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Clinical spectrum of POEMS-associated multicentric Castleman disease with renal involvement: a diagnostic challenge

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ABSTRACT

Background: Castleman disease (CD) is a rare and heterogeneous lymphoproliferative disorder with a wide variety of clinical presentations and outcomes. Human herpesvirus-8 (HHV-8) related CD corresponds to the most common subtype of the multicentric Castleman disease (MCD). However, if HHV-8 is negative, POEMS (peripheral neuropathy, organomegaly, endocrinopathy, monoclonal gammopathy, and skin changes) associated with MCD or idiopathic MCD are the cause in a subgroup of patients. Considering the rarity of POEMS and MCD association, we herein describe a patient with a typical presentation based on clinical, laboratory and tissue biopsy data.

Case Presentation: We report a diabetic patient who presented with asthenia, edema, skin lesions manifested by scarring in chiropodactyls, multiple lymph node enlargement in the neck, armpits and inguinal areas, splenomegaly, severe anemia, thrombocytopenia, and mixed polyneuropathy. Hematuria and proteinuria were detected. The patient developed progressive renal failure requiring dialysis. Renal biopsy showed mesangial expansion with mesangial hypercellularity, and lymphoplasmacytoid cells focally distributed in tubules and interstitium, which were compatible with acute tubulointerstitial nephritis. In immunofluorescence, no deposits of IgG, IgA, IgM, C1q, C3 or fibrinogen were found, and kappa and lambda were also negative. Lymph node biopsy revealed lymphoid tissue with follicular hyperplasia, sinusoidal and medullary infiltration of plasma cells. Immunohistochemistry confirmed positivity for B lymphocytes, T lymphocytes, and plasma cells in sub-capsular and para-follicular areas. The patient was diagnosed as POEMS-associated MCD variant, and chemotherapy with cyclophosphamide, doxorubicin, vincristine, and prednisone was started. The patient did not recover renal function and remained dialysis-dependent.

Conclusions: To date, the renal involvement in MCD and POEMS syndrome seems to be uncommon as reported in few case series. Its pathophysiology is not well understood. In the spectrum of MCD, decreased renal function may have impact in patient survival. Early diagnosis and treatment are needed to control the systemic manifestations, and most importantly to avoid chronic organ damage.

Implication for health policy/practice/research/medical education:

CD is a rare and heterogeneous lymphoproliferative disorder with a wide variety of clinical presentations and outcomes. To date, the renal involvement in multicentric CD and POEMS (peripheral neuropathy, organomegaly, endocrinopathy, monoclonal gammopathy, and skin changes) syndrome seems to be uncommon as reported in few case series. Its pathophysiology is not well understood. In the spectrum of MCD, decreased renal function may have impact in patient survival. Early diagnosis and treatment are needed to control the systemic manifestations, and most importantly to avoid chronic organ damage.

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1. Background

Castleman disease (CD) are described as an angiofollicular lymph node hyperplasia, and was first reported in 1954 by Benjamin Castleman. Histologically, CD consists of three variants; hyaline vascular, plasmacytic or mixed cellularity (1). The localized form of CD is referred to as unicentric CD (UCD), and the systemic form as multicentric CD (MCD). These entities share pathologic similarities, regarding germinal centers, follicular dendritic and plasma cell prominence and vascularity within lymph nodes, but are featured by specific clinical, pathologic and biological abnormalities (1). MCD presents with fever, asthenia, pleural effusion, ascites, multiple lymph nodes, and hepatosplenomegaly, and UCD with local lymph node enlargement or solitary mass, and few systemic symptoms (1,2). MCD presents with two subgroups, human herpesvirus-8 (HHV-8) and idiopathic MCD. The pathogenic mechanisms that leads to MCD are not fully understood, and may differ based on the etiology and the clinical presentation (2).

