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A rare subtype of poems syndrome: IGG4 subtype

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Objective: There is very limited data concerning the relationship between POEMS syndrome and IgG4-related disease.

Case report: A 40 year-old male patient presented with a 3 month history of progressive weakness and numbness in his lower extremities, impotence, diarrhea and weight loss. Complete blood count was as follows: WBC: 7.3×10^9/L, Hgb: 16.5 g/L, platelet 543×10^9/L. Liver enzymes, renal function, electrolytes and routine urine examination were normal. Ig G level was 14.5 g/dL (normal: 7–16 g/L). Serum immunofixation electrophoresis showed IgG λ monoclonality. Endocrine laborotory tests showed hipergonadotropic hipogonadism. Echocardiography showed pericardial effusion. Abdominal USG showed hepatomegaly and splenomegaly measuring 200 mm and 174 mm on longitudunal axis, respectively. On contrast enhanced MRİ, a 6 cm × 3.5 cm mass showing bone destruction was detected in the left sacral ala extending into the pelvis. PET CT scan demonstrated high FDG uptake (SUVmax: 10.5) for the sacral mass lesion. Based on these findings, a diagnosis of POEMS Syndrome was considered. Funduscopic examination showed no papiloedema. Vascular endothelial growth factor (VEGF) was very high (>700 pg/mL, normal: <96 pg/mL). Trucut biopsy of the mass lesion consisted of a nonneoplastic fibrous tissue and a dense infiltrate of mature plasmacytes with dense eosinophilic cytoplasm and eccentrically placed nuclei. Also, perivascular accumulation of sclerotic collagen like substance was noted. On immunohistochemical staining, neoplastic cells showed diffuse positivity for Ig G and Ig G4. Neoplastic cells were CD138(+), κ(−), λ(+), CD38(+), CD30 (−), ALK(−), CD20(−), CD10(−), CD23(−), CD45(−), CD56(−), CD57(−). Bone marrow biopsy showed a 3% monoclonal λ(+) plasma cell infiltration. Diagnosis of POEMS syndrome was confirmed. Taking into consideration high IgG4 expression in the neoplastic mass, IgG4 levels in serum was checked and found to be high 6.34 g/L (normal <1.35 g/L).

Methodology: POEMS syndrome and IgG4 related diseases show similarities including organomegaly and systemic organ damage. Polyneuropathy and bone lesions associated with IgG4 related diseases has not been reported. PET/CT detects bone lesions and lymph nodes in patients with suspected POEMS syndrome. In IgG4 related disease on the other hand, PET/CT identifies multiple lymph node enlargements/organomegaly with normal metabolic activity.

Results: Our patient had an osteosclerotic mass lesion demostrated by PET/CT and histopathological examination. Our patient had high serum IgG4 level and showed IgG4 plasmacyte tissue infiltration, yet her plasmacytes were shown to be monoclonal by bone marrow immunohistochemical staining and serum immunofixation electrophoresis. Therefore, final diagnosis was POEMS syndrome but not IgG4 related disease.

Conclusion: We propose this patient has a subtype of POEMS syndrome because he showed high serum IgG4 levels and a monoclonal IgG4 plasmacyte tissue infiltration. Monoclonal hyperglobinemia is not a feature of IgG4 related disease. It is not clear whether IgG4-positive plasma cell tissue infiltration and elevated serum IgG4 concentrations are origins or outcomes of IgG4 related diseases. To our knowledge, this is the second presumed case of POEMS syndrome-IgG4 subtype. Further research and collecting more cases are essential. We suggest every suspected POEMS patient should be tested for their serum IgG4 concentration.

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Monoclonal gammopathy of undertemined significance and solitary plasmacytoma: progression factors in population of gomel region in belarus

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Objective: To define progression factors of MGUS and SP in population of Gomel region in Belarus.

Case report: Solitary plasmacytoma (SP) and monoclonal gammopathy of undetermined significance (MGUS) are characterized by the presence of less than 10% of tumor cells in the bone marrow and the absence of CRAB criteria. Both diseases have a high risk of progression to multiple myeloma due to certain factors.

Methodology: The study included 106 patients: MGUS ($n = 90$) and SP ($n = 16$) of Gomel region (Belarus) in 2017–2019. The average age was 60.5 years; female patients prevailed All patients underwent aspiration biopsy with IPT and FISH, trepanobiopsy of the ilium wing with immunohistochemical examination of the bone marrow. (Bone marrow aspirates IPT and FISH, and biopsies were obtained for cytological and histopathological evaluation of PC infiltration, including immunohistochemical). The determination of the ratio of light chains of immunoglobulins (kappa/lambda) in blood serum was carried out. Results were assessed after 3 years of observation. The signs of progression include the appearance of any one of the CRAB-criteria.

