

Association of Multiple Sclerosis and Castleman Disease: A Case Report and Literature Review

Maroua Melliti*, Malek Mansour, Amel Kacem, Ines Bedoui and Ridha Mrissa

Department of Medicine, Military Hospital of Instruction of Tunis, Tunisia

Abstract

Castleman Disease (CD) is an uncommon lymphoid hyperplasia occurring in the mediastinal lymph nodes, and less frequently in the neck lymph nodes. Several factors, likewise Multiple Sclerosis (MS), are reported to be involved in the mechanism of each of the diseases.

Keywords: Castleman disease • Multiple sclerosis • Human Herpes virus

Introduction

We report the case of a patient with CD and MS and we review variants of CD, possible triggering factors and other association cases. We describe the case of a 27-year-old man with no family or personal history, presented with progressive gait disorder which had developed within six month with no extra-neurologic symptoms such as asthenia, fever or night sweats.

Case Report

Neurologic examination revealed a static and kinetic cerebellar syndrome with posterior cord syndrome. Magnetic Resonance Imaging (MRI) revealed multiple hyper intense T2 and FLAIR lesions in both cerebral periventricular and juxtacortical, some with confluent characteristics (plaque aspect) (Figure 1), and medullar cord with no active lesion in contrast-enhanced T-weighted images, with a parapharyngeal isointense T1 and hyperintense T2 mass (Figure 2). Histologic investigation was undergone after excisional biopsy revealing lymph node hyperplasia and follicles with hyalinized foci. Chest and abdomen CT scan did not show mediastinal or abdominal lymphadenopathies. Serological studies for HIV, Hepatite C Virus (HCV) and Human Herpes virus (HHV)-8 were negative with final diagnosis of Unicentric Castleman Disease (UCD) as extensive workup studies failed to show other localization outside the excised lymph node. Immunologic assessments as well as labial gland biopsy were negative. Cerebrospinal Fluid (CSF) immune electrophoresis revealed the presence of oligoclonal bands as well as increased concentration of CSF IgG. Diagnosis of Multiple sclerosis and UCD was established. He was treated by beta interferon with favourable outcome.

Discussion

Castleman disease was first described by Benjamin Castleman in 1954 as an unusual lymphoid hyperplasia occurring predominantly in mediastinum and neck of young to middle age patients [1]. According to histopathological features and clinical data, three variants are universally accepted [2]: a Uni Centric Variant (UCD) with Hyaline-Vascular (HV) features, a UCD Plasma Cell (PC) type with sheets of polytypic PC in the inter follicular area and a multicentric-type CD (MCD) predominantly showing histological features of the PC type. Similarly to Multiple Sclerosis (MS), the pathogenesis of CD is still

a matter of debate. Both environmental and genetic factors are involved in the etiology of MS. A role for some viral infections, such as HHV-8 has been proposed in MS which, associated with HIV infection, has a fundamental role in Multicentric Castleman disease [3,4]. In contrast, the majority of patients with HV UCD patients do not have laboratory abnormalities which is the case of our patient [5]. Reported associated diseases to UCD encompass paraneoplastic pemphigus and follicular dendritic cell sarcoma. The association with Hodgkin Disease (HD) is commonly described with PC variant histology and an interfollicular variant of HD [5].

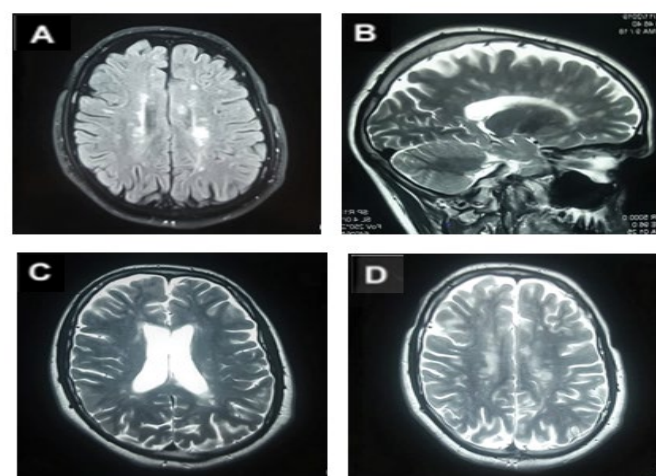


Figure 1. Brain MRI axial FLAIR (Arrow A) and T2 (Arrows C and D), sagittal T2-weighted images (Arrow B) show hyper intense periventricular and juxtacortical lesions suggestive for MS.