POEMS (peripheral neuropathy, organomegaly, endocrinopathy, monoclonal gammopathy, and skin changes) syndrome is a paraneoplastic disease due to an underlying plasma cell neoplasm, manifested by polyradiculoneuropathy, clonal plasma cell disorder, sclerotic bone lesions, elevated vascular endothelial growth factor, and the presence of CD (3). Organomegaly, endocrinopathy, skin changes, papilledema, anemia, thrombocytosis/polycythemia, and extravascular fluid overload are minor features of the whole syndrome (3). Here, we report a patient with the POEMS-associated MCD variant who presented with macroscopic hematuria, proteinuria and deterioration of renal function requiring dialysis, according to CARE guidelines for clinical case reporting (4).

2. Case Presentation

A 32-year-old woman presented to the nephrology division with edema and paresthesia in both legs, generalized weariness, amenorrhea and macroscopic hematuria. In addition, the patient exhibited asymptomatic lesions in different stages of scarring in chiropodactyls, with pitting scars that had appeared initially as bullous lesions and later evolved into small dry ulcers accompanied by nail falls in the past month. She reported that the symptoms started one year before and were getting progressively worse. In the past history, she had type 2 diabetes mellitus (T2DM) diagnosed ten years ago, and was managed with an insulin regimen. The physical examination revealed splenomegaly and diffuse lymphadenopathy. Patellar reflexes and Achilles reflex symmetrically diminished. Lower limb showed asymmetry in mechanical muscle function. Large lymph nodes in the neck, armpits and

inguinal areas with rubbery consistency, mobile, and non-sensitive were detected. Initial investigation revealed advanced renal failure with a serum creatinine of 3.56 mg/dL, urea of 118 mg/dL, metabolic acidosis (bicarbonate 17 mEq/L), and hyperkalemia (potassium 6.0 mEq/L). Besides that, severe anemia (hemoglobin levels of 5.9 g/dL), elevated C-reactive protein (29.4 mg/L), thrombocytopenia (140.000 platelets per microliter of blood), and hypoalbuminemia (3.2 g/dL) were found. Urinalysis revealed hematuria (+++/ 547 μ L; normal 0-27 μ L), proteinuria (++/ 4+) and dysmorphic red blood cells, but no cylinders or other abnormalities was detected. The measured protein/creatinine ratio in urine sample was 5.0. A polyclonal gammopathy was characterized by serum protein electrophoresis which revealed a broad diffuse band of the gamma-globulin zone (Figure 1), though immunofixation was negative for monoclonal bands both in serum and urine. Kappa/lambda ratio was in the normal range (0.51, normal values; 0.31-1.56).

An ultrasound scan showed that both kidneys had a normal size and morphology, and were non-obstructed. Chest computed tomography showed discrete pericardial effusion with lymph nodes up to 1cm and an enlarged axillary lymph node measuring 2.3 cm. Abdominal and spine computed tomography revealed para-aortic and perirenal adenomegaly, splenomegaly, a free fluid in the pelvis, and mixed lytic osteosclerotic sacral lesions. Echocardiography showed an ejection fraction of 44% and diffuse left ventricular hypokinesia. Electroneuromyography was then performed, showing severe mixed polyneuropathy with axonal degeneration. Based on clinical picture and additional investigations, POEMS syndrome was first suspected, but the presence of only on major criteria for the diagnosis of POEMS (polyneuropathy, without monoclonal plasma cell-proliferative disorder) did not meet criteria for the diagnosis of POEMS syndrome (3).

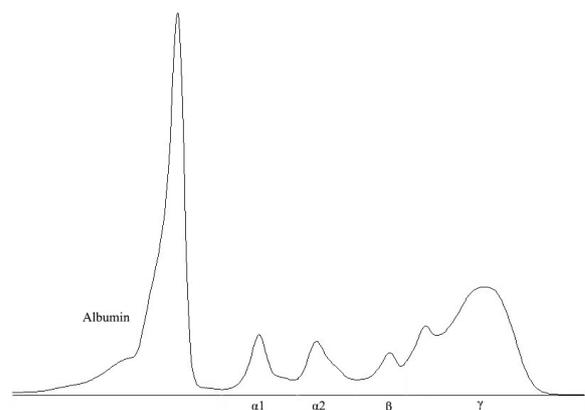


Figure 1. Serum protein electrophoresis showing a polyclonal gammopathy, characterized by a broad diffuse band of the gamma-globulin zone.

