POEMS Syndrome: Report of Three Cases with Review of the Literature

POEMS Sendromu: Üç Olgu Sunumu ve Literatürün Gözden Geçirilmesi

Somanath Padhi[1], Tara Roshni Paul[2], Rajlaxmi Sarangi[3], Shantveer Uppin[2], Sundaram Challa[2], Putcha Deekshanti Narayan[4]

[1]Pondicherry Tıp Bilimleri Enstitüsü, Patoloji Bölümü, Pondicherry, Hindistan
[2]Nizam Tıp Bilimleri Enstitüsü, Patoloji Bölümü, Panjagutta, Hyderabad, Hindistan
[3]MKCG Tıp Fakültesi, Biyokimya Bölümü, Berhampur, Orissa, Hindistan
[4]Nizam Tıp Bilimleri Enstitüsü, Nöroloji Bölümü, Panjagutta, Hyderabad, Hindistan

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ÖZET

Polinöropati (P), organomegali (O), endokrinopati (E), monoklonal gammopati (M) ve deri bulguları (S) ile karakterize POEMS sendromu plazma hücre diskrazileri ile birlikte görülen nadir bir multisistem hastalığıdır. Literatürde yüzlerce hasta bildirilmesine rağmen prevalansı tam olarak bilinmemektedir. Burada bildirilen üç hasta (iki erkek bir kadın) Ocak 2005-Aralık 2009 tarihleri arasındaki beş yılda görülmüştür. Üç hastanın klinik, patolojik, radyolojik, laboratuvar ve terapötik özellikleri literatür bilgileri eşliğinde gözden geçirilmiştir. Tanıya ulaşmak için bu hastalık tablosunun farkında olmak ve multidisipliner yaklaşım gereklidir.

Anahtar Kelimeler: POEMS sendromu, polinöropati, radyoloji, tedavi, sonuç.

ABSTRACT

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Somanath Padhi[1], Tara Roshni Paul[2], Rajlaxmi Sarangi[3], Shantveer Uppin[2], Sundaram Challa[2], Putcha Deekshanti Narayan[4]

[1]Department of Pathology, Pondicherry Institute of Medical Sciences, Pondicherry, India
[2]Department of Pathology, Nizam's Institute of Medical Sciences, Panjagutta, Hyderabad, India
[3]Post Graduate Department of Biochemistry, MKCG Medical College, Berhampur, Orissa, India
[4]Department of Neurology, Nizam's Institute of Medical Sciences, Panjagutta, Hyderabad, India

Polyneuropathy (P), organomegaly (O), endocrinopathy (E), monoclonal gammopathy (M), and skin changes (S) (POEMS) syndrome is a rare multisystemic disease that occurs in the setting of plasma cell dyscrasia. Several hundred cases have been reported in the world literature. The exact prevalence is not known, as the syndrome may be underreported. We report three such cases (2 males, 1 female) over a period of five years (January 2005 to December 2009). The clinicopathological, radiological, biochemical, and therapeutic outcome data of all three cases are presented with a review of the literature. Awareness of this entity and a multidisciplinary approach are essential to make a diagnosis in these patients.

Key Words: POEMS syndrome, polyneuropathies, radiology, treatment outcome.

INTRODUCTION

POEMS syndrome is a rare paraneoplastic multisystemic disorder that occurs in the setting of plasma cell dyscrasia (1). The acronym of POEMS syndrome, coined by Bardwick et al., includes peripheral polyneuropathy (P), organomegaly (O), endocrinopathy (E), monoclonal-protein in serum and/or urine (M), and skin changes (S) (2). Several important features not represented in the acronym are sclerotic bone lesions, Castleman disease, papilledema, pleural effusion, edema, ascites, and thrombocytosis (3-5). Unlike multiple myeloma, the peak incidence of POEMS syndrome is in the 5^{th} to 6^{th} decade, with a male to female ratio of 1.4/1, though there have been cases reported at a very young age (6). Although several hundred cases have been recorded, the exact incidence of this syndrome may be underreported because the syndrome may remain unrecognized (3-5,7). In this paper, we analyzed, retrospectively, the clinical presentations, radiological findings, laboratory data, and treatment outcome of three new cases, with a review of the literature. The aim of this paper was to highlight the varied presentation of patients with POEMS syndrome and to create an awareness about an underreported condition.

