CHAGASIC MENINGOENCEPHALITIS IN THE IMMUNODEFICIENT


ABSTRACT - Based on their own experience and on the literature, the authors compare the brain pathology due to HIV+ associated *Trypanosoma cruzi* reactivated infection to that described for the natural history of the Chagas’ disease (CD). The peculiar focal necrotizing chagasic meningoencephalitis (MECNF) which appears only in immunodeficient chagasics, especially when the deficiency is due HIV is a safe criterion for reactivation of CD. MECNF morphologic findings are unlike to those found either for some cases of acute phase CD or for chronic nervous form of CD.


During the last decades, various events such as the use of cytostatic agents and immuno-suppressors, the progress in organ transplantation and, especially, the advent of acquired immunodeficiency syndrome (AIDS) have set conditions for the reactivation of infection by *Trypanosoma cruzi*. This prompted some24 to revive the old concept of acute exacerbations of Chagas´ disease (CD), proposed by Chagas in 19113 but discarded later by himself4.

In 1994, we analyzed the main pathologic findings in 23 chagasic patients infected with human immunodeficiency virus (HIV), with or without AIDS26. Following that paper many other addressed the topic2,5,7,9,11,18,21,27,28. From those reports and the others presented in meetings, 29 of 75 (38.6%) patients with *T. cruzi* infection had reactivation involving the central nervous system (CNS).

The morphologic features of chagasic meningoencephalitis (CME) in patients with chronic CD accompanying AIDS is sometimes similar to those described for chagasics with other immunosuppressive conditions13. They are much alike the description by Queiroz in 197325. The latter did not refer to immunosuppression. However, his patient was clinically diagnosed as having mycosis fungoides,
nowadays a well-known T-cell lymphoma related with immunosuppression⁶. CME in some immunodeficient chagasic patients, especially when the immunodeficiency is due to HIV, has its own special features, which are clearly distinct from either acute³,30,31 or chronic¹⁶,²⁰,²²,²⁹ CD involving the CNS.

The present paper compares the morphological alterations of reactivated *T. cruzi* infection in brains of HIV+ patients with those classically described for natural history of CD.

**Brain morphology in acute chagasics**

Classical studies³,30, recent data⁸,¹⁰,¹⁴,¹⁶,²⁰,²²,²⁹ and our experience indicate that some acute phase chagasics present with serious neurological manifestations. These acute chagasic patients develop CME including multifocal brain lesions in white and gray matters, accompanied by a diffuse lymphocytic leptomeningitis with few plasma cells, macrophages and polymorphonuclear leukocytes. The parenchymal CNS lesions, particularly in the deeper cortical layers as well as in the sub-cortical white matter, include perivascular inflammatory cell infiltrates in addition to foci of microglial proliferation, swollen oligodendrocytes and astrocytes, neuronophagy and small hemorrhages. The inflammatory infiltrates are usually more severe within the white matter and are sometimes accompanied with small foci of demyelination. Amastigote forms of *T. cruzi* are found within glial cells in most cases. Neuronal parasitism is scant or usually absent. Necrosis of the nervous tissue is minimal if it ever occurs.

**Brain morphology in chronic chagasics**

The great majority of the chagasic patients survive their acute disease, which gradually merges into the chronic phase. It is our experience that during the chronic phase chagasic patients may present with mild encephalitis with few inflammatory foci¹⁷. Those foci may either remain as such or be replaced by glial scars or completely disappear. Pittella²² has demonstrated foci with scant inflammatory cells without surrounding nervous tissue lesions in 6% of brains from chronic chagasic patients. In his opinion those might be residual lesions from the acute phase.

During chronic CD clinical CNS manifestations may be detected⁸ and anti-*T. cruzi* antibodies and auto-antibodies may also be found in the cerebro-spinal fluid¹⁵. In spite of these evidences, Pittella²² admits that “no anatomical basis exists that might characterize the existence of chronic nervous form of CD”.

We feel that detailed morphological studies of the CNS from chronic chagasic patients with close neurological follow-up is needed to prove or disprove an anatomical basis for the existence of a neurological form of chronic CD¹⁷.

**Brain morphology in immunodeficient chagasics**

The brains of immunodeficient chagasic patients, especially those with HIV infection, show an increased weight and volume with enlargement and flattening of the gyri and narrowing of the sulci. They present with softened, hemorrhagic and poorly limited areas ranging up to several centimeters in diameter involving both white and gray matters (Figs 1 and 2). It appears that white matter is the preferred site of involvement. The lesions are mostly located in the cerebral lobes and, less frequently, in the cerebellum and brain stem. To the best of our knowledge no basal ganglia lesions were ever described. Especially in the softened areas, microscopy shows meningoencephalitis with tendency to necrosis and hemorrhage (Fig 3). Encephalitis seems to be the primary lesion. Microglial nodules are found within the white and gray matters in nearly all cases. Edema, necrosis, recent or old focal hemorrhages and focal astrocytic gliosis, mostly within the white matter, are usually also found. In addition there are dense exudates of macrophages, lymphocytes and plasma cells and, to a lesser degree, neutrophilic granulocytes within the perivascular spaces. Vascular necroses are frequent but thrombosis seems to be rare. Amastigotes of *T. cruzi* (Fig 3, detail) are easily found within the glial cells and macrophages, especially around necrohemorrhagic areas,
Fig 1. Frontal plane brain section showing poorly delimited necrohemorrhagic areas (arrows). Edema of the right cerebral hemisphere displacing the mid-line structures (bar = 1cm).

Fig 2. Detail of the Figure 1 (bar = 1cm).
around the blood vessels and free floating in the interstice. Neuronal parasitism is rare. Leptomeningitis is apparently an extension of the subjacent necrotic lesions. The leptomeningitis ranges from slight to moderate. Macrophages, lymphocytes, fewer plasma cells, and neutrophilic granulocytes, are found within the leptomeningeal lesions.

The foregoing findings, support the concept that CME in some immunodeficient chagasic patients, especially when the immunodeficiency is due to HIV, is different from the meningoencephalitis occurring either in the acute phase or in the nervous form of chronic phase of CD. It is a safe pathological indication of CD reactivation.

We propose the label **focal necrotizing chagasic meningoencephalitis** for the CME of HIV+ immunosuppressed patients herein described because of its similarity to focal necrotizing toxoplasmic encephalitis, as described, among others, by Post et al.\(^2\), Navia et al.\(^{19}\), Bertolli et al.\(^1\) and Lazo\(^{12}\).

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