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Case Report

Report on Successful Treatment of Refractory MAC 2 Lung Disease in Two Elderly Patients with Inhaled Liposomal Amikacin (ALIS) at Half the Standard Dose

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Abstract

“Nontuberculous mycobacteria” (NTM) is a general term for mycobacteria other than the *Mycobacterium tuberculosis* complex and *Mycobacterium leprae*. In Japan, 90% of pulmonary NTM disease cases are caused by two species, *Mycobacterium avium* and *M. intracellulare*, which are collectively referred to as *Mycobacterium avium* complex (MAC) due to their biochemical similarity. Pulmonary MAC disease is broadly classified into fibrocavitary and nodular/bronchiectatic types, each of which exhibits distinctive pathological features. The pulmonary NTM disease incidence has been found to be 14.7 cases per 100,000 population per year, suggesting that Japan has the highest incidence of this disease in the world, and its incidence has also been shown to have already exceeded that of pulmonary tuberculosis. In addition, many elderly people have weakened immune systems, which often causes a decline in comprehension, and many medications for this have side effects, making it difficult to continue taking them and leading to treatment difficulties. The two cases reported here were both elderly women with refractory MAC lung disease, but they had different phenotypes: a fibrocavitary type and a long-standing, progressive nodular and bronchiectatic type. Treatment was performed with a regimen using liposomal amikacin (ALIS), which is an aminoglycoside antibiotic that works by binding to bacterial ribosomes and inhibiting protein synthesis. Using amikacin liposomal technology and a specialized inhaler, ALIS efficiently reaches alveolar macrophages, directly killing the MAC bacteria within. However, the unique administration method requires inhaler cleaning, making continued use difficult given the characteristics of patients with refractory MAC pulmonary disease. Even when treatment is possible, frequent side effects, such as hoarseness and dysphonia, while not severe, further contribute to the difficulty of initiating treatment. In both cases reported here, continued administration of rifampicin was difficult due to side effects such as liver damage and loss of appetite, and the patients’ conditions were also resistant to treatment, so ALIS was chosen, as it is thought to be more effective than other drugs and to have fewer systemic side effects. The patient had a limited understanding of how to clean the inhaler and how to inhale, making continued treatment difficult; therefore, we explained the efficacy and safety of ALIS to the patient’s family. Inhalation therapy is an effective method for delivering medication directly to the lungs, where the disease is located, while reducing systemic side effects. Until now, no inhalation therapy has existed for pulmonary MAC disease, and inhalation therapy itself is still a groundbreaking treatment administration method. This is the first case in the world where therapeutic efficacy has been confirmed with fewer than half the number of treatments required for standard treatment. Furthermore, as a new drug delivery method,



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<内容要約>

非結核性抗酸菌 (NTM) は、結核菌群およびらい菌以外の抗酸菌の総称です。わが国では、肺NTM症の90%はMycobacterium aviumとM. intracellulareの2種によって引き起こされ、生化学的類似性からMycobacterium avium complex (MAC) と総称されています。

肺MAC症は線維空洞型と結節性・気管支拡張型に大別され、それぞれ明確な病態像を示します。わが国の肺NTM症発症率は人口10万人当たり年間14.7人と世界で最も多く、その発症率は既に肺結核を上回っていることが明らかになっています。

今回報告した2症例は、いずれも性質の異なる難治性MAC肺疾患の高齢女性でした。

治療は、細菌のリボソームに結合してタンパク質合成を阻害するアミノグリコシド系抗生物質であるリボソームアミカシン (ALIS) を用いたレジメンで実施しました。アミカシンリボソーム技術と専用の吸入器を使用することで、ALISは効率的に肺胞マクロファージに到達し、内部のMAC菌を直接殺菌します。

問題点→この独特な投与方法では吸入器の洗浄が必要となり、難治性MAC肺疾患の患者の特性を考えると継続使用が困難でした。治療が可能であっても、嚔声や発声障害といった重篤ではないものの頻発する副作用が、治療開始を困難にする一因となっている。

今回の2症例では、通常治療が困難であり、患者の状態も治療抵抗性であったため、他剤と比較して有効性が高く、全身的な副作用が少ないと考えられるALISが選択されました。

患者は吸入器の洗浄方法や吸入方法の理解が不十分で治療継続が困難であったため、患者家族にはALISの有効性と安全性について説明しました。吸入療法は、全身的な副作用を軽減しながら、病巣である肺に直接薬剤を届ける有効な治療法です。

これまで肺MAC症に対する吸入療法は存在せず、吸入療法自体が画期的な治療投与方法です。

標準治療の半分以下の治療回数で治療効果が確認された症例は世界初となります。さらに、新しい薬物送達方法として、吸入は、既存の薬剤が利用できない、または何らかの理由で効果がない場合に新しい治療オプションを提供し、高齢の患者にも安全に使用できる可能性がありますという実臨床でのデータを加味した論文です