CASE

The clinical presentation, examination findings, radiological features, laboratory data, management, and clinical outcome of the three patients with POEMS syndrome are summarized in Table 1. Informed consent was obtained from all three patients.

DISCUSSION

Associations between plasma cell dyscrasia and peripheral neuropathy are well recognized (8). About one-third to one-half of patients with osteosclerotic myeloma have neuropathy and half of all patients with myeloma and peripheral neuropathy have osteosclerotic bone lesions (3,9-11).

Correlation between disparate symptoms and signs supplemented with a panel of diagnostic tests is essential to reach the diagnosis. The diagnosis of POEMS syndrome requires the presence of two major and one minor criteria as described by Dispenzieri et al. (3). All three patients fulfilled the diagnostic criteria for POEMS syndrome.

Table 2 shows the comparison between our patients' characteristics with those of the three largest series published in the literature (3-5). Peripheral polyneuropathy is the most common manifestation and a defining feature in POEMS syndrome (3-5). However, cases without polyneuropathy (atypical POEMS syndrome) have also been reported in the literature by Morizane et al. (11). All three patients presented with peripheral polyneuropathy (painful in case 1), which was slowly progressive, bilateral, symmetric, ascending type, involving the lower limbs more than the upper and with a predominant motor component, as has been described in the literature (3). Nerve conduction studies from the right ulnar, median, tibial, and common peroneal nerves revealed marked slowing of conduction velocities along with prolongation of distal latencies in all three cases. F-wave latencies were prolonged in the right ulnar, median and peroneal nerves in all cases, whereas F-waves were not elicitable in the lower limbs in cases 1 and 2. Compound motor axon potential (CMAP) amplitude was normal in all the tested nerves in case 1, and mildly reduced in the right median and peroneal nerve in case 2, and in the right tibial nerve in case 3. Sensory nerve axon potential (SNAP) amplitudes were normal in all the tested nerves in cases 1 and 2, whereas median and ulnar SNAP were not elicitable in case 3. Sensory velocities were reduced in the right median and ulnar nerve in case 1, and in the right median, ulnar and sural nerve in case 2, whereas normal SNAP amplitude and reduced velocity were noted in the right sural nerve in case 3. No evidence of conduction block was noted in any of the nerves tested. It was typically a chronic, large fiber sensorimotor neuropathy of both axonal and demyelinating type and resembled chronic inflammatory demyelinating polyneuropathy (CIDP) clinically (3,12). Left vastus lateralis muscle biopsy from one patient (case 1) was suggestive of myoneuropathy along with type 2 fiber atrophy, which was due to steroid use.

By definition, all three patients had a very small amount of detectable M-protein in serum electrophoresis (SEP). The rate of detection of M-spike by SEP is less (50-100%) compared to immunofixation (75-100%), and it can be missed in up to one-third of cases (3-5). Immunofixation was not done in any of the cases; urine test for Bence-Jones protein was negative in all. As opposed to classic multiple myeloma, the percentage of

Table 1. The clinical presentation, examination findings, radiological features, laboratory data, management, and clinical outcome of the three patients with POEMS syndrome

	Age (years)/ Sex	Clinical findings	Investigations	Treatment	Follow-up
Case 1	50/Male	Dyspnea, pain in both thighs, difficulty in climbing stairs-6 months Loss of appetite and weight (4 kg in 2 months) **Examination findings:** Pallor Wasting of UL & LL muscle power (LL= 3/5; UL= 4/5) Sluggish DTR in LL No sensory or cranial nerve abnormality Maculopapular rash over trunk, B/L pedal edema, ascites, & B/L pleural effusion Splenomegaly	**EMNG:** S/o demyelinating polyneuropathy **Radiology:** Multiple sclerotic lesions in ribs (left 3^{rd}, 4^{th} & 10^{th}) Bone scan-Increased uptake in left 3^{rd} & 4^{th} ribs, posterior end of left 10^{th} rib **Laboratory findings:** Hb - 6.5 g/dL TLC - 8.6 x 10^9/L Plt - 450 x 10^9/L ESR-10 mm/1^{st} hour SEP-Small "M" spike Urine BJP-Negative LFT & RFT-WNL Hormonal evaluation-NAD BMA-6% plasma cells Bx of lesions-Not done Muscle Bx-Neurogenic pathology Nerve Bx-Not done	Oxygen inhalation Intravenous broad spectrum antibiotic (ceftriaxone, amikacin, imipenem) Pulsed dose steroid Packed red cell transfusion (4 units) Tablet calcium and multivitamins	Died of sepsis and MOF on 10^{th} day after admission
Case 2	37/Male	Progressive weakness in both LL, tingling and numbness over both feet, swelling of both ankles & feet, pigmentation over both LL and palm, and hoarseness of voice-4 months	**EMNG:** S/o demyelinating polyneuropathy **Radiology:** Lytic lesion with sclerotic rim-lower end of left femur Bone scan-Solitary photopenic area with surrounding avid uptake, lower end of left femur	Tablet cobalamin, calcium Injection heparin 5000 Unit subcutaneous Pulsed dose steroid Tablet L-thyroxine 100 µg daily External beam RT to the femoral lesion (30 cG in 3 fractions) Physiotherapy	Regression of the femoral lesion at 3 months post RT, marked improvement in the neurological symptoms, Stable disease at 2years from diagnosis

