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ARACHIDONIC ACID (AA)-DERIVED LIPID MEDIATORS ARE INCREASED IN THE BONE MARROW PLASMA FROM POLYCYTHEMIA VERA AND ESSENTIAL THROMBOCYTHEMIA PATIENTS

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Arachidonic acid (AA)-derived lipid mediators like prostaglandins (PG), prostacyclins, thromboxanes (TX), leukotrienes (LT), and lipoxins (LX), are eicosanoids that act as key regulators of a wide variety of physiological responses and pathological processes. AA controls many important cellular processes, including cell proliferation, apoptosis, metabolism and migration. Eicosanoids seems to modulate hematopoiesis and stem cell function and stemness. Therefore, we decided to quantify eicosanoids levels in bone marrow plasma from myeloproliferative neoplasms patients and healthy subjects and to correlate the results with hematological parameters. Nine polycythemia vera (PV), ten essential thrombocythemia (ET) patients and eight healthy bone marrow donors (controls-CT) were investigated. Patients and controls were from Ribeirão Preto Medical School Hospital (HC-FMRP-USP), University of São Paulo, Ribeirão Preto, SP, Brazil. The CT group was composed of four males and four females at average age of 43 years. The PV group was composed of 5 males and 4 females at average age of 61 years and the ET group was composed of 1 male and 9 females at average age of 58 years. Plasma samples were obtained by centrifugation of bone marrow and used to measure the levels of eight lipid mediators (TXB2, 5-HETE, AA, 12-HETE, 11-HETE, 15-HETE, EPA, 15-OXO-ETE) by high performance liquid chromatography. The results showed higher production of 5-HETE by ET patients than CT group ($p = 0.0058$). For EPA, the highest production was observed in PV patients in comparison with ET ($p = 0.0339$) and CT ($p = 0.0450$). 11-HETE was higher in PV patients ($p = 0.0464$) compared to CT. Moreover, a mediator is considered important for a given group/disease when more than 50% of the individuals in that group are high producers for that mediator. The analysis of high and low producers showed that for the CT group none of the mediators can be considered important. In PV group, seven mediators (TXB2, 5-HETE, AA, 12-HETE, 11-HETE, EPA, 15-OXO-ETE) seem to play an important role in disease pathogenesis. In ET group, five mediators (5-HETE, 12-HETE, 11-HETE, 15-HETE, 15-OXO-ETE) were considered important. The correlation analysis between the levels of lipid mediators and hematological parameters showed in PV negative correlation between TXB2 and red blood cells count ($p = 0.0429$; $r = -0.6167$), 5-HETE and hematocrit ($p = 0.0484$; $r = -0.6000$), AA and hematocrit ($p = 0.0150$; $r = -0.7311$), 15-HETE and platelets count ($p = 0.0429$; $r = -0.6167$). There is also positive correlation between 15-OXO-TEE and hemoglobin ($p = 0.0328$; $r = 0.6471$). In ET there was positive correlation between 15-HETE levels and platelets count ($p = 0.0075$; $r = 0.7576$). The results suggest that the lipid mediators, analyzed here, play a role in oncoinflammatory process in myeloproliferative neoplasms. **Keywords:** Lipid mediators; Polycythemia vera; Essential thrombocythemia; Pathogenesis; Oncoinflammation. **Funding:** CAPES (Code 001), CNPq and FAPESP (2018-01756-5; 2018/19714-7).

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ASSOCIAÇÃO ENTRE SÍNDROME POEMS E DOENÇA DE CASTLEMAN: RELATO DE CASO

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Introdução: A síndrome de POEMS (poliradiculoneuropatia, organomegalia, endocrinopatia, proteína monoclonal e alterações de pele) é uma entidade paraneoplásica rara, decorrente de uma proliferação de células plasmáticas. O diagnóstico é feito pela presença dos critérios maiores obrigatórios (polineuropatia e proliferação monoclonal) e pelo menos um dos outros critérios menores (doença de Castleman, lesão osteoesclerótica, organomegalia, endocrinopatia, alterações cutâneas, papiledema). A doença de Castleman (DC), por sua vez, é um distúrbio linfoproliferativo raro, com envolvimento ganglionar unifocal ou sistêmico, que está presente em 11-30% dos casos de POEMS. O presente trabalho relata a dificuldade de diagnóstico da Doença de Castleman e sua posterior evolução para Síndrome de POEMS. **Relato de caso:** Homem, 64 anos, apresentava numerosas pápulas e nódulos eritêmato-violáceas no tronco e membros há 5 anos. Contudo, procurou hematologista em 2016 após presença de linfonodomegalias cervicais, sudorese noturna e perda ponderal de 10 quilos em 45 dias. Associado a isso, observou polineuropatia sensitivo motora das extremidades e fraqueza muscular progressiva. Realizou biópsia de linfonodo cervical, cujo resultado revelou Doença de Castleman, com componente hialino vascular. Os exames de estadiamento revelaram uma positividade para VDRL, mas como havia história de tratamento prévio, aventou-se a possibilidade de se tratar de uma reação cruzada imunológica. Posteriormente exames de estadiamento, deu-se seguimento ao tratamento com R-CHOP (Rituximabe, Ciclofosfamida, Doxorrubicina, Oncovin, Prednisona). Durante a quimioterapia (QT) o paciente apresentou piora da neuropatia e fraqueza muscular, sendo necessária internação, na qual o paciente evoluiu perda do movimento dos membros inferiores e dor intensa na elevação do membro superior. Fez nova TC que evidenciou lesão osteolítica occipital (critério