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Research Article

Amikacin Liposome Inhalation Suspension (ALIS) as part of the initial regimen in the treatment of non-tuberculous mycobacteria (NTM) treatment

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Abstract

Managing non-tuberculous mycobacterial (NTM) lung disease poses challenges due to the extended treatment duration and frequent occurrence of adverse effects. Amikacin Liposome Inhalation Suspension (ALIS) is a liposomal form of amikacin, delivered through inhalation directly to the lungs. Recently published guidelines now recommend the use of (ALIS) as a component of the treatment regimen for Mycobacterium avium complex (MAC) lung disease in cases of refractory disease. However, no data exist supporting its inclusion in the initial regimen. In this case report, we present a patient with a newly diagnosed M. intracellulare infection and extensive bilateral disease who received ALIS due to the precarious use of parenteral amikacin. A 64-year-old female patient, with impaired kidney function due to kidney cancer and nephrectomy presented with cough and malaise over the last three months. The CT scan performed demonstrated multiple bilateral nodules and infiltrates, as well as bronchiectasis. A bronchoscopy was conducted and M.intracellulare was isolated from the bronchoalveolar lavage. Given the extensive nature of the disease, even in the absence of a cavity and given the impaired kidney function, the patient was administered a therapy regimen including azithromycin, rifampicin, ethambutol, and ALIS. The patient benefited the most of the treatment in terms of clinical, microbiological and imaging aspects while avoiding serious adverse effects due to amikacin. It is necessary to always consider the best treatment for the patient even beyond established guidelines in order to achieve the best outcome. ALIS is a promising new treatment that needs to be studied further.

Keywords: Non-tuberculous mycobacteria; pulmonary disease; chronic obstructive

Introduction

Non-tuberculous mycobacteria (NTM) constitute a diverse group of environmental bacteria found ubiquitously. NTM lung disease is a chronic, often progressive, and potentially life-threatening condition. It primarily affects individuals with immunodeficiency or pre-existing chronic lung conditions, such as bronchiectasis, chronic obstructive pulmonary disease (COPD), cystic fibrosis, or a prior–tuberculosis infection. However, NTM infections can also occur in individuals who are immunocompetent with no identified health conditions. Managing NTM lung disease, including *Mycobacterium avium* complex (MAC) infections, poses a challenge since achieving microbiological eradication usually entails a prolonged course of a multidrug antibacterial regimen with elevated toxicity and increased risk of adverse effects.

The guidelines provided by the American Thoracic Society (ATS) and Infectious Diseases Society of America (IDSA) for treating MAC lung disease recommend a three-drug regimen for patients with macrolide-susceptible MAC isolates that includes a macrolide, preferably

azithromycin, ethambutol, and a rifamycin (either rifampin or rifabutin). According to ATS/IDSA treatment guidelines, in patients with severe disease or a history of treatment failure, the addition of an injectable agent (amikacin or streptomycin) should be considered (1). However, the use of these intravenous aminoglycosides is often restricted due to the associated risk of systemic toxicities, especially toxicities affecting the kidneys and hearing. When dealing with refractory NTM disease, therefore in cases where sustained culture conversion is not achieved despite ≥ 6 consecutive months of the base-line guided multidrug regimen, there are limited alternative therapeutic options and a more individualized and targeted approach is required.

Amikacin Liposome Inhalation Suspension (ALIS) constitutes a liposomal formulation of amikacin, administered through inhalation. In this manner ALIS enables targeted drug delivery to the lungs, thereby reducing systemic exposure and minimizing the risk of potential adverse effects. The medicine is delivered to the patient by oral inhalation and taken up by alveolar macrophages, which represent an intracellular niche where NTM can reside (2).

Currently, approval is obtained for use as part of a combined antibacterial drug regimen against MAC lung disease for patients with refractory disease. To date, it has not been documented as part of the initial treatment regimen for a patient undergoing their first therapeutic intervention for a MAC infection, ouside of clinical trials.

In this case report, we present a patient with a newly diagnosed M. intracellulare infection and extensive bilateral disease who received ALIS due to the precarious use of parenteral amikacin.

Case Description

A 64-year-old female patient, previously diagnosed with right kidney cancer leading to nephrectomy and subsequent impaired kidney function, with a baseline glomerular filtration rate (GFR) of 35 ml/min, presented with a persistent cough and malaise over the last three months. As part of the initial diagnostic evaluation, the patient underwent a chest X-ray, which revealed bilateral infiltrates. Subsequently, a CT scan was conducted, demonstrating multiple bilateral nodules, perivascular and bronchovascular infiltrates, as well as bronchiectasis, without any evidence of lymph node enlargements. The patient initially received standard antimicrobial regimens on an outpatient basis. A subsequent CT scan was performed, revealing consistent findings alongside the emergence of consolidation in the right middle lobe. Consequently, the patient underwent bronchoscopy, and the culture from the washing and bronchoalveolar lavage (BAL) isolated M. intracellulare, demonstrating sensitivity to macrolides and aminoglycosides. Considering the extensive nature of the disease, even in the absence of a cavity and given the impaired kidney function, the patient was administered a therapy regimen including azithromycin, rifampicin, ethambutol, and ALIS. The patient tolerated the medication well with no serious adverse effect, except for dysphonia. After six months of the abovementioned prescribed treatment, a subsequent CT scan and bronchoscopy were performed. The CT scan showed improvement, while bronchoscopy yielded negative results in all cultures. The treatment is on track to be completed after 18 month.

Discussion

In this case report we describe the first patient outside a clinical trial that received ALIS for MAC lung disease since the initiation of the treatment. According to guidelines the patient should have received only azithromycin, rifampicin and ethambutol since macrolide resistance and cavities were not present (1). Despite the absence of a cavity, the extensive nature of the disease prompted physicians to considerate the addition of an extra drug to the guideline-based treatment, such as amikacin. Given that the patient was mononephric with an already impaired renal function, alternative options other than parenteral amikacin were sought. In Greece, the availability of drugs beyond those strictly prescribed based on approved indications can be considered by the authorities, provided there is an evidence-based justification and the absence of viable alternatives.

The patient tolerated the treatment and no major adverse effects were observed apart from voice hoarseness that was conservatively treated and gruadually faded without been necessary for the patient to interrupt the treatment. According to existing data localized adverse effects, such as disorders of the pharyngolarynx appear in most patients (3,4). Despite not being common, nephrotoxicity has been reported in clinical trials in patients treated with ALIS and is contradicted when severe renal impairment is present (5). Our patient was informed and willingly consented to participate in a treatment regimen associated with a higher likelihood of success. Close monitoring of renal function was agreed upon as part of the treatment plan. Given that the patient did not experience any other adverse event she was able to complete treatment firstly without any interruptions and secondly without any need for extra healthcare resource utilization.

Conclusion

In conclusion, our patient benefited the most out of an off-guideline drug regimen without experiencing any notable adverse events. ALIS emerges as a promising new medication with potential applications that extend beyond the current established guidelines. Given that knowledge is continuously evolving, it is essential to record real-life experience from ALIS use. Considering both patient outcomes and economic factors, the overall benefits outweigh the incremental drug costs. Consequently, local authorities could consider an easier access to this medication.

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