Table 1. The clinical presentation, examination findings, radiological features, laboratory data, management, and clinical outcome of the three patients with POEMS syndrome (continued)

	Age (years)/ Sex	Clinical findings	Investigations	Treatment	Follow-up
		Examination findings: Mild pallor, white nails, hypertrichosis Hyper-pigmentation over both legs, elbows and palms B/L pedal edema Wasting of small muscles of hand power (LL= 1/5; UL= 5/5) Paresthesia & Absent DTR in LL Splenomegaly	**Laboratory findings:** Hb-10 g/dL TLC-11.5 x 10^9/L Plt-500 x 10^9/L ESR-18 mm/1^{st} hour SEP-Small "M" spike Urine BJP-Negative LFT & RFT-WNL Hormonal evaluation-Hypothyroidism (TSH= 7.8 µIU/mL) BMA-8% plasma cells Bx of lesions-Plasmacytoma with adjacent sclerotic bone IHC-CD138-positive & λ- chain-positive Muscle Bx-Not done Nerve Bx-Not done		
Case 3	48/Female	Weakness of both LL-18 months Paresthesia of both LL -6 months Low backache-3 months Swelling over both feet-3 months Hyper-pigmentation over face & around eyes-3 months	**EMNG:** S/o demyelinating polyneuropathy **Radiology:** Sclerotic lesion involving L5/S1 Bone scan-Solitary photopenic area with surrounding avid uptake at L5/S1	Pulsed dose steroid, multivitamins and calcium, tablet L-thyroxine 100 µg daily, physiotherapy	Refused local RT and hospital stay Lost to follow up

Table 1. The clinical presentation, examination findings, radiological features, laboratory data, management, and clinical outcome of the three patients with POEMS syndrome (continued)

Age (years)/ Sex	Clinical findings	Investigations	Treatment	Follow-up
	Examination findings:	**Laboratory findings:**		
	Hyper-pigmentation over face & around eyes	Hb-14 g/dL		
		TLC-5.5 x 10^9/L		
	Decreased power in both LL	Plt-270 x 10^9/L		
	Sensory loss up to mid leg (vibration, pressure & touch)	ESR-10 mm/1st hour		
		SEP-Small "M" spike		
	Sluggish DTR in LL	Urine BJP-Negative		
	Tenderness over L5-S1 region	LFT & RFT-WNL		
	B/L pedal edema	Hormonal evaluation-Hypothyroidism (TSH= 6.3 µIU/mL)		
	Hepato-splenomegaly	BMA-14% plasma cells		
		Bx of lesions-Plasmacytoma with adjacent sclerotic bone		
		IHC-Not done		
		Muscle Bx-Not done		
		Nerve Bx-Not done		

EMNG: Electromyoneurogram, MOF: Multi-organ failure, UL: Upper limb, LL: Lower limb, DTR: Deep tendon reflex, NAD: No abnormality detected, Hb: Hemoglobin, TLC: Total leukocyte count, Plt: Platelet, ESR: Erythrocyte sedimentation rate, SEP: Serum electrophoresis, BJP: Bence Jones protein, M-spike: Monoclonal spike, WNL: Within normal limit, LFT: Liver function test, RFT: Renal function test, TSH: Thyroid stimulating hormone, BMA: Bone marrow aspiration, Bx: Biopsy, S/o: Suggestive of, RT: Radiotherapy, IHC: Immunohistochemistry, λ: Lambda, L-thyroxine: Levothyroxine, B/L: Bilateral.