In sequence, lymph node, bone marrow and kidney tissue examinations were done. Axillary lymph node biopsy revealed lymphoid tissue with follicular hypoplasia, presenting sinusoidal and medullary infiltration of plasma cells, and absence of granulomas or blast infiltration (Figure 2). The HHV8-negative MCD plasmacytic variant was identified through immunohistochemistry that revealed positivity for B lymphocytes (CD20+), T lymphocytes (CD3+), plasma cells (Kappa+, lambda+ polyclonal) in subcapsular and parafollicular areas, and negativity for HHV8. There was no evidence of thrombocytosis, hyperplastic change, or infiltration of lymphoproliferative neoplastic cells in the bone marrow sample.

Kidney biopsy showed 13 glomeruli, 2 of which with global sclerosis, and 11 glomeruli with mild mesangial matrix expansion and increased cellularity, thickening of the glomerular basement membrane and of the Bowman's capsule, and also a focal basement membrane wrinkling (Figure 3B and 3D). The lymphoplasmacytoid cells were focally distributed in the cortex and also in the medulla, and were composed by lymphocytes, neutrophils, eosinophils and plasmocytes; focal arteriolar hyalinosis and hypertrophy were observed (Figure 3C). A marked interstitial fibrosis and tubular atrophy was described in 50% of the cortical parenchyma (Figure 3A). In immunofluorescence no deposits of IgG, IgA, IgM, C1q, C3 or fibrinogen were found, while kappa and lambda were also negative. Final histological diagnosis was acute tubulointerstitial nephritis and diabetic nephropathy, with severe chronic damage.

At the end of the investigation, the clinical, laboratorial,

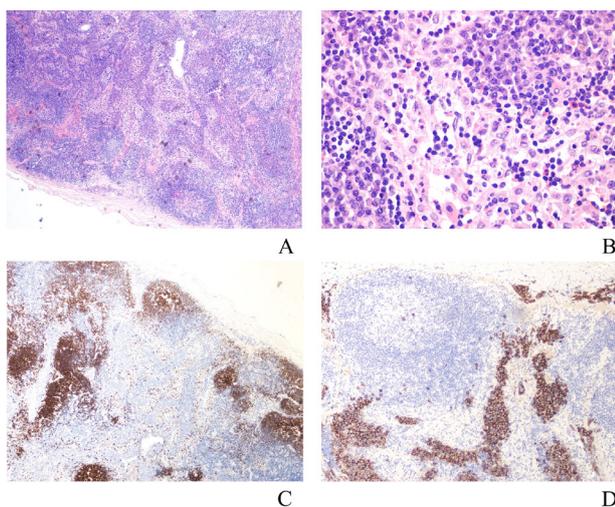


Figure 2. Lymph node biopsy. (A,B) Lymphoid tissue with follicular hypoplasia, presenting sinusoidal and medullary infiltration of lymphocytes and plasma cells. (A) Haematoxylin-eosin staining, x40 magnification. (B) Haematoxylin-eosin, x400 magnification. (C,D) Immunohistochemistry showing positivity for (C) CD20+ B lymphocytes and (D) CD138+ plasma cells.

image and tissue samples in conjunction were compatible with POEMS-associated MCD variant. The patient underwent three weekly hemodialysis sessions, and soon after the diagnosis was made CHOP-chemotherapy (cyclophosphamide, doxorubicin, vincristine, and prednisone) was started. Treatment protocol was the following; day 1; (a) cyclophosphamide 750 mg/m² diluted in 250 mL saline 0.9% intravenously over 30 minutes; (b) doxorubicin 50 mg/ m² diluted in 50 mL saline 0.9% intravenously over 5 minutes; (c) vincristine 1.4 mg/ m² diluted in 50 mL saline 0.9% intravenously over 15 minutes (maximum dose: 2 mg); Day 1 to 5: prednisone 100 mg orally administered 30 minutes prior to chemotherapy on day 1, then every 24 hours on days 2 to 5. Two cycles were made so far, with a planned 6-cycle in total. Up to now, there was no recovery of renal function and the patient remained dialysis-dependent.

