

CASTLEMAN DISEASE: A BRAZILIAN MULTICENTRIC COHORT OF A RARE HEMATOLOGICAL DISORDER

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INTRODUCTION: Castleman disease (CD) is a rare and sometimes difficult to diagnose hematological condition, with a pathophysiology not fully understood and a wide clinical spectrum. Unicentric CD (UCD) patients have an excellent prognosis contrasting with the multicentric presentation, which may be life-threatening. Some advances in CD understanding and management have been achieved recently. Data of CD in Brazilian patients' is still limited.

METHODS: We retrospectively collected data of patients with biopsy-proven CD in three large Brazilian centers (Hospital das Clínicas da Faculdade de Medicina da USP, Hospital A Beneficência Portuguesa de São Paulo and Instituto Hemomed) from January 2008 to July 2020.

RESULTS: Twenty-nine patients with confirmed CD were included, 14 patients had UCD (48.3%) and 15 had multicentric CD (MCD) (51.7%), further divided into POEMS associated MCD (20%), HHV-8 positive MCD (20%) and idiopathic MCD without TAFRO syndrome (iMCD)(60%). Median age at diagnosis was 46.1 years (19.1-87.9) and 58.6% were male. The histological variants were hyaline vascular in 14, plasma cell in 7 and mixed in one patient. Median time to diagnosis after onset of symptoms was 18.5 months. All UCD patients had lymph node disease and underwent to surgery, either for diagnostic or therapeutic reasons. One UCD patient had a localized relapse requiring another surgery. MCD patients' symptoms at diagnosis more commonly were multicentric lymphadenopathy (93.3%), weight loss (40%), fever (40%) and night sweats (33.3%). First line therapies employed in iMCD patients were: steroids (55.5%), rituximab alone (11.1%) and thalidomide plus cyclophosphamide and prednisone (11.1%). Watch and wait strategy was indicated in two oligosymptomatic iMCD patients. One POEMS-MCD patient received rituximab alone and one received cyclophosphamide monotherapy. Rituximab plus liposomal doxorubicin was administered in 2 of the 3 HHV-8 positive MCD patients. Eight MCD patients needed additional treatment due to progressive disease, with a median time to next treatment of 16.5 months. Siltuximab was administered in 22.2% patients with iMCD during disease course. Other therapies delivered for iMCD patients were chemotherapy with CHOP or CHOP-like protocols in 6 patients, radiotherapy and tocilizumab each one in one patient. Median follow-up duration was 59 months. Median progression free survival (PFS) was 43 months for UCD and 14 months for MCD patients. Median overall survival (OS) for UCD patients was not reached and was 92 months for MCD patients. At 2 years, PFS for UCD patients was 100% and 37.5% for MCD patients. Three MCD patients died of CD progression and one UCD patient died of unrelated infection. All deaths occurred in patients treated in public healthcare service.

DISCUSSION AND CONCLUSION: This is the largest Brazilian cohort of CD patients reported to date, to our knowledge. Patients experienced a long time between the onset of symptoms and the diagnosis of CD. As described by other groups, our UCD patients' results showed good prognosis. Therapies for MCD were heterogeneous due to lack of a specific treatment until recently. However,

most MCD patients still do not have access to recommended first-line therapies, particularly in public healthcare, with a negative impact in their outcomes. The development of a national registry of CD patients in Brazil may raise awareness to this rare entity.