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Case Report

Acute ST elevation myocardial infarction after intravenous immunoglobulin infusion in a young patient: a rare but probable adverse effect of immunoglobulin

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ABSTRACT

Intravenous immunoglobulin (IVIG) is used in the treatment of a variety of disorders, including autoimmune conditions. IVIG has been considered a safe medication, with minor and transient adverse effects. With the wider use of IVIG, the reported rate of adverse effects has been increased, some of them are potentially fatal cardiovascular reactions due to induction of hypercoagulable state. We report a 40-year-old female treated with IVIG for Guillain-Barre syndrome, who developed chest pain 1 hr following IVIG infusion. The symptoms were associated with ST elevation in anterior leads on electrocardiogram. This anterior wall myocardial infarction (MI) is compatible with IVIG-induced hypercoagulability and considered as a probable adverse effect of this medication. To the best of our knowledge, this is probably the first case report where a young patient developed acute MI without any cardiac risk factors after IVIG infusion.

Keywords: Immunoglobulin, Myocardial infarction, Probable adverse effect

INTRODUCTION

Intravenous immunoglobulin (IVIG) is a highly purified globulin preparation obtained from the pooled plasma of thousands of healthy donors. Although initially given as replacement therapy for patients with primary and secondary immunodeficiency states, IVIG has proven to be effective in the treatment of various autoimmune and inflammatory disorders. IVIG have been considered a safe medication, the majorities of adverse effects are mild, self-limited, and related to the speed of infusion. These effects include headache (50%), back pain (4-6%), chills, myalgia (4%), cough (2%), fever (1%), or chest discomfort and do not usually necessitate discontinuation of therapy.[1] With the wider use of IVIG, the reported rate of side-effects has increased, some of them being potentially fatal thrombotic complications including myocardial infarction (MI) and stroke. Although an association between IVIG administration and MI has not been yet established in prospective clinical trials, clinical experience suggests that elder individuals or those with ischemic heart disease are potentially at risk for cardiac ischemia with IVIG administration.[2,3] We report a case of probable IVIG-induced acute MI in a young female without any cardiac risk factors, occurring during treatment for Guillain-Barre syndrome.

CASE REPORT

A 40-year-old female admitted in the medical ward due to weakness in all four limbs since 3 days. After detailed history and neurological examination probable diagnosis of Guillain-Barre syndrome was made. Her past medical history is not significant. Blood investigations showed normal electrolytes levels, normal hemogram, normal renal function tests, and other biochemistry was also unremarkable. Baseline electrocardiogram showed normal sinus rhythm (Figure 1). Diagnosis of Guillain-Barre syndrome was confirmed by nerve conduction study, which was suggestive of demyelinating pathology. Hence, IVIG 0.4 g/kg/day for 5 days was planned. After 1 hr of

initiation of an infusion of 5% IVIG at infusion rate of 20 ml/hr, patient was started having chest pain radiating to the left arm along with shortness of breath and perspiration. At the patient's request, the infusion rate was decreased; the infusion was subsequently discontinued when the symptoms did not resolve. Electrocardiogram was done, which revealed ST elevation in anterior precordial leads, suggestive of acute anterior wall MI (Figure 2) and two-dimensional echocardiography showed regional wall motion abnormality in anterior territory. Patient was offered thrombolytic therapy, but she refused for this, so treatment with aspirin, clopidogrel, Enoxaparin along with intravenous nitroglycerine was initiated. Patient got relief in pain after 3-4 hrs. During hospitalization patient undergone plasmapheresis treatment and improved. She was refused for further cardiac evaluation.

DISCUSSION

We report here a rare case of ST elevation MI after IVIG treatment in a young female patient without any cardiac risk factors. Although several case reports of MI after the use of IVIG were published, it is not generally considered an adverse effect of IVIG. According to adverse effects probability scale developed by Naranjo et al.,[4] there was a probable association between IVIG administration and occurrence of ST elevation MI in this patient. Rapid administration of IVIG may cause flushing altered heart rate, blood pressure. Medical literature showed a very low rate of thromboembolic events in young patients with MS

