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Case Study

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# EFFECTIVENESS OF LENALIDOMIDE IN A PATIENT OF POEMS SYNDROME WITH THROMBOCYTOSIS: A CASE REPORT

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## ABSTRACT

POEMS syndrome is a rare multisystem disease associated with plasma cell dyscrasia. We report herein a case of POEMS syndrome with thrombocytosis who had multiple hospitalizations during five year interval. The patient was treated under five chemotherapy regimen. We focus on progress of her disease and effect of Lenalidomide on blood platelets. Thrombocytosis is seen in almost 50% of the cases of POEMS syndrome and use of Lenalidomide chemotherapy regimen may lower the increased blood platelets.

**KEYWORDS;** POEMS syndrome, lenalidomide, plasma cell dyscracia.

## INTRODUCTION

POEMS syndrome is a rare paraneoplastic syndrome caused by disorder of plasma cell, clinically described by the acronym (POEMS): Polyneuropathy, Organomegaly, Endocrinopathy, Monoclonal plasma cell disorder, and Skin changes.[1] It is a rare but fatal multisystem disease potentially associated with substantial deterioration of quality of life.[2] Though the cause of POEMS syndrome is unknown but the major feature related to this syndrome are chronic overproduction of pro inflammatory and other cytokines such as VEGF.[3] The diagnosis of POEMS syndrome is made through three classified criteria. a) Mandatory criteria: Polyneuropathy, and Monoclonal plasma proliferative disorder. b) Other major criteria: Sclerotic bone lesions, Elevated VEGF and Castleman's disease. c) Minor criteria: Organomegaly, Edema, Endocrinopathy, Skin changes, Papilledema and Thrombocytosis. For the confirmation of diagnosis of POEMS syndrome the prerequisite is the presence of both mandatory criteria including polyneuropathy and a monoclonal plasma cell-proliferative disorder, and at least one major and one minor criterion.[4]

## CASE REPORT

A 47- year-old female, known case of POEMS syndrome with thrombocytosis, diagnosed 8 years back in another hospital was admitted in our hospital for 7 times in five years interval from 2014 to 2019. Back in 2011, she visited Tongji hospital with complain of fatigue and lower limb numbness for 6 months. Later she was diagnosed as POEMS syndrome with thrombocytosis in August 2013 on the basis of clinical presentation, monoclonal gammopathy and additional physical findings. Bone marrow examination was normal. There was no evidence of Castleman's disease. After five courses of Melphalan chemotherapy she came to our hospital for further treatment. We present this patient with monoclonal gammopathy, polyneuropathy, organomegaly, endocrinopathy, skin changes and thrombocytosis which later developed sclerotic bone lesions. In this case report, we emphasis on effectiveness of Lenalidomide addition in chemotherapy regimen on increased platelets. After 8 months of diagnosis of POEMS syndrome the patient was presented with dull pain in left shoulder for 3 months. Excluding mild hepatosplenomegaly no other abnormalities were detected. Routine blood tests including platelets were tested. Some significant lab reports of each admission are listed in table 1. Other tests performed were Immunofixation electrophoresis which revealed IgA-lambda type monoclonal immunoglobulin disease. Deep vein angiography of both lower extremities was normal. Patient was treated with MPTC (Melphalan, Prednisone, Thalidomide and Cyclophosphamide) chemotherapy regimen. Tab. Aspirin to prevent thrombosis and Levothyroxine sodium for hypothyroidism was continued in each visit. Blood platelets tested after chemotherapy were still elevated. Same chemotherapy TD (Thalidomide and Dexamethasone) was used as discharge medication for each visit. During her second admission, CT chest and abdomen reported Right upper lung inflammation, right pleural hypertrophy and hepatosplenomegaly. Inner diameter of dorsal pedal artery of left lower extremity was smaller than normal in color doppler ultrasound and decreased Left ventricular