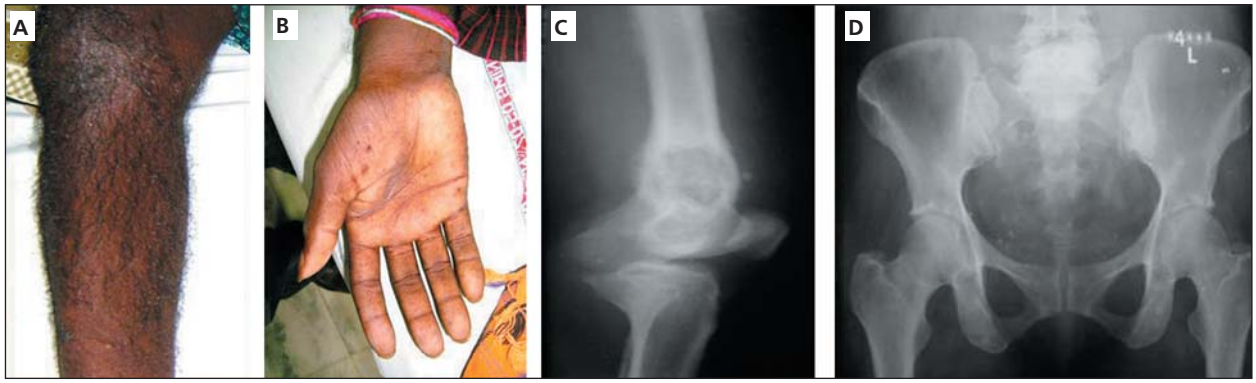

Figure 1. Clinical photographs showing hypertrichosis **(A)**, and palmar hyperpigmentation **(B)**. Lateral **(C)** plain radiograph of the left knee showing a lytic lesion with surrounding sclerosis involving the distal metaphysis of the femur. Anterior plain radiograph of the pelvis showing sclerotic lesion involving the 5th lumbar and 1st sacral vertebrae **(D)**.

