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POEMS SYNDROME: A CASE REPORT

Sirirat Anutrakulchai MD.*
Pisaln Mairiang Bsc. MD. FRCPT*
Kitti Chunlertrith MD. FRCPT*
Suthipun Jitpimolmard MD. FRCPT*
Chawalit Pairotkul MD.**
Kitiwan Vipulakorn MD.***

* Department of Medicine
** Department of Pathology
*** Department of Orthopaedics
Faculty of Medicine
Khon Kaen University
Khon Kaen 40002

POEMS Syndrome, a case report. [polyneuropathy, organomegaly, endocrinopathy M-protein and Skin change]

ศิริรัตน์ อนุตระกูลชัย*
พิศาล ไม้เรียง*
กิตติ จันทร์เลิศฤทธิ์*
สุทธิพันธ์ จิตพิมลมาศ*
ชวลิต ไพโรจน์กุล**
กิติวรรณ วิปุลากร***

* ภาควิชาอายุรศาสตร์
** ภาควิชาพยาธิวิทยา
*** ภาควิชาออร์โธปิดิกส์
คณะแพทยศาสตร์
มหาวิทยาลัยขอนแก่น
จังหวัดขอนแก่น 40002

ผู้ป่วยหญิงอายุ 42 ปี อาชีพทำนา มารับการตรวจรักษาที่โรงพยาบาลศรีนครินทร์ ในปี พ.ศ. 2535-2537 ด้วยอาการท้องเสียเรื้อรัง และมีไข้ต่ำ ๆ เป็น ๆ หาย ๆ ร่วมกับสังเกตว่าผิวหนังมีสีคล้ำและตึงขึ้น หน้าแดง และมีขนเพิ่มขึ้นที่แขนขา และใบหน้า หลังจากที่มีอาการท้องเสียประมาณ 18 เดือน ผู้ป่วยเริ่มมีอาการบวมตามตัว ชาที่มือและขา 2 ข้าง และมีอาการอ่อนแรงของขา โดยเป็นมากขึ้นเรื่อยๆ จากเท้าขึ้นไปถึงต้นขา จากการตรวจร่างกายและตรวจวินิจฉัยเพิ่มเติม พบมีตับม้ามโต มี Monoclonal hypergammaglobulinemia และพบมี mixed osteosclerrotic and osteolytic ที่กระดูกก้นกบข้างขวา ซึ่งเมื่อทำการตัดชิ้นเนื้อพิสูจน์ทางพยาธิวิทยา ลักษณะเข้าได้กับ plasmacytoma เมื่อรวมอาการและสิ่งตรวจพบต่างๆ ในผู้ป่วยรายนี้ สามารถจัดเข้าในกลุ่มอาการ "POEMS" ซึ่งอาการของกลุ่มนี้พบน้อยมากที่จะมาด้วยอาการท้องเสียเรื้อรังเป็นอาการเริ่มแรกดังในผู้ป่วยรายนี้ ผู้ป่วยได้รับการรักษาด้วย การฉายแสงบริเวณรอยโรคของกระดูกก้นกบข้างขวา และได้รับสเตอรอยด์ ฮอร์โมน หลังการรักษาอาการอ่อนแรงของผู้ป่วยดีขึ้น

Address reprint request to : Pisaln Mairiang, Department of Medicine, Faculty of Medicine, Khon Kaen University Khon Kaen, Thailand 40002

Introduction

"POEMS Syndrome" associated with plasma cell dyscrasia, is an acronym that stands for uncommon syndrome involving multisystem. The major features are chronic progressive sensorimotor polyneuropathy, organomegaly (mainly hepatomegaly and lymphadenopathy) endocrinopathy (especially gonadal failure and diabetes mellitus), monoclonal gammopathy and skin changes. In typical case, papilledema, high CSF pressure and CSF protein, anasarca and clubbing of fingers are found.(1,2) Most cases were reported from Japan, and rarely reported from United States, Europe and other parts of Asia (3,4,5). We report a Thai woman who initially presented with chronic diarrhea, edema and skin changes, then the other complete features of POEMS Syndrome were revealed later.

Case report

A 42 year-old woman had two years history of chronic watery diarrhea, low grade fever, fatique, night sweating, facial plethora and flushing. She noticed that her skin was edematous, thickening and hyperpigmented. She had hypertrichosis at extremities and face. She lost 5 kilograms of her weight. At that time, she was admitted at Srinagarind hospital and had been investigated for the cause of chronic diarrhea. The result of stool examination, small bowel study, and malabsorption tests were not diagnostic. The duodenal and jejunal biopsy showed the villous atrophy and increased plasma cell infiltration. Her biochemical tests were shown on table I. The abnormal biochemical test were hypoalbuminemia, low cholesteral level and high alkaline phosphatase. Thyroid function test and muscle enzymes were normal. Antinuclear antibody, anti RNF and LE cell were negative.