systolic function was recorded in echocardiography. Along with MPTC, Hydroxyurea was also added in chemotherapy regimen but it was ineffective for thrombocytosis. Radioactive Iodine Uptake Testing was done on her third visit and was found to be normal. The patient was treated with MPTC plus Hydroxyurea. As formerly, blood platelets were elevated tested before and after treatment. In next visit, she was presented with aggravated pain and edema on lower limb for 10 days. Color Doppler ultrasonography demonstrated inner diameter of dorsal pedal artery of left lower extremity was smaller than normal. Same chemotherapy regimen MPTC and Hydroxyurea was used and her lower limbs edema was alleviated but platelets were still elevated. On her fifth admission her physical strength decreased significantly and slightly reduced weight was observed. Diffuse cutaneous hyperpigmentation along with anterior pitting tibial edema of both lower extremities were also noted. In chemotherapy regimen Melphalan was stopped and CTD regimen and Hydroxyurea was continued. After treatment, edema of both lower limbs was alleviated but thrombocytosis persist. During her 6$^{th}$ admission, echocardiography stated Left atrial enlargement with 70% ejection fraction. This time with CTD regimen the patient was treated with interferon alpha as an alternative of hydroxyurea but that was also ineffective for lowering the platelets. On her last admission she was presented with numbness on her both hands and edema on both lower limbs aggravated for 1 month. Physical examination revealed cachexic face and palpable liver and spleen**.** The fingertips of both hands were numb. Leukonychia with edema on both hands (more on right) as shown in figure (1) and ankle edema was seen. Diffuse hyperpigmentation, Seborrheic keratosis on face and glomeruloid hemangioma in right lower abdomen as shown in figure (2) was also detected. Routine blood tests were sent and blood platelets was elevated as usual. Echocardiography revealed slight enlargement of left ventricle, mild tricuspid regurgitation, mild pulmonary hypertension and mild mitral regurgitation. Chest CT revealed bilateral pulmonary infection, pericardial effusion and bilateral minimal pleural effusion. Left nephrolithiasis, bilateral kidney enlargement with slight perirenal exudation, unclear retroperitoneal structure and bilateral pleural effusion with hepatosplenomegaly was reported in abdominal CT. Spine MRI scanned Cervical and lumbar degeneration on C5/6, C6/7, L4/5, L5/S1 lumbar intervertebral disc posterior mild bulging; sacral cyst. New chemotherapy regimen (CtX + Dex + R) Cyclophosphamide, Dexamethasone and Lenalidomide was started. Repeat routine blood tests including Platelets were tested few days after using Lenalidomide. For the first time her blood platelets was dropped to normal range as shown in table 1**.** This might be due to addition of Lenalidomide in new chemotherapy regimen.