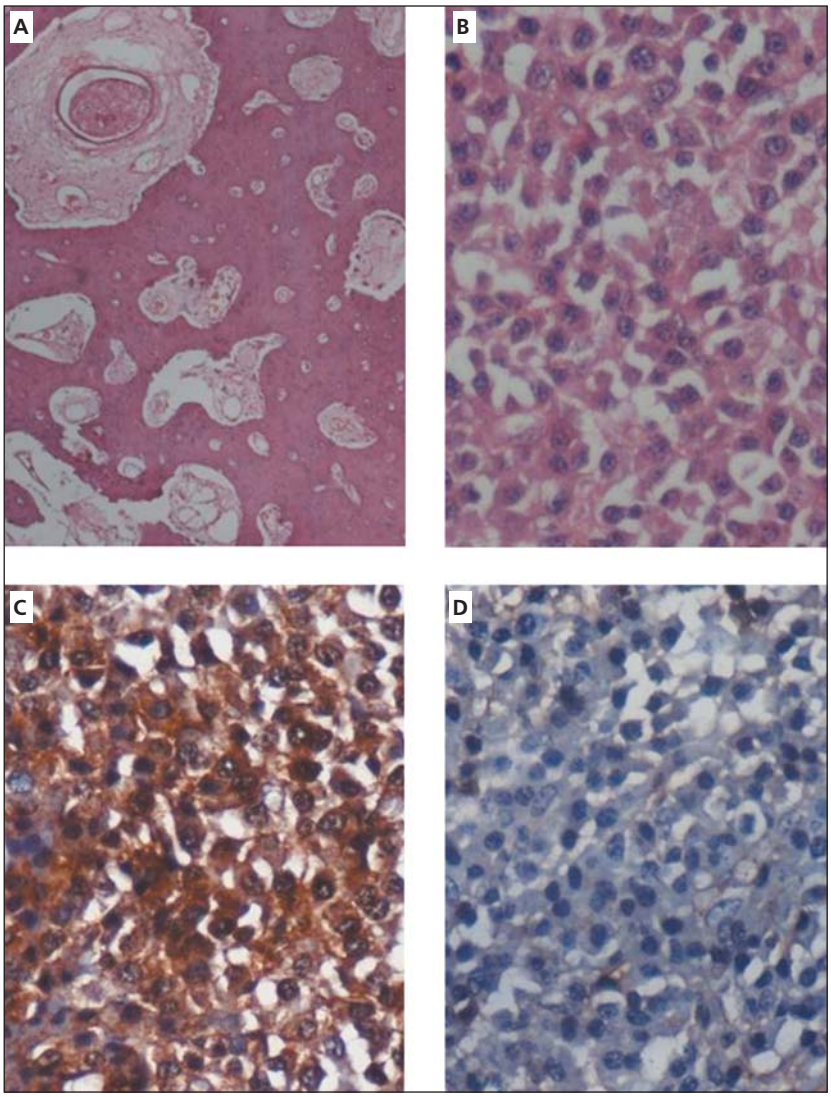

Figure 2. (A) Irregularly thickened anastomosing woven bony trabeculae with intervening fibrous tissue (HE x100). **(B)** Photomicrographs of lesion showing diffuse sheets of plasma cells with eccentric nuclei and moderate amount of eosinophilic cytoplasm (HE x400). Immunohistochemical findings: **(C)** CD138 showing diffuse cytoplasmic positivity (x400). **(D)** Negative staining with κ light chain (x400).

Table 2. Comparison of major and minor criteria of patients in the present series and 3 other series

Characteristic	Case 1	Case 2	Case 3	Dispenzieri et al.[3], % (n= 99)	Nakanishi et al.[4], % (n= 102)	Soubrier et al.[5], % (n= 25)
Polyneuropathy	Present	Present	Present	100	100	100
M-spike (serum)	Very thin	Very thin	Very thin	85 (Lambda) 1.1 g/L	75 (Lambda) Very small	100 (Lambda) Very small
Bone lesion*	Multiple (S)	Solitary (L + S)	Two lesions (S)	S-47, L + S-51, L-2 Solitary-45	S-56, L + S-31, L-13 Solitary-45	S-41, L + S-59, L-0 Solitary-41
Castleman disease	Absent	Absent	Absent	11	19	24
Organomegaly**	Spl	Spl	H + Spl	H (24), Spl (22)	H (78), Spl (35)	H (68), Spl (52)
Endocrinopathy	Absent	Hypothyroid	Hypothyroid	Gonadal (55) Adrenal (16) Hypothyroid (14)	Hypothyroidism-NR DM (25)	Hypothyroid (36) DM (36)
Skin changes	Maculo-papular rash	Hyper-pigmentation Hypertrichosis White nails	Hyper-pigmentation	Hyper-pigmentation Hypertrichosis	Hyper-pigmentation Hypertrichosis	Hyper-pigmentation Hypertrichosis
Edema	PE Ascites	B/L pedal edema	B/L pedal edema	Peripheral edema PE	Peripheral edema PE	Peripheral edema PE

* L: Lytic, S: Sclerotic, L + S: Lytic and sclerotic,

** H: Hepatomegaly, Spl: Splenomegaly, H + S: Hepatosplenomegaly, NR: Not reported, DM: Diabetes mellitus, PE: Pleural effusion, B/L: Bilateral.

plasma cells in the bone marrow aspirate was less than 15%, which accounted for the very small M-spike in SEP, low sedimentation rate and absence of rouleaux formation (13). As has been described by Dispenzieri et al., bone marrow examination from all three patients revealed hypercellularity (for age) and was reported as "reactive" (13).

On presentation, about 95% of patients can have bone lesions detected by radiological survey. Bone lesions may be purely sclerotic, mixed sclerotic and lytic, or purely lytic, and these can be either solitary or multiple (3-5). case 1 had multiple sclerotic lesions involving the ribs and case 2 had solitary mixed lytic and sclerotic lesion of the left lower end of the femur, whereas case 3 had two sclerotic lesions involving the lumbosacral spine (Figures 1C, 1D). This is in comparison to the findings in other series where lesions were solitary in 45% of the cases and multiple in the remainder (Table 2) (3-5). Lesion biopsies from cases 2 and 3 demonstrated sheets of plasma cells consistent with solitary plasmacytoma with adjacent sclerotic bony trabeculae (Figures 2A, 2B). On immunohistochemistry (IHC), the lesional cells showed intense positivity with CD138 antibody (Biogenex) and lambda (λ) light chain (Dako) (case 2), whereas IHC with kappa light chain monoclonal antibody was negative in the cells (Figures 2C, 2D) (3,4). Biopsy was not done in case 1 because of the patient's poor condition and the location of the lesions (ribs).