According to the histology of duodenum and jejunal mucosa that revealed villous atrophy and increased plasma cell infiltration, the diagnosis of Immunoproliferative small intestinal disease (IPSID) was made.(6) The patient was treated with tetracycline without improvement.

Table I show results of biochemical tests

FBS	105	mg%	(70-110)
Na	139	mEq/L	(130-147)
K	4.4	mEq/L	(3.4-4.7)
HCO3	2.4.2	mEq/L	(20.6-28.2)
Cl	109	mEq/L	(96-107)
Cholesteral	97	mEq/L	(127-269)
Albumin	3.4	gm%	(3.6-54)
SGOT	27	sigma U	(0-28)
SGPT	15	sigma U	(0-21)
BUN	8.6	mg%	(5.8-19.1)
Cr	0.6	mg%	(0.8-2.3)

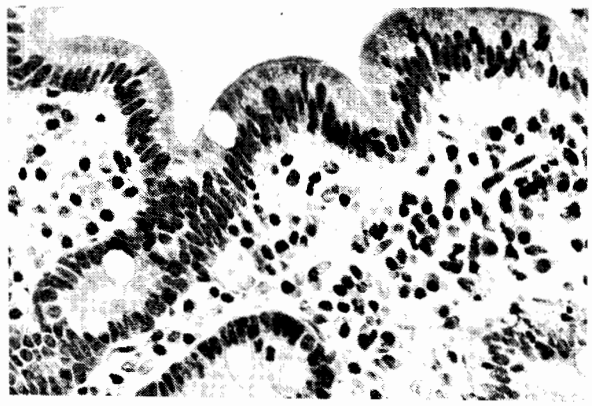

Figure 1 Duodenal mucosal biopsy showed diffuse plasma cell infiltration with villous atrophy.

She had been followed up as out-patient regularly. There was no significant clinical improvement. One year later, she developed new symptoms including symmetrical motor weakness of extremities, Raynaud's phemomenon and polyarthralgia.

In the past, she had thyroidectomy for hyperthyroidism ten years ago and was being well. Three years ago she had pain at right buttock when she walked and still had this pain until last admission.

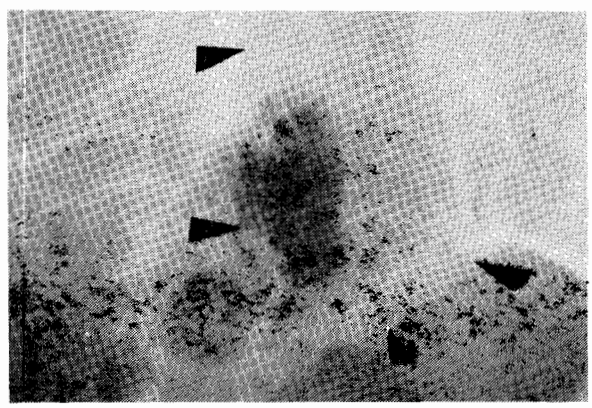

Figure 2 Radiography of pelvic bone shows osteolytic lesion with sclerotic border.

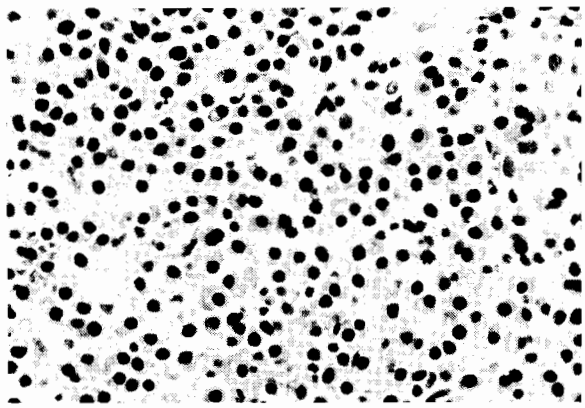

Figure 3 Shows plasmacytoma of pelvic bone

Since her symptoms were progress, she was admitted in the hospital again. On last admission she had gereralized edema, hyperpigmented skin, hepatosplenomegaly, motor weakness, areflexia of both lower extremities, decreased touch and pain sensation. She has no papilledema, no clubbing of fingers, no lymphadenopathy and no signs of diabetes mellitus, adrenal insufficiency or thyroid diseases.

According to her right buttock pain, she was sent for pelvic x-ray and this revealed osteolytic lesion with surrounding sclerotic border at sacrum (Fig. 2). The result of bone and soft tissue pathology was plasma cell infiltration compatible with plasmacytoma (Fig. 3).

