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Case Report

Canakinumab For The Treatment of Amyloidosis Secondary to Lung Cancer

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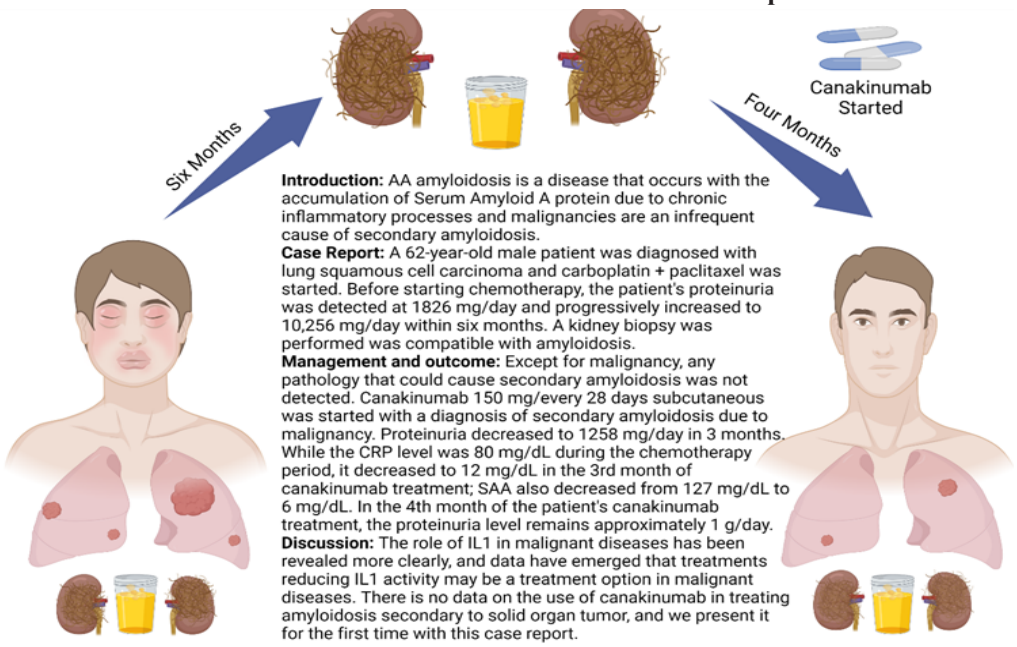

ABSTRACT

AA amyloidosis is a disease that occurs with the accumulation of Serum Amyloid A protein due to chronic inflammatory processes. Malignancies are an infrequent cause of secondary amyloidosis; therefore, there is not much data on the treatment of amyloidosis in these patients. We present a 62-year-old male patient was diagnosed with AA amyloidosis secondary to lung squamous cell carcinoma and successfully treated with canakinumab. Ramipril was started for the patient because of the 2 gram/day proteinuria at the time of lung cancer diagnosis. However, in the follow-ups, the proteinuria increased to 10 g/day, and the kidney biopsy was compatible with amyloidosis. Canakinumab (150 mg every 28 days) treatment was started, and proteinuria regressed below 1 g/day in 3 months. As the role of IL 1 in malignant diseases has become clear, data have emerged suggesting that treatments reducing IL 1 activity may be a treatment option in these diseases. There is no data on the use of canakinumab in treating amyloidosis secondary to solid organ tumor, and we present this usage for the first time with this case report.

Keywords: Amyloidosis, canakinumab, inflammation, lung cancer, proteinuria

INTRODUCTION

Amyloidoses are characterized by misfolded polypeptides in which proteins acquire an alternative and relatively misfolded state at subsequent aggregate. AA amyloidosis (secondary amyloidosis) is a disease characterized by deposition of serum amyloid A-derived fibrils as a result of chronic inflammation. The main goal of treatment is the treatment of the underlying chronic inflammatory disease (1).

The most prominent pro-inflammatory activities of A-SAA include the induction of the synthesis of IL-1α, pro-IL-1β and IL-6 (2). Canakinumab is a monoclonal

antibody to interleukin-1 (IL-1β) beta, often used to treat autoinflammatory diseases. Canakinumab has been used in treating secondary amyloidosis in various patient groups, such as colchicine-resistant familial Mediterranean fever or rheumatoid arthritis. It has been shown to provide effective control of the underlying inflammatory condition (3,4).

To our knowledge, this is the first case to demonstrate the success of the IL-1 antagonist canakinumab in reducing proteinuria in treating secondary amyloidosis in a patient with a solid organ tumor.

