POEMS syndrome: A rare paraneoplastic presentation of spinal plasmacytoma

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SUMMARY

The acronym POEMS syndrome was coined for a unique multisystem disorder characterised by peripheral neuropathy, organomegaly, endocrinopathies, monoclonal gammopathy and skin changes. We report a male patient presenting to us with spinal plasmacytoma complicated with paraplegia. He was subsequently diagnosed to have POEMS syndrome and successfully treated with thalidomide and dexamethasone. Post treatment, he is able to ambulate independently.

INTRODUCTION

In 1980, the acronym POEMS syndrome was suggested for a unique multisystem disorder characterized by Peripheral neuropathy, Organomegaly, Endocrinopathies, Monoclonal gammopathy and Skin changes.[1] As it is a rare disorder, we are of the opinion that POEMS syndrome is underreported in Malaysia. We report here a young male patient with features of this rare disorder after he presented to us with spinal plasmacytoma complicated with paraplegia.

CASE REPORT

A 32-year-old Malay man, an office clerk presented with progressive bilateral lower limb weakness for five-month duration. It was associated with gradual painless abdominal distension without lower limb swelling. He denied any history of trauma, back pain or high-risk behaviour. Systems review was significant for erectile dysfunction with loss of libido.

Clinically, he was bedbound, hyperpigmented (Figure 1A), clubbed, with facial lipodystrophy. There was bilateral sensorimotor peripheral neuropathy over both upper and lower limbs where power of the lower limbs until hips were 1/5 bilaterally while upper limbs were 3/5. Anal tone and cranial nerves examination were normal with no papilloedema. Abdominal examination revealed ascites and splenomegaly one centimetre below costal margin. Sub-centimetre cervical and axillary nodes are palpable. Lung examination revealed bilateral pleural effusions (Figure 1B).

Nerve conduction study showed symmetrical demyelination sensorimotor polyneuropathy while electromyogram showed neuropathic changes.

Abdominal ultrasonography revealed splenomegaly and ascites but no features of portal hypertension.

Abdominal paracentesis revealed non-portal hypertensive cause of ascites with serum albumin ascites gradient of nine while pleural tapping was transxudative with no positive culture or cytology. Viral hepatitis and human immunodeficiency screen were negative. Sputum acid fast bacilli, Mantoux testing and sputum *Mycobacterium tuberculosis* were negative. Serum free lambda light chain with very low level of paraprotein was detected by immunofixation. Basic blood parameters are listed in Table I. Urine protein electrophoresis was not done.

Computed-tomography (CT) scan of the spine revealed L2-L4 vertebrae spinal mass with L3 osteosclerotic lesion (Figure 1C). Skeletal survey was performed to look for other bony lesions but was normal. As he refused excisional biopsy of cervical node, fine needle aspiration cytology was performed and was inconclusive.

Biopsy of the spinal mass stained strongly for CD 138 and showed lambda light chain restriction. Bone marrow trephine showed no osteosclerosis or paratrabecular fibrosis while aspiration revealed 6% plasma cells with no abnormal forms of plasma cells. Bone marrow immunophenotyping showed 0.6% plasma cells expressing both kappa and lambda light chain.

Diagnosis of POEMS syndrome was made where five fractions of radiotherapy (20 Grays) were delivered to the spinal mass before he underwent posterior instrumentation and tumour debulking. He underwent six cycles of thalidomide-dexamethasone as the main treatment in view of our limited resources.

After completion of chemotherapy, objective clinical assessment of the disease parameters improved. Clinically, there was no pleural effusion, ascites or palpable spleen. Neurologically, he is no longer bedbound and is currently ambulating independently. Repeated nerve conduction study 18 months later showed improvement. Repeated paraproteinemia revealed no significant interval change. Currently he is under regular haematology clinic follow up with oral gabapentin and thalidomide. A CT scan of the spine was arranged for him previously to assess radiological response; however, he defaulted the CT appointment and a newer appointment has been scheduled where he has been counselled on the importance on being compliant to treatment.

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Table I: Investigation results

Full Blood Count	Result	Others	Result
Haemoglobin (g/dL)	17.5	ESR*(mm/Hr)	35
Haematocrit (%)	53%	C-Reactive Protein (mg/L)	4.8
Total White Cell, x 10^3 cells/ml	9.7	HIV / Hep Bs Ag / Hep C	NR
Platelet count, x 10^3 cells/ µL	399	Tumor markers (CEA, AFP, PSA, LDH)*	Normal
Renal Profile		Liver Function Test	
Serum urea (mmol/L)	5.4	Total protein	77
Serum sodium (mmol/L)	131	Serum albumin (g/L)	42
Serum potassium (mmol/L)	4.4	Globulin	35
Serum chloride (mmol/L)	98	Aspartate aminotransferase (U/L)	12
Serum creatinine (µmol/L)	58	Alanine aminotransferase (U/L)	6
		Alkaline phosphatase (U/L)	75
		Total serum bilirubin (µmol/L)	10.5
Endocrinology		Echocardiography	
Serum testosterone (nmol/L)	0.6	ECHO Ejection Fraction	55%
Luteinizing Hormone (mIU/L)	5.2	- Global pericardial effusion	1.3cm
Follicle Stimulating Hormone (IU/L)	7.1	- No valvular lesions	Normal
HbA1c (%)	5.2		
Fasting Blood Sugar (mmol/L)	4.8		
Thyroid Stimulating Hormone (mIU/mL)	4.38		
Free thyroxine (pmol/L)	13.03		

