EUR REV MED PHARMACOL SCI
2025; 29: 383-386

EFFECTIVE AND SAFE USE OF ALIROCUMAB IN SPINAL AND BULBAR MUSCULAR ATROPHY WITH HIGH CARDIOVASCULAR RISK: A CASE REPORT

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ABSTRACT – ***Background:*** Spinal and bulbar muscular atrophy (SBMA) is a rare X-linked neuromuscular disorder characterized by progressive muscle weakness and endocrine abnormalities. Beyond its classic neurological presentation, SBMA is increasingly associated with metabolic and cardiovascular comorbidities, including dyslipidemia and insulin resistance.

Case Report: We present the case of a 54-year-old male with genetically confirmed SBMA and high cardiovascular risk, in whom statins and ezetimibe were contraindicated due to persistently elevated creatine kinase levels and underlying muscle involvement. Coronary CT angiography revealed subclinical atherosclerosis. Alirocumab, a PCSK9 inhibitor, was initiated at a dose of 150 mg every 2 weeks. After six months, LDL cholesterol was reduced by 54.9% without adverse effects or functional decline, and CK levels remained stable.

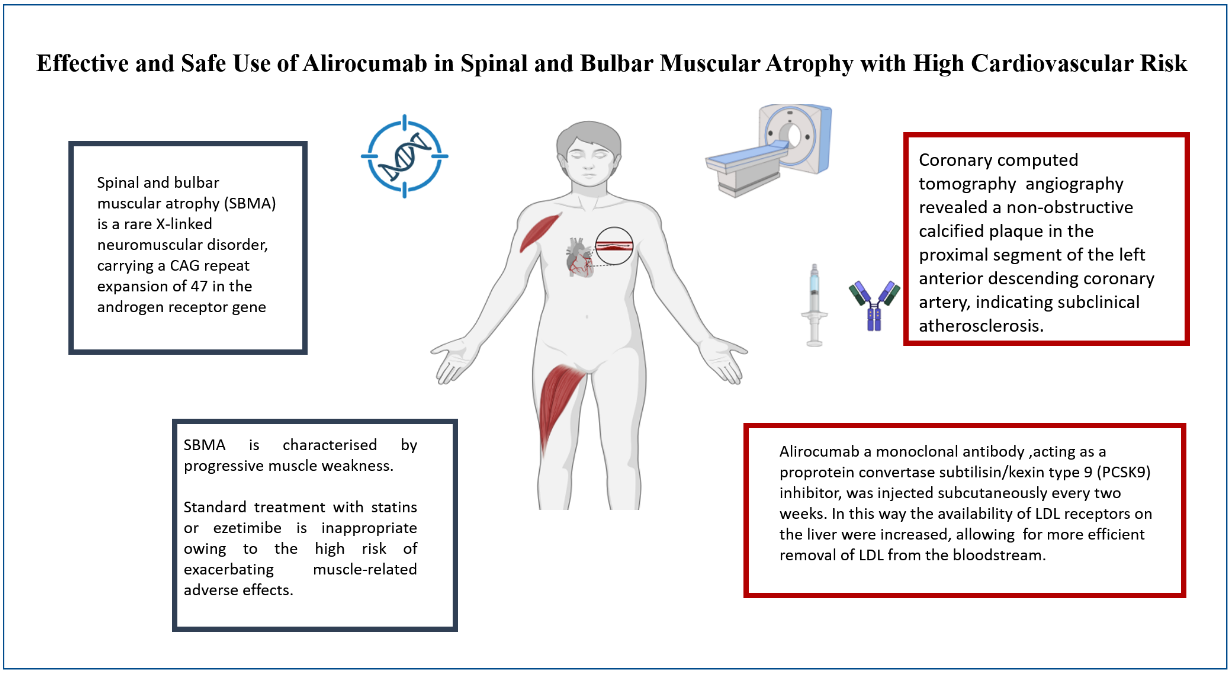
Conclusions: This case highlights the potential role of PCSK9 inhibitors as a safe and effective lipid-lowering option in patients with neuromuscular disorders at high cardiovascular risk, for whom traditional therapies are not feasible. It also highlights the importance of integrated cardiovascular care in managing multisystem diseases, such as SBMA.

KEYWORDS: Alirocumab, Spinal and bulbar muscular atrophy, SBMA, PCSK9 inhibitor.

INTRODUCTION

Spinal and bulbar muscular atrophy (SBMA), also known as Kennedy's disease, is a rare X-linked neuromuscular disorder with an estimated prevalence of 1-2 per 100,000 individuals[1]. It is caused by a trinucleotide (CAG) repeat expansion in the androgen receptor (AR) gene, which leads to the production of a mutant AR protein with toxic effects on both lower motor neurons and skeletal muscle[2]. Clinically, SBMA is characterized by progressive muscle weakness and wasting, bulbar dysfunction, and endocrine abnormalities such as gynecomastia, infertility, and testicular atrophy[3].

