Castleman’s disease (CD) is a rare lymphoproliferative disorder of unknown cause. In even rarer circumstances, it can be associated with POEMS (peripheral neuropathy, organomegaly, endocrinopathy, monoclonal gammopathy and skin changes) syndrome. We report a case of multicentric plasma cell CD with POEMS syndrome, who presented with inguinal masses and lower extremity weakness for years. Computed tomography (CT) demonstrated widespread enlarged lymph nodes with homogenous enhancement, as well as splenomegaly and gynecomastia. Recognition of the CT findings in patients with appropriate clinical settings is helpful in suggesting the diagnosis of multicentric CD associated with POEMS syndrome.

Castleman’s disease (CD), also known as angiofollicular hyperplasia or benign giant lymph node hyperplasia, is a rare usually benign lymphoproliferative disorder of unknown cause [1, 2]. It was first reported as localized mediastinal lymph node hyperplasia by Castleman in 1954 [2, 3]. Clinically, it can be divided into unicentric and multicentric types. Histologically, three variants, hyaline vascular, plasma cell, and mixed, have been described. The hyaline vascular pattern subtype is the most common and usually presents as a unicentric lesion. In contrast, the plasma cell variant accounts only for approximately 10 to 20% of cases and usually presents as a multicentric form [4, 5].

POEMS syndrome is a multisystemic disorder characterized by polyneuropathy, organomegaly, endocrinopathy, monoclonal gammopathy, skin changes and various other systemic clinical signs. POEMS syndrome is a rare disorder with uncertain prevalence [6, 7]. Although the association between POEMS syndrome and CD is yet unclear, it has been reported that about 19 to 24% of patients with POEMS syndrome are associated with CD [6, 8]. The imaging findings of plasma cell CD with POEMS syndrome have scarcely been reported [4, 9]. In this report, we demonstrate the computed tomography (CT) findings of multicentric plasma cell CD associated with POEMS syndrome.

CASE REPORT

A 63-year-old man presented to the clinic because of progressive gait disturbance, which occurred about 2 years ago while aggravated recently. He had the history of left renal stones with renal atrophy and ischemic heart disease as well as palpable left inguinal masses for more than 10 years.
Multicentric Castleman’s disease with POEMS syndrome

Physical examination showed multiple subcutaneous nodules in bilateral inguinal areas. Neurological examination revealed weakness and numbness symmetrically involving bilateral lower extremities. The laboratory investigations showed mild anemia (13.8 g/dL), impaired renal function (Cr, 2.2 mg/dL), hypothyroidism (TSH 9.2 μIU/mL, Free-T4 0.78 ng/dL) and the presence of IgA monoclonal gammopathy (558 mg/dL). A bone marrow examination demonstrated plasma cell infiltration. Electromyogram and nerve conduction studies revealed sensorimotor polyneuropathy involving all four extremities. Contrast-enhanced CT scan from the chest to the inguinal region showed enlarged lymph nodes in the left inguinal, left iliac, paraaortic, celiac, porta hepatis and to a lesser degree, the mediastinal and axillary regions (Fig. 1). All nodes were of homogeneous soft-tissue attenuation without calcifications, and exhibited intense, homogeneous enhancement after administration of contrast medium. Splenomegaly was demonstrated, as well as prominent breast tissues suggestive of gynecomastia.

The patient underwent excisional biopsy for an inguinal lymph node. Pathological examination of the specimen revealed an enlarged lymph node with many endothelial venules and numerous plasma

Figure 1. a and b. Enhanced axial CT scan of the chest, abdomen and pelvis demonstrated extensive enhancing lymphadenopathy in the inguinal (a, arrows), paraaortic, celiac, porta hepatis (b, arrows), mediastinal and axillary regions.

Figure 2. High-power photomicrograph (original magnification, 400X; H-E stain) shows a great deal of plasma cells infiltrating among interfollicular areas with many venules, conforming to the manifestations of plasma cell type of Castleman’s disease.

Figure 3. High-power photomicrograph (original magnification, 400X; Lambda stain) indicates that numerous plasma cells (brown) with lambda light chain restriction.
cells in the expanded interfollicular areas (Fig. 2). Lambda light chain restriction was shown on immunohistochemical staining (Fig. 3). The histopathological diagnosis was plasma cell type CD.

Due to the impaired performance status, the patient was treated with corticosteroids as a single agent without chemotherapy or radiotherapy. In the following two years, his symptoms persisted with mild progression. He also had experienced an episode of pneumonia. Follow-up CT showed no significant interval changes of the existing lesions, and newly developed pleural effusion, pericardial effusion and ascites.

DISCUSSION

CD was first reported as localized mediastinal lymph node hyperplasia by Castleman in 1954 [2, 3]. It may present in either local unicentric form or widespread multicentric form. The former is often asymptomatic and may occur anywhere along the lymphatic chain such as the neck, axilla, mesentery, thorax, pancreas, spleen, adrenal, retroperitoneum, and, most commonly, mediastinum [10, 11]. The multicentric form is characterized by polylymphadenopathy and multiorgan involvement. Histologically, CD is divided into the hyalinized vascular form, the plasma cell variant and mixed type [5, 12]. The hyaline vascular subtype is the most common; the plasma cell predominance variant is found in only 10 to 20% of cases [5]. The plasma cell type usually presents as multicentric form at an elderly male patient and is associated with various clinical manifestations including fever, fatigue, anemia, polyclonal hypergammaglobulinemia, and bone marrow plasmacytosis [1, 5, 13].