Results: There were no statistically significant differences between groups of patients with MGUS and SP according to signs (presence of tumor plasma cells, CD95+, CD200+, CD27+,

CD56+, IHC of CD138+ plasma cells, presence of M-protein in bone marrow) (Fisher p ranged from 0.292 to 0.73). An aberrant phenotype or the presence of clonal plasma cells <10% in SP patients was detected in 31%. According to the secretion of immunoglobulins: with MGUS, IgG secretion (53.3%) was most common, with SP, we observed non-secretion variant (37.5%), IgG secretion (31.5%). During the observation period, disease progression into MM was recorded in 18.8% in SP and in 16% MGUS patients. Disease progression in SP patients was associated with the presence of cytogenetic changes (the presence of del13) in combination with IHC of CD138+ >10%, an abnormal ratio of κ/λ chains. High expression of CD27+ was observed. In one patient with SP (iliac plasmacytoma), the disease transformed into MM within six months in the presence of risk factors: clonal plasma cells in the bone marrow −3.1%, CD56+ 93.1%, CD95+ 3.8% by IPT, del13, IHC CD138+ 20%. With MGUS, disease progression was associated with the presence of a combination of CD138+ >10% (76.5% vs. 23.6%; $p < 0.0001$), CD95+ <20% (44.0% vs. 71.4%; $p < 0,083$), CD56+ >20% according to IPT (27.3% vs. 78.0%; $p < 0.0001$), loss of CD27+ expression (66.7%), abnormal ratio κ/λ of chains $p < 0.001$.

Conclusion: Our study showed that a combination of such indicators as the presence of cytogenetic changes (in particular, the presence of del13), CD138+ cells >10% according to IHC, CD56+ >20%, CD95+ <20% according to IPT in combination with an abnormal ratio of κ/λ chains can have prognostic value in transformation into MM in both MGUS patients and SP patients.

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Poems syndrome: a "multifaceted" entity of plasma cell disorder

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Objective: The objective of this study is to reveal patients with misdiagnosed POEMS syndrome in the group of patients with polyneuropathy and to stratify the right form of the plasma cell disease. POEMS syndrome (polyneuropathy, organomegaly, endocrinopathy, M-protein, skin changes) is a rare paraneoplastic disorder caused by plasma cell proliferative disease. The exact incidence of POEMS syndrome is unknown as diagnosis of POEMS syndrome is prolonged and complicated due to variety and non-specific symptoms. In accordance to some sources the incidence of POEMS syndrome is 0.3 per 100,000, however the disease rate may be higher due to missed diagnosis. POEMS syndrome is a plasma cell disorder and the medications used for the treatment are similar to multiple myeloma treatment regimens. However this is a distinct entity with disease process nuances, that's why the selection of the right medication could be crucial for the wellness and survival of patient with POEMS syndrome.

Case report: The first case of POEMS syndrome is diagnosed in Armenia in 2019. The rate of plasma cell disorders that is mainly presented with multiple myeloma is 1.3 per 100,000 in Armenia. In the last decade there is a tendency of increasing of multiple myeloma cases in Armenia. This fact is associated with the improvement of diagnostic methods. The first reported patient with POEMS syndrome is a young men suffering of severe pain in the legs. He was diagnosed with chronic demyelinating polyneuropathy and treated with plasmapheresis and immunoglobulin for 6 months. No efficacy was observed. The progressive neuropathy and new symptoms such as edema, shortness of breath caused patients' disability and his admission to intensive care department. The CT scan, USD examination, bone marrow biopsy, echocardiography, serum protein electrophoresis, CBC, blood chemistry were performed. The examination results were not consistent with multiple myeloma disease, monoclonal gammapathy of undetermined significance (MGUS) and chronic inflammatory demyelinating polyneuropathy (CIDP). The deviations that were revealed during analysis were compared with POEMS syndrome diagnostic criteria and made the diagnosis of POEMS syndrome.

Methodology: 13 patients not responding to the standard treatment protocols for polyneuropathy and 4 patients not corresponding with classic multiple myeloma criteria were included in this study. The spectrum of standard examinations included bone marrow biopsy, immune fixation electrophoresis, CT scan, echocardiography, CBC, Blood chemistry, Interleukin 6 and Interleukin 12 levels detection.

Results: The results were promising. In 3 patients treated for polyneuropathy, not responding to treatment and taking morphine due to severe pain the blood electrophoresis revealed low quantity of monoclonal immunoglobulin (M-spike) with Lamda component detected by immune fixation and the CT show sclerotic lesions in the bones. 2 patients with uncommon myeloma symptoms such as specific pulmonary impairment show high level of Interleukin 6 and Interleukin 12, that can cause the pulmonary hypertension.

Conclusion: The new examinations must to be involved in the list of obligatory analysis for neurology disease. The spectrum of analyses (diagnostic criteria) adopted for plasma cell disorder have to be extended including echocardiography and analyses of interleukin 6 and interleukin 12 for the right diagnosis and target therapy.

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