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A CASE REPORT ON ERYTHROPOIETIN INDUCED MACULOPAPULAR RASHES

General Medicine

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ABSTRACT

Erythropoietin is a hormone produced by the kidneys. It acts on red blood cells to protect them against destruction. It stimulates the bone marrow to produce more blood cells.3 Chronic renal failure is usually associated with a moderate to severe hypoproliferative anemia. Red cells are typically normocytic and normochromic. Reticulocytes are decreased. The anemia will occurs as there is a reduction in the adequate amounts of erythropoietin as well as red blood cell survival.4 Several adverse effects are reported with erythropoietin. In this case report we are emphasizing on erythropoietin induced maculopapular skin rash, one of the rare adverse effects associated with erythropoietin.

KEYWORDS

INTRODUCTION

Erythropoietin stimulating agents are used to treat anemia caused by Chronic Kidney Disease,certain anti-cancer drugs and certain treatment for HIV.Adverse effects to erythropoietin occurs rarely.1 Erythropoietin is a glycoprotein produced in the kidney which stimulates red blood cell production and stimulates the division and differentiation of committed erythroid progenitors in the bone marrow. Epoetin alfa consists of 165 amino acid glycoprotein manufactured by recombinant DNA technology. It has the same biological effects as endogenous erythropoietin. molecular weight of EPO 30,400 daltons . EPO is formulated as a sterile, colorless liquid in an isotonic sodium chloride/sodium citrate buffered solution or a sodium chloride/sodium phosphate buffered solution for intravenous (IV) or subcutaneous (SC) administration.2 They have been shown to be associated with venous thromboembolism and cardiovascular events. Erythropoietin induced maculopapular skin rash is a rare adverse reaction.

Case Report

A 68 year old male patient with Hypertension, Type 2 Diabetes Mellitus, Dyslipidemia and Chronic Kidney Disease and was prescribed subcutaneous injection of epoetin-α for the treatment of anemia due to Chronic Kidney Disease. Currently taking medications are Glimipiride and Metformin, Atorvastatin, Telmisartan, Cilinidipine, Sodium bicarbonate, Ferrous fumerate, Folic acid ,Zinc. About 2 weeks after the injection of epoetin-α, he developed erythematous pruritic rash. Physical examination revealed, generalized erythematous pruritic maculopapular rashes on his body and limbs without mucosal involvement. Laboratory investigations showed white blood cell count 6700/microliter(4000-11000), neutrophil 80% (43-72), lymphocyte 11% (19-48), eosinophil 9% (0-7), hemoglobin 8.8 g/dl (13.00-18.00), packed cell volume 25.8% (38-48) ,platelets 4.05 lakh/microlitre (1.5-4.5), creatinine 2.21 mg/dl(0.9-1.2) Ferritin 233.4 ng/mL(24 - 336) and % TSAT 11%(25-50) , Drug discontinuation was suggested due to the suspicion of delayed allergic reaction to epoetin-α and was resolved by itself within 2 days without any treatment

DISCUSSION :

Erythropoietin (EPO) is a glycoprotein hormone, produced naturally by the renal cortex (peritubular cells) of the kidney, which stimulates red blood cell production. Erythropoietin stimulating agents (ESAs) are recombinant versions of EPO produced pharmacologically .ESAs are very useful in stage 5 CKD (who receive dialysis) as well as patients soon to need dialysis. Examples of ESAs are epoetin and darbepoetin.Endogenous erythropoietin and erythropoietin stimulating agents stimulate the division and differentiation of erythropoietin progenitor cells.

The surface of CD34+ hematopoietic stem cells and erythrocytes, contains EPO receptors . Endogenous EPO or ESAs bind to these receptors thereby creates a cellular signaling cascade, which activates genes that promote cell proliferation and prevent apoptosis. This results in an increase in total body hemoglobin and hematocrit.The time to reach peak concentration is slower via the subcutaneous route than the intravenous route. subcutaneous injectable erythropoietin has much lower bioavailability (20 to 40%) than that of the intravenously administered product.Volume of distribution of intravenous epoetin alfa was ranging from 40 -63.80 mL/kg.Erythropoietin and epoetin alfa are cleared via the EPO-R-expressing cells, and may also involve other cellular pathways in the interstitium, probably via cells in the reticuloendothelial scavenging pathway or lymphatic system .Small amount of unchanged epoetin alfa is excreted through urine .The half life is approximately 4 hours who receiving an intravenous injection.5

Masahiro Sakaguchi et al, reported that patient in their study first received a new EPO product (epoetin-α) that contained gelatin and immediately showed symptoms of severe anaphylaxis. After recovery, she received a conventional EPO product with HSA and had no allergic reaction. When she again received an EPO product with gelatin, she showed similar symptoms of anaphylaxis.She had antigelatin IgE. These results suggest that the anaphylaxis to EPO products were associated with hypersensitivity to gelatin included in the products.6 In our study, the patient presented with maculopapular rashes after administering Inj. EPO and showed delayed reaction.It was resolved after the discontinuation of drug.

CONCLUSION

ESA hypersensitivity has been reported as both immediate and delayed allergic reactions varying in severity ranging from mild to fatal reactions. The above case report represents a rare incidence of maculopapular skin rash caused by erythropoietin.However the mechanism of erythropoietin induced maculopapular skin rash is unknown.The patient may present with either acute or delayed reaction and drug is withdrawn if the patient develops reaction towards the drug.In this case ,the patient developed delayed reaction after the administration of erythropoietin and thus the drug was stopped .The reaction abated within 2 days.

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CONFLICT OF INTEREST

The authors declare that there is no conflict of interest

ABBREVIATIONS

ESA-Erythropoietin Stimulating Agent

EPO-Erythropoietin
CKD-Chronic Kidney Disease
HAS-Human Albumin Serum

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