardiosis in a patient undergoing palliative chemotherapy for advanced glioblastoma. Nocardia spp. are obligatory aerobic, gram-positive, and partially acid-fast, branched filamentous rods that are found ubiquitous in the environment. They can cause superficial cutaneous, pulmonary, or disseminated infections, which usually progress to abscess. The risk of hematogenous spread and systemic

dissemination is particularly relevant in immunocompromised patients.[4] Tuberculosis, atypical mycobacteriosis or infections with aerobic or anaerobic actinomycetes (such as Nocardia spp.) should therefore always be considered in the case of abscess-forming, nodular, or cavernous infectious processes without evidence of fast-growing bacteria and/or failure of standard therapy. Since Nocardia spp. grow rather slowly, aimed diagnostic procedures should be specifically requested if there is any suspicion. The microscopic image in the gram preparation can play a role in routine diagnostics.[7] Sometimes Nocardia spp. are found, when searching for mycobacteria, since they are also partially acid-resistant.

According to German guidelines, microbiologic testing should be conducted when treating hospitalized patients with community-acquired pneumonia (exception: palliative therapy situation), nosocomial pneumonia and pneumonia under immunosuppression.[2,3,9]. In these cases, the selection of an effective therapy can be difficult, as a significantly broader spectrum of pathogens is to be expected (compared to community-acquired pneumonia in otherwise healthy patients).[2,10]

In the case of severe infections under immunosuppression, one pillar of therapy is the restoration of a functioning immune system. Often, however, a balance must be found in order not to jeopardize the life-sustaining or life-prolonging therapy of the underlying disease. In this case, the already strictly palliative situation regarding the advanced glioblastoma led to a modified therapy goal of nocardiosis. The focus was not on the permanent elimination of the pathogens, but rather on a temporary suppression of the infection process.

Regarding the ideal antibiotic therapy of nocardiosis, there are still many uncertainties. Recommendations are largely based on single case reports or very small case series. To make matters worse, the individual Nocardia spp. differ significantly in terms of their antibiotic sensitivity and geographical distribution.[4,5] For example, the Robert Koch Institute recommends using imipenem plus amikacin for empirical therapy in Germany, since sulfonamides are often poorly effective in the species frequently found here.[4] Following this recommendation, we added amikacin to the therapeutic regime. After the antibiogram was available, therapy could be modified accordingly. The strain was sensitive to sulfamethoxazole/trimethoprim, while the MIC for imipenem was very high (>32 mg/L). To optimize therapeutic decisions, Nocardia spp. thus should be differentiated down to the species level and an antibiogram should be obtained. In our case, the differentiation at species level obtained by mass spectrometry (Nocardia pseudobrasiliensis) could not be confirmed by molecular biology. However, as the antibiogram matched well with the MALDI-TOF result, the infection was most likely caused by N. pseudobrasiliensis.[5,7]

As a rare cause of melting processes, nocardiosis should be considered as a differential diagnosis, especially in immunosuppressed or tumor patients. Promptly collected, suitable material and a specific request are necessary for the diagnosis.

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