All three patients had palpable liver and/or spleen without lymphadenopathy. Liver biopsy done postmortem in case 1 revealed no histological abnormalities, as described in the literature.

Endocrine abnormalities are the defining feature of the POEMS syndrome. Diabetes mellitus and gonadal dysfunction are the most common endocrinopathies (3-5,13,14). Gandhi et al., in their evaluation of 64 patients with POEMS syndrome, found hypogonadism as the most common abnormality (54/64, 84%), followed by hypothyroidism (28/64), abnormalities in glucose metabolism (impaired fasting glucose in 16, diabetes in 8), hypocalcemia (14/51, 27%), and adrenal insufficiency (6/9) (14). Twenty-nine (54%) of 54 patients had evidence of multiple endocrinopathies in the four major endocrine axes (gonadal, thyroid, glucose, and adrenal). Hypothyroidism was the only endocrine abnormality seen in two of our patients (cases 2 and 3), whereas case 1 had no detectable endocrine abnormality.

Skin changes in the first patient were in the form of maculopapular rash over the trunk. As described in the literature hyperpigmentation was seen in cases 2 and 3, and hypertrichosis and white nails were seen additionally in case 2 (Figures 1A, 1B) (3-5).

Extravascular volume overload in the form of pleural effusion and ascites was seen in case 1, whereas bilateral pitting edema of both feet was seen in all three patients. As an additional feature weight loss and mild thrombocytosis were observed in case 1 and case 2, respectively (3).

The course of POEMS syndrome is chronic, and median survival is four times that of patients with multiple myeloma. At the Mayo Clinic, 99 patients treated without peripheral stem cell transplantation had a median survival of 13.8 years. With the exception of extravascular volume overload and fingernail clubbing, no other features, including the number of presenting features, was predictive of survival. The most common causes of death were cardiorespiratory failure, progressive inanition, infection, capillary leak-like syndrome, and renal failure (3-5).

During the short hospital stay of case 1, bilateral pleural effusion leading to dyspnea, ascites and pedal edema suggestive of cardiorespiratory compromise dominated the clinical picture more than myoneuropathy, for which he was managed with oxygen inhalation, intravenous broad spectrum antibiotics, packed red cell transfusion, calcium, and vitamins. However, the patient's condition deteriorated and he finally succumbed to cardiorespiratory failure and sepsis. Case 2 was managed with external beam radiotherapy (30 cGy in 3 fractions) to the femoral lesion, along with steroids, multivitamins, calcium, and tablet L-thyroxine (3,10). Follow-up radiograph showed regression of the femoral lesion at three months' post-radiotherapy with marked improvement in the neurological symptoms at two years from the diagnosis, and the patient presently has stable disease (3). Case 3 was managed with steroids, calcium, L-thyroxine, and physical therapy; no local radiotherapy was given to the spinal lesions because of the patient's refusal, and she was subsequently lost to follow-up.

The exact pathogenesis of POEMS syndrome is unknown. The role of lambda light chains in the pathogenesis of this disorder has been postulated because of their unexpected frequency (95% of cases), though a histopathologic review of affected organs and nerves does not support a deposition disorder (4,5). The most plausible hypotheses regarding the pathogenesis of POEMS syndrome are those implicating cytokines, more specifically, vascular endothelial growth factor (VEGF). (3-5,15,16). Patients with POEMS syndrome tend to have increased levels of interleukin 1-beta (IL-1β), tumor necrosis factor-alpha and IL-6 than observed in multiple myeloma. Plasma and serum levels of VEGF are increased in patients with POEMS syndrome, which correlates with disease activity. It is postulated that VEGF is secreted from the plasma cells and the platelets promoting vascular permeability, angiogenesis and monocyte/macrophage migration. In addi-

tion, VEGF is implicated in the pathogenesis of the edema, organomegaly and skin changes seen in POEMS syndrome, and the level in plasma/serum tends to fall following therapy. The role of VEGF in polyneuropathy is less clear, though microthrombosis of the endoneurial vessels is suggested (5,15). The role of human herpes virus-8 (HHV-8) in POEMS syndrome has been postulated, as antibodies to HHV-8 have been reported in up to 22% of patients without Castleman disease (17).