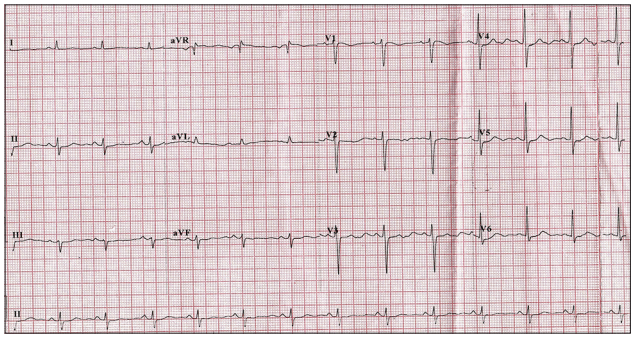

Figure 1: Baseline electrocardiogram showed normal sinus rhythm.

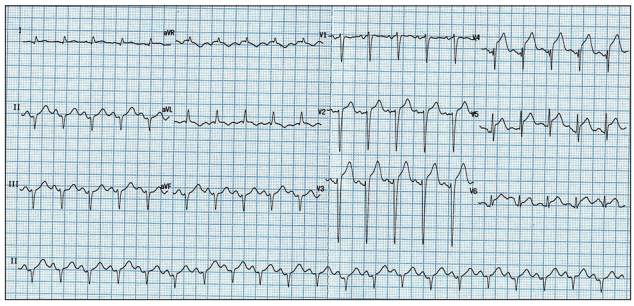

Figure 2: Electrocardiogram after complaining of chest pain showed ST elevation myocardial infarction in anterior leads.

treated with low-rate infusion.[5] The recommended initial infusion rate is 0.5 mL/kg/h for a 5% IVIG solution and may be titrated up to 4 mL/kg/h as tolerated.[6] The first report of serious thrombotic events occurring during treatment with IVIG was published in 1986.[6] In spring 2002, on the basis of 28 published studies and internal medication safety monitoring data, US Food and Drug Administration, issued safety warnings regarding the possible association of IVIG with serious thrombotic events.[7]

A recent review summarized published cases of serious thromboembolic events, including 12 that were fatal, occurring during or after IVIG infusion.[8] Thromboembolic complications were more common in association with higher IVIG doses (>400 mg/kg daily) or more rapid infusion rates. The pathophysiology of IVIG-induced thrombosis is not well-recognized. Proposed mechanisms consist of platelet or endothelial cell activation and increased blood viscosity, which is a significant determinant of subendocardial oxygen delivery.[9,10]

Reductions in IVIG doses and administration at lower infusion rates may be advisable for patients with underlying cardiovascular disease or those who experience anginal symptoms during or after IVIG infusion. Manufacturer guidelines strongly recommend that when there is a potential risk of a thrombotic event, the concentration of IVIG should not exceed 5%, the infusion should be initiated at a rate of 0.5 mL/kg/hr, and the infusion rate should be increased slowly to a maximum of 4 mL/kg/hr as tolerated.[7] In patients with known cardiovascular disease or thrombotic risk factors, IVIG should be administered in a setting in which monitoring by 12-lead electrocardiography can be performed. Patients should be monitored for symptoms characteristic of cardiac events, such as chest pain or shortness of breath. Continuous telemetry monitoring may be ideal for high-risk patients, but probably precludes IVIG administration in many outpatient settings. Complaints of angina around the time of infusion should trigger prompt discontinuation of IVIG therapy, and the symptoms should be investigated for cardiac events in light of the published cases. Patients experiencing IVIG-associated MI should be treated according to the current standard of care and treatment guidelines. IVIG should not be administered during MI or the subsequent recovery period. Clinicians should consider decreasing future IVIG doses and/or infusion rates if cardiac events appear to be related to immunoglobulin administration. Preventive treatment with antiplatelet or anticoagulant agents has been suggested;[8] but, there are no clear data to support this recommendation.

CONCLUSION

It is difficult to calculate the true incidence of MI and other thrombotic complications of IVIG treatment because few cases are reported, which are highly variable in the details provided. Cardiovascular evaluation is not routinely recommended before IVIG treatment; however, it should

be routinely performed in elderly patients or with risk factors for cardiovascular disease who are candidates for IVIG treatment. Although fatal coronary events due to IVIG administration are still considered rare, the potential seriousness of these events necessitates caution and vigilance on the part of the clinician.

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