The POEMS syndrome, also known as osteosclerotic myeloma or Crow-Fukase syndrome, is a rare disease of unknown cause. Its diagnosis is established on the linkage of various signs and symptoms. The coexistence of sensorimotor peripheral neuropathy and evidence of a monoclonal plasma proliferative disorder bring up the possibility for the diagnosis. Additional symptoms would help distinguish POEMS syndrome from neuropathy associated with monoclonal gammopathy of undetermined significance, which include sclerotic bone lesion, lymphadenopathy, organomegaly, endocrinopathy, edema (peripheral edema, ascites, or effusions) and skin changes. Pulmonary hypertension, renal failure, thrombotic events, and congestive heart failure have also been reported to be part of the syndrome. CD is one of the diseases recognized to be associated with POEMS syndrome [7, 14]. They share certain clinical presentations [15], as well as pathogenesis factors including IL-6 and VEGF [16]. However, the interconnection between these two diseases is yet to be determined.

Typically, the CT finding of unicentric hyaline vascular CD is a localized mediastinal mass with homogeneously intense contrast enhancement, reflecting the hypervascularity of the lesion [13]. Occasionally, there are associated calcifications, central necrosis, and degeneration, especially in a larger sized lymph node [13, 17]. The typical CT findings of multicentric plasma cell CD are multiple adenopathy and splenomegaly. The enhancement pattern of the affected lymph nodes usually varies from mild to moderate degree, which is histopathologically related to plasma cells infiltration and vascular proliferation [10, 18]. Our case exhibited dense contrast enhancement, which was relatively unusual to the previous reports [10, 11, 19]. The pathological finding of numerous venules in the interfollicular areas explained the imaging character (Fig. 2). There have been few reported about the imaging findings of multicentric CD associated with POEMS syndrome [4, 9]. Kirsch et al reported a case of POEMS syndrome with multicentric CD of mixed plasma cell and hyaline vascular type in a 53-year-old woman, in whom CT showed extensive nodal enlargement with focal calcification and dense contrast opacification, splenomegaly, pleural effusion and skin thickening [4]. Eisenbarth et al reported another case of POEMS syndrome with multicentric CD of hyaline vascular type in a 45-year-old woman in whom CT showed widespread adenopathy and ascites [9]. To our knowledge, CT features of multicentric plasma cell CD associated with POEMS syndrome have not previously been reported.

Unicentric CD is generally treated by surgical removal of the mass with excellent prognosis. Radiotherapy has been used for either residual disease after incomplete resection or unresectable lesions, while chemotherapy is usually unnecessary [20]. The optimal treatment for multicentric CD is still controversial. Various treatments have been reported, including corticosteroids, chemotherapy, radiotherapy, surgery, antiviral therapy and immunotherapy [12]. Surgery seems to be the least beneficial because of the diffuse nature of the disorder [20]. The prognosis is worse than unicentric CD, with median survival of 2 to 3 years [19]. As far as the POEMS syndrome is concerned, there is also
no standard treatment for this disorder. According to the large scale retrospective review from Mayo Clinic, the course of POEMS syndrome is chronic and patients survive for many years with overall median survival of 165 months [7]. Concurrent multicentric CD with POEMS syndrome seems to have a favorable prognosis than pure multicentric CD alone. However, more observation from long-term follow-up and large scale studies are necessary before conclusion can be made.

Our patient is a 63-year-old man with POEMS syndrome associated with multicentric plasma cell CD. He presented with inguinal subcutaneous nodules, polyneuropathy, anemia, renal failure, skin hyperpigmentation, hypothyroidism, and IgA monoclonal gammopathy. CT confirmed the inguinal nodules to be markedly enlarged lymph nodes, and also disclosed clinically occult iliac, retroperitoneal, abdominal, mediastinal and axillary adenopathy. Furthermore, it revealed splenomegaly and gynecomastia that were initially overlooked on clinical examination. Thus, in patients having clinical presentations of POEMS syndrome, CT is helpful in confirming the clinical diagnosis and assessing the extent of the disease. Although lymphoma had a likewise CT appearance, the longstanding course of the inguinal mass made it less likely. Histopathological examination was still needed to confirm CD and to verify the histological subtype. CT can also help determining the treatment response and the clinical course of POEMS syndrome associated multicentric plasma cell CD. In our patient, the follow-up CT in the following two years showed persistent lymphadenopathy and newly developed pleural effusion, pericardial effusion and ascites, indicating poor response of the disease to steroid treatment.

REFERENCES

多發性漿細胞型的 Castleman 氏病合併 POEMS 症候群：電腦斷層影像

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Castleman 氏病是一種原因不明而且罕見的淋巴結增生疾患。多發型的 Castleman 氏病可同時合併 POEMS 症候群（周邊性神經病變、器官腫大、內分泌異常、單株免疫球蛋白、皮膚的變化），此情況更為少有。此報告為一多發性漿細胞型 Castleman 氏病同時合併 POEMS 症候群病例，臨床症狀為多年的鼠蹊部腫塊和下肢無力。電腦斷層檢查出有全身散在性的淋巴結腫大，施打顯影劑後有均勻的增強顯影，另外還發現有脾腫腫大以及男性女乳症。在有著特定臨床表現的患者身上，利用電腦斷層找出這些影像特徵將有助於診斷多發性 Castleman 氏病合併 POEMS 症候群。