While the neuromuscular manifestations of SBMA are well documented, the disease may also involve other systems, including metabolic and cardiovascular pathways. Patients with SBMA often present insulin resistance, dyslipidemia, and increased visceral adiposity, contributing to an elevated cardiovascular risk profile[4,5].



Graphical Abstract. A 54-year-old male with genetically confirmed spinal and bulbar muscular atrophy (SBMA), elevated cardiovascular risk, and contraindications to statins and ezetimibe due to persistently high creatine kinase levels, underwent coronary CT revealing subclinical atherosclerosis. Treatment with alirocumab, a PCSK9 inhibitor, led to a 54.9% reduction in LDL-C without adverse effects or neuromuscular deterioration. This case underscores the safety and efficacy of PCSK9 inhibitors in neuromuscular patients with high cardiovascular risk.

CASE PRESENTATION

A 54-year-old male with genetically confirmed spinal and bulbar muscular atrophy (SBMA), carrying a CAG repeat expansion of 47 in the androgen receptor gene, was referred for cardiovascular risk assessment. His clinical history included gynecomastia, dysarthria, and slowly progressive proximal muscle weakness, which had been evident since his early forties. Neuromuscular symptoms were stable under regular follow-up, and the patient reported no current functional limitations beyond moderate exertional fatigue.

Routine laboratory investigations revealed elevated levels of low-density lipoprotein cholesterol (LDL-C), measuring 153 mg/dL, along with a markedly increased creatine kinase (CK) concentration of 1,782 U/L. A coronary computed tomography (CT) angiography revealed a non-obstructive calcified plaque in the proximal segment of the left anterior descending coronary artery, indicating subclinical atherosclerosis and reinforcing the need for lipid-lowering therapy.

However, due to the pre-existing neuromuscular disorder and the persistently elevated CK levels, treatment with statins or ezetimibe was deemed inappropriate owing to the high risk of exacerbating muscle-related adverse effects. After a multidisciplinary evaluation, we decided to initiate alirocumab, a proprotein convertase subtilisin/kexin type 9 (PCSK9) inhibitor, at a dosage of 150 mg, administered subcutaneously every two weeks.

The therapy was well tolerated, with no reported muscular complaints or functional decline. After six months of treatment, lipid profiling showed a substantial improvement: total cholesterol had decreased to 157 mg/dL, LDL-C had dropped to 69 mg/dL, representing a 54.9% reduction, HDL-C was 77 mg/dL, and triglycerides were 88 mg/dL. CK levels remained stable at 1458 U/L. No signs of clinical deterioration or new-onset symptoms emerged during follow-up.

DISCUSSION

This case highlights the potential utility of PCSK9 inhibitors in patients with neuromuscular disorders where statin use is contraindicated. Statin-induced muscle symptoms (SAMS) are a common reason for discontinuation, and patients with neuromuscular disorders, such as SBMA, may be particularly vulnerable[6]. PCSK9 inhibitors, such as alirocumab and evolocumab, offer an effective alternative for lowering LDL-C in these cases, without the risk of muscle toxicity[7-9]. By inhibiting PCSK9, alirocumab increases the number of LDL receptors on liver cells, enabling more efficient removal of LDL cholesterol from the bloodstream. They are administered by