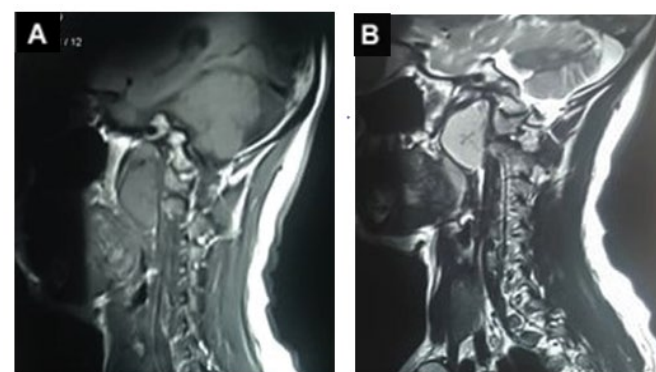


Figure 2. Sagittal MRI images shows isointense T1 (Arrow A) and hyperintense T2-weighted images (Arrow B) parapharyngeal mass with central linear hypointense septate suggestive for lamellar fibrosis.

*Address for Correspondence: Melliti M, Department of Medicine, Military Hospital of Instruction of Tunis, Tunisia, E-mail: mellitimaroua2602@gmail.com

Copyright: © 2021 Melliti M, et al. This is an open-access article distributed under the terms of the Creative Commons Attribution License, which permits unrestricted use, distribution, and reproduction in any medium, provided the original author and source are credited.

Association of CD and MS was reported in rare cases [6,7]. UCD variant was described in a 54-year-old female suffering from MS since the age of 44 and treated with beta interferon, developing a lymph node hyaline-vascular type CD relapsing in the skin after 24 months. The second case was of a 57-year-old female who was shown to have an episode with fever, sweating, lumbalgia and purpuric rash of the right leg, which was diagnosed with MCD, and who then developed gait and speaking disorder within one month and was diagnosed with MS after cerebral and medullar MRI [7]. For our patient, MS was inaugurated with gait disorder however UCD was totally asymptomatic. UCD typically presents as a solitary mass with a progressive enlargement and indolent course. It can be asymptomatic or may have symptoms due to compression of adjacent structures. It occurs equally for men and women and the median age of presentation is 30 years and 34 years old [5]. Approximately 75% to 90% of patients with UCD have HV histologic subtype whereas 10% to 25% patients have variants. Imaging studies typically showed a solitary lesion, as the case of our patient, which may mimic a lymphoma. There is no reliable diagnostic method and its definitive diagnosis is based on histopathology report [5]. CD was also described in three cases of alemtuzumab-treated patients suffering from active relapsing-remitting MS, as potentially life-threatening secondary autoimmune event.

The diagnosis of idiopathic MCD (iMCD) and TAFRO (Thrombocytopenia, Anasarca, Myelofibrosis, Renal failure, Organomegaly) subtype (typical histopathologic findings, HHV-8 negative immunohistochemistry, thrombocytopenia, fever, organomegaly, absence of hypergammaglobulinemia (0.8 g/d) was established after histopathologic studies of lymph node revealing hyperplasia, germinal centre regression, plasma cell expansion and hyalinised vessels [8]. The disease onset has been reported at 28 to 41 months after alemtuzumab initiation [9-12]. As association with different malignancies can occur before, concurrent with or after iMCD (with an incidence of up to 19%), a thorough clinical follow up is required especially beyond 48 months after the last alemtuzumab infusion [13]. However, patients with UCD variant have excellent prognosis which confers 10-year overall survival rates of more than 95% [14] especially after complete resection of the mass. If complete resection is not possible, radiation therapy can be considered with an overall survival rate of 82% at 20 months with limited data on long-term response rate [15]. Systemic therapeutic options for MCD, such as chemotherapy, rituximab or anti-Interleukin-6 (IL-6) therapy can be considered for patients with UCD who cannot be treated with surgery or radiotherapy or for those who fail to respond to such treatment. The peculiarity of the present case bases itself on the association of UCD discovered incidentally in treatment free MS-patient which is to our best of knowledge, the first reported case of such a possible association.