She also had nerve biopsy which revealed slightly decreased of myelinated nerve fibers. Her serum showed monoclonal pattern of immunoglobulin. The diagnosis of POEMS syndrome was made. She then received prednisolone initially 60 mg/day and reduced to 10 mg per day, and also had 30 cGy total radiation at sacrum. In first month of treatment she was able to walk and the pain at buttock was decreased.

Discussion

A patient with neuropathy, sclerotic myeloma and skin pigmentation was first described in 1938(4) but the term of POEMS syndrome had just been used since 1980.(7) The age of onset for this syndrome is 40-50 years old. (ranges from 27 to 80). The ratio of male to female is about 2:1.

The full pictures of POEMS syndrome were shown on table 2 (8). Most of reported cases had only 2 or 3 features of this syndrome plus plasma cell dyscrasia (5).

Table 2. Systemic manifestation of POEMS syndrome

System	Incidence in four reviews (%)
Dermatologic	
Skin thickening	77-96
Hyperpigmentation	93-98
Hypertrichosis	78-85
Hyperhydrosis	66-95
Edema	91-97
Cutaneous angiomas	26-44
Digital clubbing	53-87
Neurologic	
Sensorimotor polyneuropathy	100
Papilledema	62-75
Elevated CSF protein level	94-98
Hematologic	
Monoclonal immunoglobulin	61-75
Lymphadenopathy	64-70
Splenomegaly	37-42
Hepatomegaly	67-88
Polycythemia or thrombocytosis	32-38
Osteosclerotic bone lesions	54-71
Endocrine	
Hypogonadism	73-86
Diabetes mellitus	28-41
Hypothyroidism	10-36
Miscellaneous	
Ascites/effusions	62-68
Low grade fever	48-76

The most common presenting symptom and sign of POEMS syndrome is peripheral neuropathy, which is usually a symmetrical sensorimotor polyneuropathy that starts distally and spreads slowly to more proximal part of extremities (7). In this case polyneuropathy came later in the course leading to delayed diagnosis.

The most common endocrinopathies associated with POEMS syndrome are hypogonadism (impotence, gynecomastia, secondary amenorrhea) and diabetes mellitus. The others less frequent

abnormalities are adrenal insufficiency, primary hypothyroidism and hyperthyroidism (9). We are uncertain that hyperthyroidism of this patient is one of POEMS syndrome. This may be only unrelated illness because it developed ten years ago.

Osteosclerotic lesions are the hallmark of the syndrome. Occasionally osteosclerosis is manifested as a very unimpressive sclerotic rim surrounding by a large lytic lesion,(4,10) as seen in our case. The common sites of bone involvement are spine, pelvis,ribs and long bones of proximal extremities (4).

The mechanism of multiple organ involvement in POEMS syndrome are unknown. Many reports postulate possible mechanism that abnormal immunoglobulin and other humoral substrances producing by the neoplastic plasma cells are responsible for clinical features of POEMS syndrome.Improvement of syndrome such as polyneuropathy, diabetes mellitus, hyperpigmentation, flushing, diarrhea and osteosclerotic bone lesion occur after recieving steroid or chemotherapy treating neoplastic plasma cell.(12-14) Some authors suggested that neuropathy may cause by vasculopathy (7,15).

There were few cases in literatures that first presentation with chronic diarrhea. Brent M. et al reported a case with POEMS syndrome who presented with chronic diarrhea, facial flushing similar to our case. The features might mimic carcinoid syndrome but his studies of urine-5-hydroxyindoleacetic acid,serum histamine, gastrin, vasoactive intestinal peptide, neurotensin, substance P and calcitonin levels were normal. Because of improvement of diarrhea and flushing of that reported case after receiving treatment for plasma cell dyscrasia, we believed that pathogenesis of diarrhea may be caused by humoral factors or paracrine hormone producing form neoplastic plasma cell acting on gastrointestinal tract.

Treatment for patients with POEMS syndrome has not been clearly defined. However, the single or multiple osteosclerotic lesions should be treated with radiation but widespread osteosclerotic lesion should be treated by steroid or other chemotherapy such as meplhalan or cyclophosphamide (3-5,7,13).

The mean survival of this syndrome from the presenting of symptom was reported to be about 28 months with 5 years survival rate at 20% (5).

We gave the radiation for solitary bone lesion plus prednisolone to our patient. In first month of treatment her motor weakness was improved and her bone pain was reduced.

Our report aims to present a rare and difficult case of POEMS syndrome that presented with chronic diarrhea. The wrong dignosis and treatment were made for a long time. Careful history taking and physical examination help us to correct the diagnosis later on.

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