To conclude, we present herein three cases of POEMS syndrome based on the proposed criteria. Due to the lack of awareness, varied presentation and close resemblance with CIDP, the POEMS diagnosis can be missed, which can lead to increased morbidity and mortality. The misdiagnosis may be problematic because of therapeutic implications, as therapies effective in CIDP are not effective in patients with POEMS syndrome. A multidisciplinary approach is essential for proper management and therapeutic outcome in these patients.

REFERENCES

1. *Dispenzieri A, Lacy MQ, Greipp PR. Multiple myeloma. In: Greer JP, Foestler J, Rodgers GM, Paraskevas F, Glader B, Arber DA, Means RT Jr (eds). Wintrobe's Clinical Hematology. 12th ed. Philadelphia: Lippincott Williams and Wilkins, 2009:2414-5.*
2. *Bardwick PA, Zvaifler NJ, Gill GN, Newman D, Greenway GD, Resnick DL. Plasma cell dyscrasia with polyneuropathy, organomegaly, endocrinopathy, M protein and skin changes: the POEMS syndrome. Report on two cases and a review of literature. Medicine 1980;59:311-22.*
3. *Dispenzieri A, Kyle RA, Lacy MQ, Rajkumar SV, Therneau TM, Larson DR, et al. POEMS syndrome: definitions and long-term outcome. Blood 2003;101:2496-506.*
4. *Nakanishi T, Sobue I, Toyokura Y, Kuroiwa Y, Satoyoshi E, Tsubaki T, et al. The Crow-Fukase syndrome: a study of 102 cases in Japan. Neurology 1984;34:712-20.*
5. *Soubrier MJ, Dubost JJ, Sauvezie BJ. POEMS syndrome: a study of 25 cases and a review of the literature. French Study Group on POEMS syndrome. Am J Med 1994;97:543-53.*
6. *Sevketoglu E, Hatipoglu S, Ayan I, Dogan O, Salihoglu B. POEMS syndrome in childhood. J Pediatr Hematol Oncol 2008;30:235-8.*
7. *Chan JL. POEMS syndrome. eMedicine 2009.*
8. *Crow R. Peripheral neuritis in myelomatosis. Br Med J 1956;2:802-4.*
9. *Driedger H, Pruzanski W. Plasma cell neoplasia with osteosclerotic lesions: a study of five cases and a review of the literature. Arch Intern Med 1979;139:892-6.*
10. *Iwashita H, Ohnishi A, Asada M, Kanazawa Y, Kuroiwa Y. Polyneuropathy, skin hyperpigmentation, edema, and hypertrichosis in localized osteosclerotic myeloma. Neurology 1977;27:675-81.*
11. *Morizane R, Sasamura H, Minakuchi H, Takae Y, Kikuchi H, Yoshiya N, et al. A case of atypical POEMS syndrome without polyneuropathy. Eur J Hematol 2008;80:452-5.*
12. *Kelly JJ Jr, Kyle RA, Miles JM, Dyck PJ. Osteosclerotic myeloma and peripheral neuropathy. Neurology 1983;33:202-10.*
13. *Dispenzieri A, Gertz MA. POEMS syndrome. Orphanet Encyclopedia 2005;1-7.*
14. *Gandhi GY, Basu R, Dispenzieri A, Basu A, Montori VM, Brennan MD. Endocrinopathy in POEMS syndrome: the Mayo Clinic experience. Mayo Clin Proc 2007;82:836-42.*
15. *Watanabe O, Arimura K, Kitajima I, Osame M, Maruyama I. Greatly raised vascular endothelial growth factor (VEGF) in POEMS syndrome. Lancet 1996;347:702.*
16. *Sintaro H, Hiroshi O, Shuji O, Masashi U, Atsuo T, Chihiro T, et al. POEMS syndrome with increased vascular endothelial growth factor (VEGF). Nippon Naika Gakkai Zasshi 2002;91:752-4.*
17. *Belec L, Authier FJ, Mohamed AS, Soubrier M, Gherardi RK. Antibodies to human herpes virus 8 in POEMS (polyneuropathy, organomegaly, endocrinopathy, M protein, skin changes) syndrome with multicentric Castleman's disease. Clin Infect Dis 1999;28:678-9.*

Yazışma Adresi/Address for Correspondence

Uzm. Dr. Somanath Padhi

Pondicherry Institute of Medical Sciences (PIMS) 605014

Ganapathichettykulam, Village-20,

Kalapet Puducher/India

E-posta: somanath.padhi@gmail.com

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