**Figures**

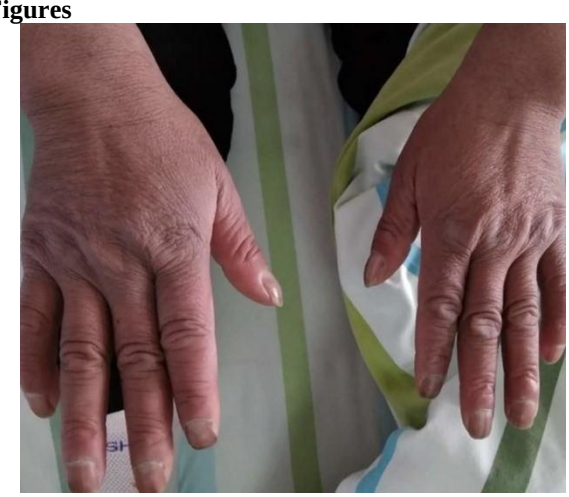

***Figure 1:*** **Edema with Leukonychia on both hands.**

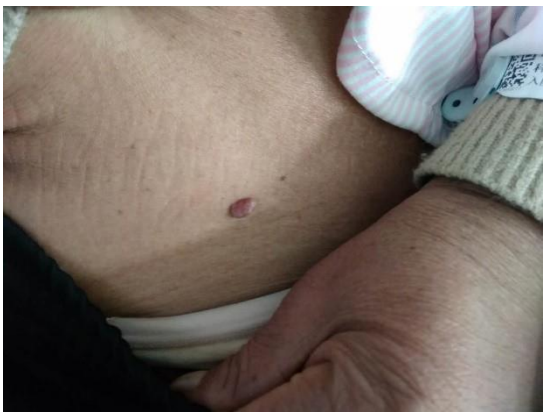

***Figure 2:*** **Glomeruloid hemangioma on abdomen.**

**Table 1: Significant laboratory values and chemotherapy regimen during each admission.**

| Lab Markers/Treatment | 1$^{st}$ admission | 2$^{nd}$ admission | 3$^{rd}$ admission | 4$^{th}$ admission | 5$^{th}$ admission | 6$^{th}$ admission | 7$^{th}$ admission | Reference range |
|---|---|---|---|---|---|---|---|---|
| **Platelets** | **430**$^{*}$ | **1240**$^{*}$ | **1131**$^{*}$ | **984**$^{*}$ | **830**$^{*}$ | **428**$^{*}$ | 310 | 125-350x($10^9$/L) |
| **VEGF** | NR | NR | NR | NR | NR | NR | **>800*** | 0-142 (pg/ml) |
| **IgA** | **6.08**$^{*}$ | **4.28**$^{*}$ | 3.62 | 3.41 | 3.49 | 2.80 | **4.87**$^{*}$ | 0.7-4 (g/L**)** |
| **FT4** | **9.69**$^{*}$ | **9.83**$^{*}$ | **9.47**$^{*}$ | **10.01**$^{*}$ | **9.53**$^{*}$ | **9.92**$^{*}$ | **8.98**$^{*}$ | 10.8-21.2(pmol/L) |
| **TSH** | **7.02**$^{*}$ | **4.52**$^{*}$ | **4.79**$^{*}$ | **5.24**$^{*}$ | **5.31**$^{*}$ | **4.81**$^{*}$ | **5.11**$^{*}$ | 0.3--4.7 (IU/mL) |
| **β2MG** | **301.95**$^{*}$ | **360.11**$^{*}$ | **365.53**$^{*}$ | **493.75**$^{*}$ | 183.92 | 216.29 | **262.19**$^{*}$ | 84—254(nmol/L) |
| **μKAP** | <18.5 | <18.5 | <18.5 | <18.5 | <18.5 | <18.5 | **137.0**$^{*}$ | <18.5 |
| **μLAM** | <50 | <50 | <50 | <50 | <50 | <50 | **104.0**$^{*}$ | <50 |
| **IL6** | NR | NR | NR | NR | NR | NR | **11.54**$^{*}$ | 0-7 (pg/mL) |
| **Chemotherapy** | MPTC | MPTC, HU | MPTC,HU | MPTC,HU | CTD,HU | CTD, INN | CDR | - |

(*****): Abnormal values, VEGF: vascular endothelial growth factor, IgA: immunoglobulin A, FT4: free thyroxine, TSH: thyroid stimulating hormone, β2MG: β2-microglobulin, μKAP & μLAM: Kappa and Lambda free light chains in urine,

IL6: interleukin 6, NR: not reported, MPTC: melphalan, Prednisone, thalidomide, cyclophosphamide, HU: hydroxyurea, D: dexamethasone, INN: interferon alpha, R: Lenalidomide.

## DISCUSSION

Thrombocytosis refers to an increased platelet count (>450 x 109/L in blood. Thrombocytosis as one of the manifestation of POEMS syndrome is seen in almost half of the patients. It can be classified into primary and secondary forms. Whereas primary thrombocytosis is observed in myeloproliferative syndromes, mutations in Janus kinase 2 (JAK2), thrombopoietin gene (TPO), secondary or reactive thrombocytosis is noted in numerous clinical situations, especially in association with inflammatory states of either infectious or noninfectious origin such as trauma and malignancy. Inflammatory thrombocytosis is thought to be related to increased interleukin-6 levels.[5] Thrombocytosis causes thrombotic and hemorrhagic complications especially in brain, hands, feet heart and lungs.

Aspirin is the commonest drug used to decrease platelet aggregation and inhibit thrombus formation. The medications used to lower the increased blood platelets in clinical practices are Hydroxyurea and Interferon alfa. Hydroxyurea suppresses bone marrow production of blood cells including platelets. But these two drugs are not always effective as in our case. As mentioned above, Hydroxyurea was used for four times and interferon alpha was used once during her hospital stay. But these both medications were fruitless. Addition of Lenalidomide to cyclophosphamide and dexamethasone lowered the increased blood platelets in our patient.

## CONCLUSION

In summary, use of Lenalidomide chemotherapy regimen in POEMS syndrome may normalize the increased blood platelets. So more treatment trials including Lenalidomide and other drugs should be executed to find the efficacy in lowering the blood platelets in POEMS syndrome.

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**Conflicts of interest**
There are no conflicts of interest.

## REFERENCES

1. M.L. Mauermann, Hematol. Oncol. Clin. North Am., 2018; 32: 153–163.
2. H. Li, Y. Huang, Y. Li, B. Zheng, J. Cui, M. Liu, BMC Endocr. Disord, 2019; 19: 1–7.
3. R.A. Kyle, 80 - Monoclonal Gammopathies, Fifth Edit, Elsevier Ltd, 2016.
4. R. Brown, L. Ginsberg, J. Neurol, 2019; 266: 268–277.
5. U.S. National Library of Medicine, (2013).