* CEA, Carcinoembryonic antigen, AFP, Alpha-feto Protein, PSA, Prostate Specific Antigen, LDH, Lactate Dehydrogenase, ESR, Erythrocyte Sedimentation Rate

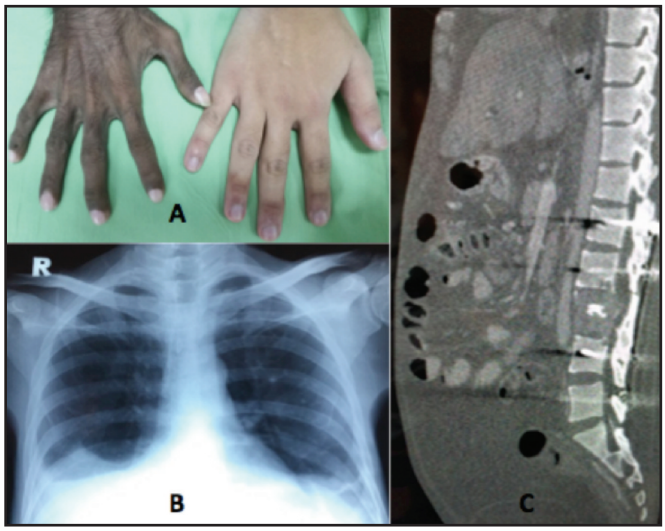

Fig. 1: (A) Comparison between patient's right hand (left) with that of the physician's (right). (B) Chest radiograph showing bilateral pleural effusion. (C) CT spine showing osteosclerotic lesions over L3 vertebrae.

DISCUSSION

Our patient has plasmacytoma while the symptoms also fulfils the criteria for diagnosis of POEMS syndrome as outline by Dispenzieri.[2] He had both mandatory criteria of polyneuropathy and Lambda restricted monoclonal plasma cell disorder. A major criterion is the osteosclerotic lesion in the CT spine while he demonstrated many minor criteria such as organomegaly, extravascular volume overload, hyperpigmentation and polycythaemia. Unfortunately, serum vascular-endothelial growth factor (VEGF), another major criterion was not done due to our limited resources.

Patients diagnosed with POEMS syndrome with only an isolated bone lesion without clonal plasma cells found may respond to radiation where symptoms may improve over the course of 3-36 months.[2] For patients with two or more bone lesions or clonal plasma cells on iliac crest biopsy, systemic therapy is recommended.

However, there are no randomized controlled trials in the systemic treatment of POEMS. Recommended chemotherapy, based on case reports, includes melphalan-dexamethasone, cyclophosphamide-dexamethasone, lenalidomide-dexamethasone, as well as bortezomib-dexamethasone.[2] Literature search for cases in Malaysia revealed only a case report by Nyunt et al., utilising melphalan-prednisolone in a tertiary teaching hospital in area around Klang Valley.3 When chemotherapy was delivered accordingly to POEMS patients, at least 50% of patients will have significant improvement.[2]

In targeting the monoclonal gammopathy, treatment strategies are based on plasma cell disorders where systemic chemotherapy includes cyclophosphamide, doxorubicin and dexamethasone. However, since our patient was too malnourished to withstand anthracycline and unable to resource mephalan, lenalidomide or bortezomib, we decided to embark on thalidomide-dexamethasone (thal-dex) as there were numerous case reports showing that this therapy improves peripheral neuropathy, extravascular volume overload and VEGF level.[4] Apart from that, a small open trial by Kuwabara et al., showed that thal-dex therapy is an effective treatment for POEMS as two-thirds of patients treated with thal-dex showed substantial clinical improvement while the rest had stabilization of symptoms during a mean follow up of 15 months.[4]

Remarkably our patient, who was bedbound for the previous one year, was able to ambulate independently after completion of six cycles of chemotherapy. Interestingly, thalidomide did not induce or worsens his neuropathy as evidenced by repeated nerve conduction study which was in accordance with previous reports.[4]

Monitoring his response according to serum paraproteinemia was difficult in view of the small size of the M-protein. Even without M-protein response, patients may have significant clinical benefit.[5] This presents another challenge for the treating physicians who have limited resources, as patients should ideally be followed up with trends of serum VEGF rather than absolute values.[2]

In the event of a relapse, bortezomib or lenalidomide based therapy with autologous stem cell transplantation may be considered for him. This is because available literature showed that 100% of surviving patients have significant clinical improvement after autologous stem cell transplantation.[2]

In conclusion, while it is difficult to diagnose the POEMS syndrome, treating and monitoring POEMS syndrome in a centre with limited resources will be a challenge. Apart from that, it appears that in such a centre with no options for lenalidomide or bortezomib, and if patients are unfit for induction with systemic chemotherapy, thalidomide might provide a cheap and safe option as treatment.

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