BSH 2020 VIRTUAL
9 -14 NOVEMBER
British Society for Haematology
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60 1960–2020

LENALIDOMIDE INDUCED ITP IN MYELOMA WITH RESPONSE TO STEROIDS AND TPO AGENTS
A Rare Important Event To Consider - Case Series From Single Institute From South India

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INTRODUCTION

Immune thrombocytopenia (ITP) is frequently encountered in patients with lymphoproliferative disorders. However this is only rarely reported in patients with multiple myeloma. The most likely explanation for this could be that monoclonal immunoglobulin (Ig), a hallmark of MM, does not exert activity as an antibody and often accompanies depressed normal Igs and consequently renders patients immuno-incompetent.[1] Though drug induced thrombocytopenia is frequently observed, it is a rare phenomenon. We report a series of Myeloma cases with ITP post therapy.

AIM

The aim of this study was to assess for the response to the various treatments in improving the platelet count in patients with lenalidomide induced ITP

METHOD

All the myeloma cases presented with associated ITP defined as “sudden, abnormal lowering of the platelet count after ruling out all possible other causes like post infection, with peripheral smear characteristics like giant platelets with normal megakaryocytes in marrow and presence of antibodies against platelets.” between 2012-2019 at single institute were taken. The clinical characteristics, treatment received, and the response were evaluated.

RESULTS

A total of 4 cases presented during the between 2012-2019 period with following characteristics (table1). The one common finding is induction with lenalidomide + dexamethasone in all the cases.

We could observe that all these cases met the “Naranjo adverse drug reaction probability scale-as high probability” and hence we postulate that all these cases are probably Lenalidomide induced ITP

CHARACTERISTCS	CASE 1	CASE 2	CASE 3	CASE 4
AGE/GENDER	65/M	42/F	54/M	69/F
DURATION OF SYMPTOMS	2 months	1 month	1 month	2 months
M BAND LEVELS	3.8 gm/dl	4.2 gm/dl	2.9 gm/dl (igA)	6.3 gm/dl
KARYOTYPING	Normal	Normal	Normal	Normal
BETA 2 MICROGLOBULIN	26.92mg/l	43.12mg/l	16.83mg/l	31.74mg/l
ISS – STAGE	Stage II	Stage III	Stage II	Stage III
SERUM CALCIUM	8.6mg/dl	8.0 mg/dl	9.1 mg/dl	7.8mg/dl
HEMOGLOBIN	10g	9.8g	9.5g	9g
SERUM CREATINIE	1.0mg/dl	0.8mg/dl	1.2mg/dl	1.1mg/dl
% MARROW PLASMA CELLS	10%	12%	10-12%	10-12%
TREATMENT GIVEN	4 cycles Vd f/b remission then on maintenance lenalidomide	4 cycles Vd then on maintenance Lenalidomide f/b HSCT	4 cycles of Vd then on Lenalidomide , on progression started on Thalidomide then underwent HSCT	4 cycles of Lenalidomide & Dexamethasone with denosumab
INTERVAL BETWEEN DRUG & ITP	2.1 months	6 months	2 months	3 months
RESPONSE TO 1ST LINE	Poor response to steroids	Received 4 weeks of rituximab	Received steroids	Recovery after 2 weeks after receiving Eltrombopag
RESPONSE TO 2ND LINE	Recovery within 2 weeks of Eltrombopag but thrombocytopenia persisted	IV Ig – short lived response for 3 months	Recovery within 4 weeks of Romiplostim	
RESPONSE TO 3RD LINE	Best response with romiplostim	Recovery within 2 weeks with weekly Romiplostim and VCR		

CONCLUSIONS

Though Lenalidomide can induce immune dysregulation & cause autoimmune diseases, ITP is extremely rare phenomenon with first reported case in 2018.[2] However, appropriate treatment was not defined by the authors and was left as “a difficult to treat condition”.

The two proposed mechanisms of this rare condition are

1. Immunoglobulin (specific against platelets) production from the myeloma cells, which were selected by the antitumor effect of Lenalidomide.
2. Antibodies from normal plasma cells, which were activated by immune dysregulation effect of Lenalidomide

In our observation- attempts like steroids or rituximab did not yield optimal results. This opens the possibility of megakaryocytic function suppression as possible mechanism and we suggest that a combination of Steroids with stimulating agents like Eltrombopag/ Romiplostim are the best choice as we could achieve best response with these agents in all the cases

ACKNOWLEDGEMENT

We acknowledge the department of pathology for their support.

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