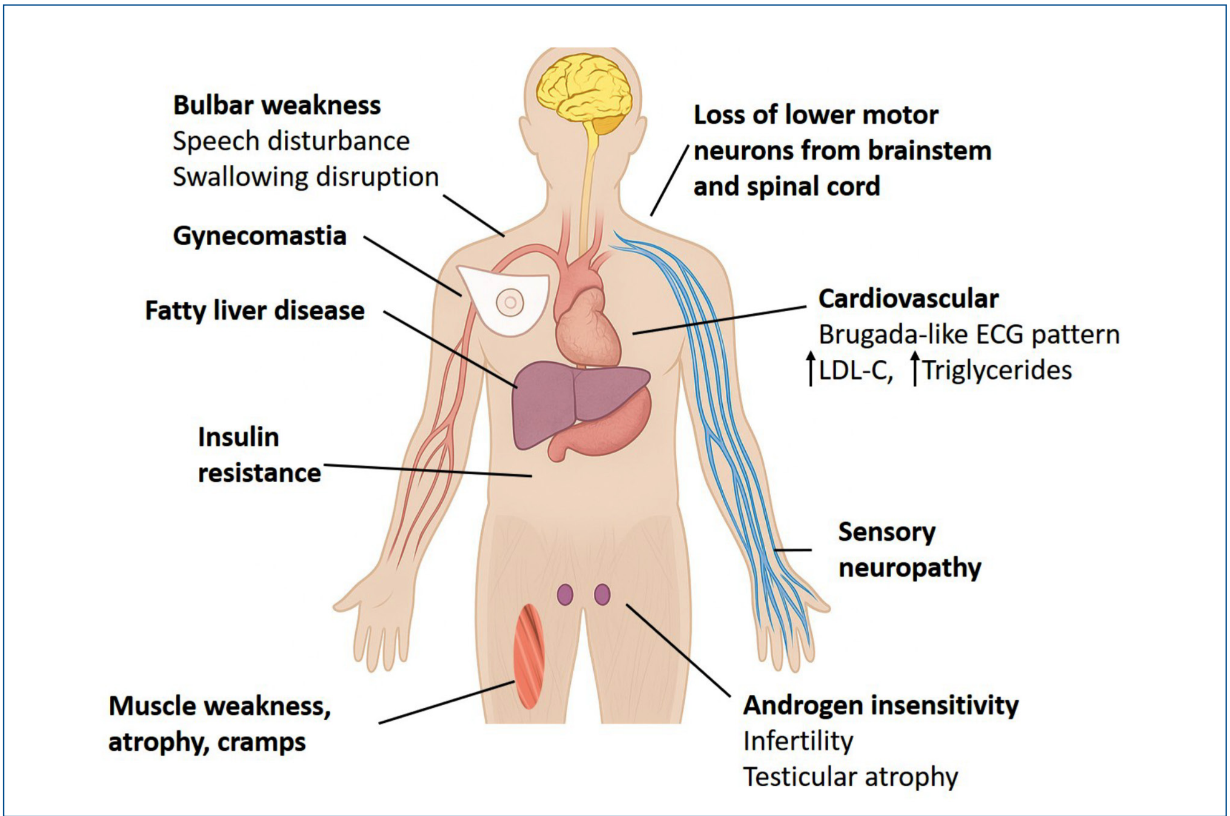


Figure 1. Multisystem involvement in Spinal and Bulbar Muscular Atrophy (SBMA). The figure illustrates the typical clinical manifestations of SBMA, a rare X-linked neuromuscular disorder. Neurological features include bulbar weakness, muscle atrophy, cramps, and sensory neuropathy, resulting from degeneration of lower motor neurons in the brainstem and spinal cord. Endocrine abnormalities, such as gynecomastia and androgen insensitivity (leading to infertility and testicular atrophy), are common. Metabolic and cardiovascular comorbidities include insulin resistance, dyslipidemia (↑LDL-C, ↑triglycerides), fatty liver disease, and a Brugada-like ECG pattern.

subcutaneous injection every 2 weeks. The initial dose is 75 mg; the dose can be increased to 150 mg if LDL-C is not sufficiently reduced. There is an alternative to the once-per-month administration of the 300 mg dose. SBMA is increasingly recognized as a multisystem disease, with evidence pointing to an adverse cardiometabolic profile that may contribute to excess morbidity[4,5]. In statin-intolerant adults, PCSK9 inhibitors such as evolocumab effectively lower LDL-C levels[9]. Moreover, in patients at high or very high cardiovascular risk, these agents reduce non-fatal myocardial infarction and stroke[7]. Despite the lack of randomized studies in this population, this case adds to the limited but growing body of literature suggesting that PCSK9 inhibitors can be safely and effectively used in neuromuscular patients with high cardiovascular risk.

CONCLUSIONS

In patients with SBMA and elevated cardiovascular risk, PCSK9 inhibitors may offer a valuable lipid-lowering option when standard therapies are not feasible. This case supports the need for broader clinical awareness and further investigation into the cardiovascular management of neuromuscular patients.

Conflict of Interest

The authors declare that they have no conflict of interest.

Funding

This research received no external funding.

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Data Availability

The data supporting the findings of this study are available from the corresponding author upon reasonable request.

Authors' Contributions

SM conceived the case report, supervised the clinical management, and critically revised the final manuscript. LC, DPK, GdB, LR, and FP contributed to the collection of clinical data and patient follow-up. RD, FM, GG, and GP carried out the literature review and supported manuscript drafting. AN, ANa, and GMS provided critical revision for important intellectual content. All authors read and approved the final version of the manuscript.

Ethics Approval and Informed Consent

In accordance with the journal's policies, we confirm that written informed consent was obtained from the patient for the publication of this case report, including any accompanying images or clinical data. The patient was made fully aware of the purpose of the publication and agreed to the disclosure of anonymised information for scientific and educational purposes. Ethics Approval is not applicable due to the design of the study.

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