3. Discussion

In this case report we described a diabetic female patient with clinical, laboratorial and immunohistochemical markers which were diagnostic for POEMS-associated MCD variant. During disease evolution, our patient presented with asthenia, edema, multiple lymph nodes, splenomegaly, severe anemia, and mixed polyneuropathy.

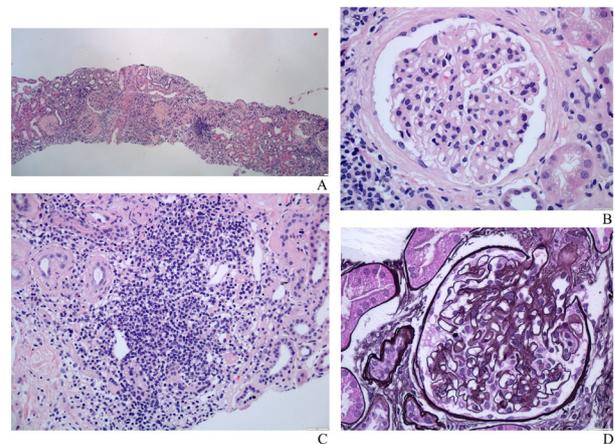


Figure 3. Kidney biopsy. (A) Renal parenchyma with lymphoplasmacytoid cells which were focally distributed in the interstitium and tubules. Some glomeruli show global sclerosis and there was a marked interstitial fibrosis and tubular atrophy in 50% of the renal parenchyma (PAS, x100 magnification). (B) Mild mesangial matrix expansion and increased cellularity, and thickening of the glomerular basement membrane are shown (Haematoxylin-eosin, x400 magnification). (C) Acute focal inflammatory cellular infiltrate in the interstitium composed by lymphocytes, neutrophils, eosinophils and plasmocytes. Focal arteriolar hyalinosis and hypertrophy were observed (Haematoxylin-eosin, x100 magnification). (D) Mild thickening of the glomerular basement membrane with mild mesangial matrix expansion (Jones methenamine silver stain, x400 magnification).

These findings with clinical and laboratorial investigations were compatible with POEMS-associated MCD variant. Interestingly, the patient presented with severe renal impairment that progressed to chronic dialysis. Renal involvement in CD is described in 25% to 54% of patients with MCD plasmacytic or mixed cellularity histological variants (5,6). Acute renal failure is the most common clinical form of presentation, though response to chemotherapy and long-term renal outcomes in affected patients are not fully understood, and few cases have been described so far.

CD is a rare entity that is frequently underdiagnosed because many systemic symptoms may not be present during its course. The estimated incidence rate for CD is 21 to 25 per million person-years, and for MCD is 5 per million per million person-years, but this statistic may change depending on the region, from 4.2 to 5.4 per million (7). Considering the variant of MCD-POEMS, the prevalence rate is estimated in 17% in North American (8) and 6% in China (9).

Multicentric CD involves multiple regions of lymph nodes, and clinical manifestations give rise to the so-called B-symptoms that include weight loss, fever, fatigue, anemia, edema, and hepatosplenomegaly, with endocrinological, cutaneous, neurological, and autoimmune disease being part of the clinical scenario (1,2,8). Currently, the proposed consensus diagnostic criteria for MCD (10) require both major criteria (lymph node histopathology and multicentric lymphadenopathy), at least two of 11 minor criteria with at least one laboratory abnormality, and exclusion of infectious, malignant, and autoimmune disorders that can mimic MCD. Our patient has both two major criteria, and more than two minor criteria manifested by; elevated C-reactive protein, anemia, thrombocytopenia, hypoalbuminemia, renal dysfunction, proteinuria, polyclonal gammopathy, constitutional symptoms, splenomegaly, edema, and skin lesions (10).

Multicentric CD is a pro-inflammatory syndrome and interleukin-6 (IL-6) is a pleiotropic cytokine that play a central role in its pathogenesis. IL-6 is a growth, differentiation, and survival factor which contributes to lymph node enlargement, plasmacytic infiltration, hepatosplenomegaly, and reactive bone marrow plasmacytosis with polyclonal hypergammaglobulinemia (2).