Conclusion

Multiple sclerosis is a myelodegenerative disease sustained by production of anti-myelin antibodies. The deregulated immune system might have favoured

the development of CD. Although many environmental factors are involved, the precise mechanism which triggers both diseases is still inconclusive. Future studies with larger sample sizes and evaluation of immune status of patients are warranted.

References

1. Benjamin Castleman, Lalla Iverson and Pardo V. Menendez. "Localized Mediastinal Lymphnode Hyperplasia Resembling Thymoma." *Cancer* 9 (1956): 822.
2. Anu Dham and Bruce A Peterson. "Castleman's Disease." *Curr Opin Hematol* 14 (2007): 354.
3. Chang Yuan, Cesarman Ethel and Patrick S. Moore. "Identification of Herpesvirus-like DNA Sequences in AIDS-Associated Kaposi's Sarcoma." *Sci* 266 (1994): 1865-1869.
4. Soulier, James. "Kaposi's Sarcoma Associated Herpesvirus-like DNA Sequences in Multicentric Castleman's Disease." *Blood* 86 (1995): 1276.
5. Wong, Raymond. "Unicentric Castleman Disease." *Hematol* 32 (2018): 65-73.
6. Buraga, Ion. "Multiple Sclerosis: Varied Symptoms, One Disease." *J Neurol Sci* 3 (2015): 357.
7. Dario Tomasini, Clementina Zampatti and Giovanni Serio. "Castleman's Disease with Numerous Mantle Zone Lymphocytes with Clear Cytoplasm Involving the Skin: Case Report." *J Cutan Pathol* 36 (2009): 887-891.
8. Leoni Rolfes and Steffen Pfeuffer, Tobias Ruck and Susanne Windhagen. "A Case of Idiopathic Multicentric Castleman Disease in an Alemtuzumab-Treated Patient with MS." *Neurol Neuroimmunol Neuroinflamm* 7 (2020): 638.
9. Jennifer Somerfield, Grant A. Hill-Cawthorne, Andrew Lin and Michael S. Zandi, et al. "A Novel Strategy to Reduce Immunogenicity of Biological Therapies." *J Immunol* 185 (2010): 763-768.
10. Aliehossadat Mostafa, Somayeh Jalilvand, Zabihollah Shoja and Ahmad Nejati, et al. "Multiple Sclerosis-Associated Retrovirus, Epstein-Barr Virus, and Vitamin D Status in Patients with Relapsing Remitting Multiple Sclerosis." *J Med Virol* 89 (2017): 1309-1313.
11. Ahmad Nejati, Zabihollah Shoja, Shohreh Shahmahmoodi and Abbas Tafakhori, et al. "EBV and Vitamin D Status in Relapsing-Remitting Multiple Sclerosis Patients with a Unique Cytokine Signature." *Med Microbiol Immunol* 205 (2016): 143-154.
12. Boddu Pillai and Hassan Anth. "Rare Case of Multicentric Castleman Disease Secondary to Alemtuzumab Therapy." *Int J Tumor Ther* 4 (2015): 1-4.
13. Amy Y Liu, Christopher S Nabel, Brian S Finkelman and Jason R Ruth, et al. "Idiopathic Multicentric Castleman's Disease: A Systematic Literature Review." *Lancet Haematol* 3 (2016): 163-175.
14. Nadia Talat, Ajay P. Belgaumkar and Klaus-Martin Schulte. "Surgery in Castleman's Disease: A Systematic Review of 404 Published Cases." *Ann Surg* 255 (2012): 677-684.
15. Kah-Lok Chan, Stephen Lade and Simon Harrison. "Update and New Approaches in the Treatment of Castleman Disease." *J Blood Med* 7 (2016): 145-158.

How to cite this article: Maroua Melliti, Malek Mansour, Amel Kacem, and Ines Bedoui, et al. "Association of Multiple Sclerosis and Castleman Disease: A Case Report and Literature Review." *Clin Case Rep* 11 (2021): 1443.