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Methylprednisolone pulse therapy induced bradycardia

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ABSTRACT

High-dose or pulse corticosteroid therapy is used as a mainstay of treatment in a number of autoimmune conditions in both children and adults. Even though it can precipitate short term dose related effects such as hyperglycemia, immunosuppression, sodium and fluid retention, the occurrence of cardiac arrhythmia is considered as a rare adverse effect associated with pulse therapy. In this report we describe a case of bradycardia that developed after the use of steroid pulse therapy. A 56 year old female patient with significant past medical history on Rheumatoid Arthritis was admitted with pain and swelling in multiple joints. She was treated with methylprednisolone pulse therapy (0.5g IV once daily) and developed bradycardia on the third day. Upon discontinuation of the steroid therapy patient's heart rate returned to normal within 48 hours.

INTRODUCTION

High-dose or pulse corticosteroid therapy is used as a mainstay of treatment in a number of autoimmune conditions in both children and adults. Evidences suggest their significant role in musculoskeletal diseases, such as rheumatoid arthritis, as well as dermatological diseases, such as psoriasis [1, 2]. The term pulse therapy arbitrarily defined as the administration of more than 250 mg prednisone (or equivalent) per day as intravenous infusion in order to augment the therapeutic effect and to minimise the long-term adverse effects [1]. It has a significant role in reduction of synovial fluid in polymorphonuclear cell, lymphocytes, immune complexes and CRP.

Even though it can precipitate short term dose related effects such as hyperglycemia, immunosuppresssion, sodium and fluid retention, the occurrence of cardiac arrhythmia is considered as a rare adverse effect associated with pulse therapy. Scarcely it can also cause other adverse effects such as seizures, sudden death and gastro intestinal ulceration or perforation [3]. About 1 to 82% of high dose corticosteroid users may experience cardiac arrhythmias during treatment and bradycardia was the most common type of arrhythmia observed in such patients. The first reports regarding the relationship between bradycardia and high-dose corticosteroids was documented in 1986 [1]. In this report we describe a patient who developed bradycardia after receiving a course of intravenous corticosteroids for the treatment of Rheumatoid arthritis exacerbation.

CASE PRESENTATION

A 56 year old female patient with past medical history of Rheumatoid Arthritis presented to OPD of General Medicine Department with complaints of pain and swelling of multiple joints which was found to be progressive in nature and aggravated since 1 week. Patient was not on treatment for the same since a few months. On physical examination the patient's heart rate was found to be 76 beats/min, BP 120/80 mmHg; she also had tender swelling of metacarpophalangeal and proximal inter phalangeal joints, bilateral knee and ankle joints along with tenderness over cervical spine and left sacroiliac joint(Tender joint count 23; swollen joint count 20). Laboratory investigation showed a random blood sugar level of 73.4 mg/dl, ESR: 105 mm/hr, RA factor: 225u/ml. She was treated with methylprednisolone pulse therapy (0.5g IV once daily) from the first day of admission. Three days after hospitalization, she complained of chest discomfort and mild dizziness which was associated with bradycardia with a heart rate of 48 bpm. Her blood pressure was 120/80 mmHg and there was an elevation in RBS level (141 mg/dl). Cardiovascular examination was otherwise normal. Electrocardiogaram revealed sinus bradycardia with no ST changes (figure: 1). Methylprednisolone pulse therapy was completed on 3rd day and methotrexate (10 mg weekly) therapy was initiated. The patient's heart rate returned to baseline 48 hours after discontinuation of steroid therapy (figure: 2), patient condition stabilized hence discharged and advised review after 1 week in case of increased joint pain or chest pain.

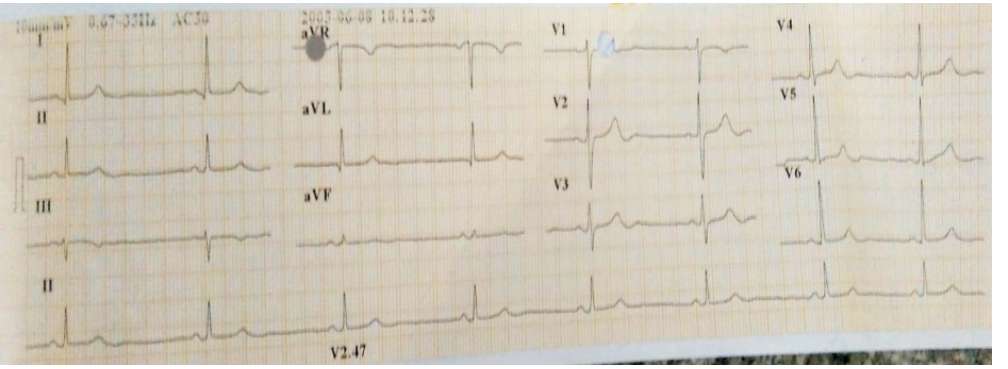

Figure 1 : ECG showing sinus bradycardia upon administration of steroid pulse therapy on the third day of hospitalization