CASE

A 62-year-old male patient with no known comorbidity was diagnosed with lung squamous cell carcinoma ten months ago. Carboplatin + paclitaxel treatment was started in the patient with liver and bone metastases. The treatment was changed to nivolumab (200 mg/2 weeks) due to the progression of the disease in the fourth month of treatment. Before starting chemotherapy, the patient's kidney function tests were normal, but proteinuria was detected at 1826 mg/day, and ramipril 2.5 mg/day was started due to proteinuria. At that time, no further research was conducted on the etiology of proteinuria. Follow-up revealed that proteinuria progressively increased to 10,256 mg/day within six months. A kidney biopsy was performed for the etiology of nephrotic syndrome, and the biopsy result was compatible with amyloidosis. Positive expression was also detected in AA amyloid staining by immunohistochemical analysis. On physical examination, the patient's blood pressure was 90/50 mmHg, and there was no skin lesion or rash suggestive of vasculitis. Laboratory tests, including anti-nuclear antibodies (ANA), anti-dsDNA, anti-neutrophil cytoplasmic antibodies (ANCA), rheumatoid factor (RF), and serum complement 3 and 4 (C3-C4) levels, were normal. Hepatitis serology was negative, and serum and urine protein electrophoresis did not reveal any pathology suggestive of plasma cell dyscrasias. Serum urea was 12 mg/dL, and creatinine was 0.68 mg/dL. Except for malignancy, no pathology that could cause secondary amyloidosis was detected. Canakinumab 150 mg/every 28 days subcutaneous therapy was started with a preliminary diagnosis of secondary amyloidosis due to malignancy. Nivolumab treatment continued with canakinumab for three months. During follow-up, proteinuria decreased to 1258 mg/day in 3 months. While the CRP level was 80 mg/dL during the chemotherapy period, it decreased to 12 mg/dL in the 3rd month of canakinumab treatment, while SAA decreased from 127 mg/dL to 6 mg/dL. During these three months, the patient required antibiotic treatment, once for a urinary tract infection and once for bacterial pneumonia. Both infections were not life-threatening. The computer tomography taken at the end of the treatment showed regression of the disease compared to before. At the 4th month of the patient's canakinumab treatment, the proteinuria level remains approximately 1 g/day.

DISCUSSION

IL-1 cytokines play critical roles in cancer development and progression, both in the tumor microenvironment and in systemic immune surveillance. It has been shown that IL1 inhibition, especially in the early stages of malignant development, provides a more potent suppressive effect on malignant cells (5). Inflammatory pathways play an essential role in tumor development and tumor progression (6). The development of amyloidosis due to chronic inflammatory conditions is also frequently encountered. Canakinumab is a monoclonal antibody to interleukin-1 (IL-1 β) beta, frequently used in secondary amyloidosis treatment (3,4). To our knowledge, no other patient in the literature canakinumab was used to treat amyloidosis secondary to solid organ tumor.

There is concern over the use of canakinumab in malignant patients, as it may cause both immunosuppressive effects and malignancy progression. However, the role of IL-1β in the development of malignancy has been revealed by numerous studies in recent years, so studies on its use in malignant patients in treatments targeting IL-1β have increased (6). The Canakinumab Anti-inflammatory Thrombosis Outcome Study (CANTOS) showed that canakinumab significantly reduced the incidence of lung cancer development in patients with high inflammatory condition (7,8).

The common point of the studies that tried the efficacy of canakinumab in patients with lung cancer is the role of IL-1β in developing malignant cells. For this reason, it is reasonable to use canakinumab, a frequently tried treatment option in malignant patients due to its anti-inflammatory properties, to treat amyloidosis secondary to malignancy. In our patient, inflammation markers (Hs-CRP and ESR) were persistently high during chemotherapy and immunotherapy periods, and decreased rapidly after canakinumab treatment. During the 3 months of canakinumab treatment, the patient encountered two opportunistic infections that could be treated with oral antibiotics, but a severe infective pathology was not encountered. The patient's malignant disease process also regressed.

Although studies investigating the use of canakinumab in malignant diseases have obtained contradictory results, the relationship between malignant diseases and canakinumab continues to attract attention (9,10). In addition to the fact that our case was the first case of amyloidosis secondary to malignancy that responded to canakinumab treatment, the significant improvement in the malignant disease process after the combined use of

nivolumab and canakinumab also gives an idea about the anti-tumor efficacy of canakinumab.

CONCLUSION

In recent years, the role of inflammatory processes in the development of solid and hematological tumors has attracted attention, and treatment agents targeting these inflammatory processes have been tried in many studies. We think that canakinumab should be kept in mind as a treatment agent that can be used if amyloidosis is detected secondary to increased chronic inflammation in patients with malignant tumors.

DECLARATIONS

Ethics Committee Approval Number: Not necessary

Informed Consent: Informed consent was taken from the patient.

Referee Evaluation Process: Externally peer-reviewed

Conflict of Interest Statement: The authors declare that they have no potential conflict of interest relevant to this article.

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