Major criteria for the diagnosis of POEMS syndrome are demyelinating polyneuropathy, monoclonal plasma cell-proliferative disorder where lambda is prevalent, CD, sclerotic bone lesions, and vascular endothelial growth factor (VEGF) elevation (3). We did not measured VEGF in this patient. Minor criteria include organomegaly, endocrinopathy (adrenal, thyroid, pituitary gonadal and pancreatic), skin changes hyperpigmentation,

acrocyanosis, hypertrichosis and white nails), papilledema, thrombocytosis, and polycythemia (1,3,11-14). Diabetes mellitus and thyroid dysfunction have a high prevalence in POEMS. Between 11% and 30% of POEMS patients who have a documented clonal plasma cell disorder also have CD typically with angiofollicular hyperplasia (12-14). The patient we reported here, despite having one mandatory major criterion, two other major criteria and three minor criteria for POEMS syndrome, did not have a detectable monoclonal plasma cell disorder as showed in serum protein electrophoresis and immunofixation. Thus, we can consider that MCD variant of POEMS syndrome without evidence of a clonal plasma cell disorder should be the correct diagnosis in this case.

Multicentric CD is a pro-inflammatory syndrome and IL-6 is a pleiotropic cytokine that play a central role in its pathogenesis. IL-6 is a growth, differentiation, and survival factor which contributes to lymph node enlargement, plasmacytic infiltration, hepatosplenomegaly, and reactive bone marrow plasmacytosis with polyclonal hypergammaglobulinemia (8,15). In the etiopathogenesis of POEMS-associated MCD, cytokine production from mononuclear plasma cells undergoing genomic events are a potential mechanism, and almost all cases present restriction to lambda light chain variable region. Signaling pathways involve the action of VEGF inducing B-cell proliferation and endothelial injury, and effector cytokines that drive POEMS symptoms include IL-6, IL-12, transforming growth factor-1 β , and tumor necrosis factor- α (1-3).

Renal involvement with or without renal failure in MCD, as reported in few published case series, varies from 25% to 54% (5,6,16,17); in POEMS is around 6% (14). Renal histology in MCD reveals glomerular and tubulointerstitial lesions, more frequently small vessel lesions with thrombotic microangiopathy (8%-60%), AA amyloidosis (20%-39%), membranoproliferative glomerulonephritis (11%), and tubulointerstitial nephritis (6%-11%) (5,16,17,18). In POEMS syndrome, histological findings are diverse, including mesangial expansion, narrowing of capillary lumina, basement membrane thickening, sub-endothelial deposits, widening of the sub-endothelial space, swelling and vacuolization of endothelial cells, and mesangiolysis (14). Immunofluorescence is negative for immune deposits. Accordingly, renal biopsy of the patient showed mesangial expansion and mesangial hypercellularity, basement membrane thickening, and severe acute tubulointerstitial nephritis with lymphoplasmacytoid cells composed of lymphocytes, neutrophils, eosinophils and plasma cells. No evidence for thrombotic microangiopathy was found in renal biopsy, such as diffuse endothelial swelling, mesangiolysis, and thrombi within capillary

loops. Unfortunately, ultrastructural examination by transmission electron microscopy was not performed, which could have excluded more accurately the features of chronic and active endothelial injury that is a common finding in the pathology of thrombotic microangiopathy. Mutneja et al (18) reported a rare case of renal thrombotic microangiopathy associated with MCD, where the patient presented acute renal failure, mild proteinuria and renal thrombotic microangiopathy. Interestingly, the renal injury was associated with inhibited expression of podocyte VEGF as shown by immunofluorescence. A dysregulated production of both pro-inflammatory VEGF and interleukin-6 was connected with proliferating plasma cells in lymph nodes causing overproduction of both cytokines (18).