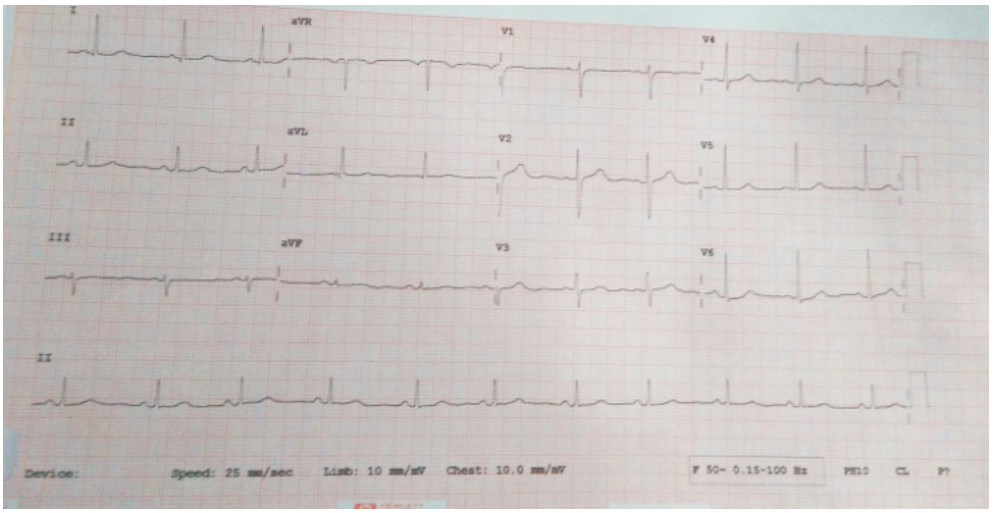

Figure 2 : Normal ECG report obtained 48 hours after the discontinuation of steroid pulse therapy.

DISCUSSION

High dose intravenous pulse methylprednisolone is mainly used for managing autoimmune disorders. A double blind placebo controlled trial by William *et al* in 20 patients with active rheumatoid arthritis showed clinical benefit in methylprednisolone 1g received group compared with placebo [4]. Methyl prednisolone pulse therapy was found to be beneficial in short term treatment of rheumatoid arthritis [5].

Variations in dosing, duration and routes of administration are known to cause severe adverse effects with corticosteroids [6, 1]. The major adverse effects include hypertension, hypokalemia, behavioural changes and infections. The most serious adverse effect reported with the use of corticosteroid includes arrhythmias and sudden death. Corticosteroids play a major role in inducing bradycardia in a small portion of patients. Such cases have been identified in both children and adults [7].

The corticosteroids involved in most of the cases were methylprednisolone, prednisone and dexamethasone [8-18].

The bradycardia associated with methylprednisolone can be symptomatic or asymptomatic. The major symptoms include dizziness and chest pain [1]. In our study the patient experienced chest discomfort and mild dizziness during methylprednisolone pulse therapy which is consistent with the case report on sinus bradycardia in women treated with pulse dose steroids for multiple sclerosis by Kundu *et al* [19]. In our patient the bradycardia was resolved on the 5th day after completion of steroid pulse therapy without any interventions. No cardiac effects were seen in our patient and her blood pressure was normal throughout the study. There was significant but temporary increase in blood sugar concentration on 3rd day which was managed suitably. No significant changes in plasma concentration of electrolytes were found.

Unless several mechanisms suggested for the steroid induced bradycardia, the actual cause was not recognised. Animal studies revealed that the cardiac effects of steroids were mediated by direct action on myocardial membrane and via alterations in cardiovascular sensitivity to catecholamines. However in humans, corticosteroids have the capacity to produce rapid electrolyte shift that may cause cardiac arrhythmias including bradycardia or it may induce changes in sodium and water physiology which further contribute to plasma volume expansion and can lead to activation of low pressure baroreceptors [1].

CONCLUSION

Even though pulse steroid therapy has been employed as an important therapeutic modality, adverse events were common with these agents. But symptomatic sinus bradycardia remains an extremely rare adverse effect of PST compared to asymptomatic

bradycardia. Our patient experienced chest discomfort and mild dizziness as symptoms suggestive of sinus bradycardia. Most cases are self-limiting that does not need any treatment and resolve after discontinuing pulse steroid therapy. Health professionals have the responsibility to provide education and monitor this rare but serious adverse effect.

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