The patient had diabetes mellitus diagnosed ten years before. Kidney biopsy findings were consistent with diabetic kidney disease, as they showed thickening of the glomerular basement membrane, mesangial cell expansion, and arteriolar hyalinosis. As there was found severe chronic damage in 50% of the renal parenchyma, it is probable that before hospitalization the patient already had advanced chronic kidney disease, thus explaining the severe renal failure and the nephrotic range proteinuria we detected in the initial presentation.

A survival analysis of 145 cases of HIV negative CD reported three risk factors that can be considered predictors for poor survival in MCD patients; a prior history of tuberculosis (HR=4.51; 95% confidence interval [CI], 1.23–16.47; $P=0.02$), the presence of POEMS syndrome (HR=3.03; 95% CI, 1.01–9.04; $P=0.047$), and estimated glomerular filtration rate (eGFR) <60 mL/min/1.73 m² (HR=4.89; 95% CI, 1.63–14.73; $p=0.005$) (9). However, multivariate Cox regression showed that only eGFR <60 mL/min/1.73 m² (HR=4.60; 95% CI, 1.50–14.12; $P=0.008$) was an independent predictor for death in MCD patients. After a median follow up of 58 months, the 1-year and 5-year survival for these patients were 92.1% and 85.5% respectively.

Different therapeutic options for MCD have been tested with variable results, as reviewed by van Rhee et al (15). Surgery, irradiation, corticosteroids, rituximab, combined chemotherapy including CHOP or CVAD (cyclophosphamide, vincristine, adriamycin, etoposide), anti-IL6 agents (tocilizumab, siltuximab), autologous stem cell transplantation, monoclonal antibodies and immunomodulatory drugs (bortezomib, thalidomide, and sirolimus). An initial therapy for mild MCD could be rituximab and steroids, and if there is an inadequate response anti-IL6 or chemotherapy are indicated. For severe cases anti-IL6 agents are first used, followed by combination chemotherapy, rituximab and/or

immunomodulatory agents as a proposed algorithm (15).

4. Conclusions

This case report highlights the value of a multidisciplinary approach in rare and heterogeneous systemic diseases affecting multiple organs. Renal involvement manifesting with hematuria, proteinuria and reduced renal function may be associated with MCD/POEMS, reflecting the importance of early diagnosis and prevention of associated comorbidities. In MCD, renal failure may be an adverse prognostic factor reducing patient survival. Therefore, patients with a compatible clinical scenario should be carefully investigated. After the results of the initial work-up, individualized treatment must be performed quickly to limit organ damage.

Availability of data and material

All data came from the medical records of Hospital de Clínicas de Porto Alegre, across the operational system called AGHUse.

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Authors' contribution

CKR and FVV did the conception, design, analysis, and interpretation of data; provided intellectual content of critical importance to the paper; drafted the article and revised it; gave final approval of the version to be submitted. FB, SES and EGB did the conception, design, analysis, and interpretation of data; gave final approval of the version to be submitted. PGS performed the histological examination and interpretation of kidney and lymph node biopsies; did the description of figure legends; gave final approval of the version to be submitted.

Competing interests

The authors declare that they have no competing interests.

Ethical considerations

Ethical issues (including plagiarism, data fabrication, double publication) have been completely observed by the authors. As a case report (and not a research article), the Ethics Committee of Hospital de Clínicas de Porto Alegre states the need only for the patient giving consent to data disclosure before the paper submission. Moreover, written informed consent for publication of their clinical details and/or clinical images was obtained from the patient. A copy of the consent form is available for review by the

Editor of this journal.

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References

- Szalat R, Munshi CN. Diagnosis of Castleman Disease. *Hematol Oncol Clin N Am* 2018;32:53-64. doi: 10.1016/j.hoc.2017.09.005.
- Fajgenbaum DC, Shilling D. Castleman Disease Pathogenesis. *Hematol Oncol Clin N Am* 2018;32:11-23. doi: 10.1016/j.hoc.2017.09.002.
- Dispenzieri A. POEMS syndrome: 2017 Update on diagnosis, risk stratification, and management *Am J Hematol*. 2017;92:814-29. doi: 10.1002/ajh.24802.
- Gagnier JJ, Kienle G, Altman DG, Moher D, Sox H, Riley D, et al. The CARE Guidelines: Consensus-based Clinical Case Reporting Guideline Development. *Glob Adv Health Med* 2013;2:38-43. doi: 10.7453/gahmj.2013.008.
- Xu D, Lv J, Dong Y, Wang S, Su T, Zhou F, et al. Renal involvement in a large cohort of Chinese patients with Castleman disease. *Nephrol Dial Transplant*. 2012;27(Suppl 3):119-25. doi: 10.1093/ndt/gfr245.
- Rieu P, Noël LH, Droz D, Beaufils H, Gessain A, Hermine O, et al. Glomerular involvement in lymphoproliferative disorders with hyperproduction of cytokines (Castleman, POEMS). *Adv Nephrol Necker Hosp*. 2000;30:305-331.
- Simpson D. Epidemiology of Castleman Disease. *Hematol Oncol Clin Am* 2018;32:1-10. doi: 10.1016/j.hoc.2017.09.001.
- Dispenzieri A, Armitage JO, Loe MJ, Geyer SM, Allred J, Camoriano JK, et al. The clinical spectrum of Castleman's disease. *Am J Hematol*. 2012;87:997-1002. doi: 10.1002/ajh.23291.
- Zhang L, Li Z, Cao X, Feng J, Zhong D, Wang S, et al. Clinical spectrum and survival analysis of 145 cases of HIV-negative Castleman's disease: renal function is an important prognostic factor. *Sci Rep*. 2016;6:23831. doi: 10.1038/srep23831.
- Fajgenbaum DC, Uldrick TS, Bagg A, Frank D, Wu D, Srkalovic G, et al. International, evidence-based consensus diagnostic criteria for HHV-8-negative/idiopathic multicentric Castleman disease. *Blood*. 2017;129:1646-1657. doi: 10.1182/blood-2016-10-746933.
- Kulkarni GB, Mahadevan A, Taly AB, Seshagiri KS, Nalini A, Satischandra P, et al. Clinicopathological profile of polyneuropathy, organomegaly, endocrinopathy, M protein and skin changes (POEMS) syndrome. *J Clin Neurosci*. 2011;18:356-360. doi: 10.1016/j.jocn.2010.07.124.
- Ye W, Wang C, Cai QQ, Cai H, Duan MH, Li H, et al. Renal impairment in patients with polyneuropathy, organomegaly, endocrinopathy, monoclonal gammopathy and skin changes syndrome: incidence, treatment and outcome. *Nephrol Dial Transplant* 2016;31:275-83. doi: 10.1093/ndt/gfv261.
- Li J, Zhou DB, Huang Z, Jiao L, Duan MH, Zhang W, et al. Clinical characteristics and long-term outcome of patients with POEMS syndrome in China. *Ann Hematol*. 2011;90:819-826. doi: 10.1007/s00277-010-1149-0.
- Dispenzieri A, Kyle RA, Lacy MQ, Rajkumar SV, Therneau TM, Larson DR, et al. POEMS syndrome: definitions and long-term outcome. *Blood* 2003;101:2496-2506. doi: 10.1182/blood-2002-07-2299.
- van Rhee F, Greenway A, Stone K. Treatment of Idiopathic Castleman Disease. *Hematol Oncol Clin N Am*. 2018;32:89-106. doi: 10.1016/j.hoc.2017.09.008.
- El Karoui K, Vuiblet V, Dion D, Izzedine H, Guitard J, Frimat L, et al. Renal involvement in Castleman disease. *Nephrol Dial Transplant* 2011;26:599-609. doi: 10.1093/ndt/gfq427.
- Nakamoto Y, Imai H, Yasuda T, Wakui H, Miura AB. A spectrum of clinicopathological features of nephropathy associated with POEMS syndrome. *Nephrol Dial Transplant*. 1999;14:2370-8.
- Mutneja A, Cossey N, Liapis H, Chen YM. A rare case of renal thrombotic microangiopathy associated with Castleman's disease. *BMC Nephrol*. 2017;18:57-61. doi: 10.1186/s12882-017-0472-2.

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