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CHAGASIC MENINGOENCEPHALITIS IN THE IMMUNODEFICIENT

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ABSTRACT - Based on their own experience and on the literature, the authors compare the brain pathology due to HIV+ associated *Trypanosoma cruzi* reactived infection to that described for the natural history of the Chagas' disease (CD). The peculiar focal necrotizing chagasic meningoencephalitis (MECNF) which appears only in immunedeficient 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.

KEY WORDS: chagasic meningoencephalitis, encephalitis, AIDS, *Trypanosoma cruzi*, Chagas´ disease.

Meningoencefalite chagásica no imunodeficiente

RESUMO - Baseados na experiência pessoal e nos dados da literatura, os autores comparam as alterações anatomopatológicas encefálicas resultantes da reativação da infecção pelo *Trypanosoma cruzi*, de paciente HIV+, com aquelas observadas e descritas na história natural da doença de Chagas (DC). A meningoencefalite chagásica necrosante focal (MECNF) que somente se desenvolve em tripanosomoticos imunodeficientes, especialmente quando a imunodeficiência é devida ao HIV, tem características peculiares e constitui parâmetro anatomopatológico seguro, de reativação da DC. Esta MECNF apresenta lesões diversas daquelas que podem ser observadas e que são descritas em casos da fase aguda e da forma nervosa crônica da DC.

PALAVRAS-CHAVE: meningoencefalite chagásica, encefalite, AIDS, *Trypanosoma cruzi*, doença de Chagas.

During the last decades, various events such as the use of cytostatic agents and immunosuppressors, 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 some[24] to revive the old concept of acute exacerbations of Chagas´ disease (CD), proposed by Chagas in 1911[3] but discarded later by himself[4].

In 1994, we analyzed the main pathologic findings in 23 chagasic patients infected with human immunodeficiency virus (HIV), with or without AIDS[26]. Following that paper many other addressed the topic[2,5,7,9,11,18,21,27,28]. 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 conditions[13]. They are much alike the description by Queiroz in 1973[25]. The latter did not refer to immunosuppression. However, his patient was clinically diagnosed as having mycosis fungoides,

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nowadays a well-known T-cell lymphoma related with immunosuppression[6]. 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 acute[3,30,31] or chronic[16,20,22,29] 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 studies[3,30], recent data[8,10,14,16,20,22,29] 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 foci[17]. Those foci may either remain as such or be replaced by glial scars or completely disappear. Pittella[22] 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 detected[8] and anti-*T. cruzi* antibodies and auto-antibodies may also be found in the cerebro-spinal fluid[15]. In spite of these evidences, Pittella[22] 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 CD[17].

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,

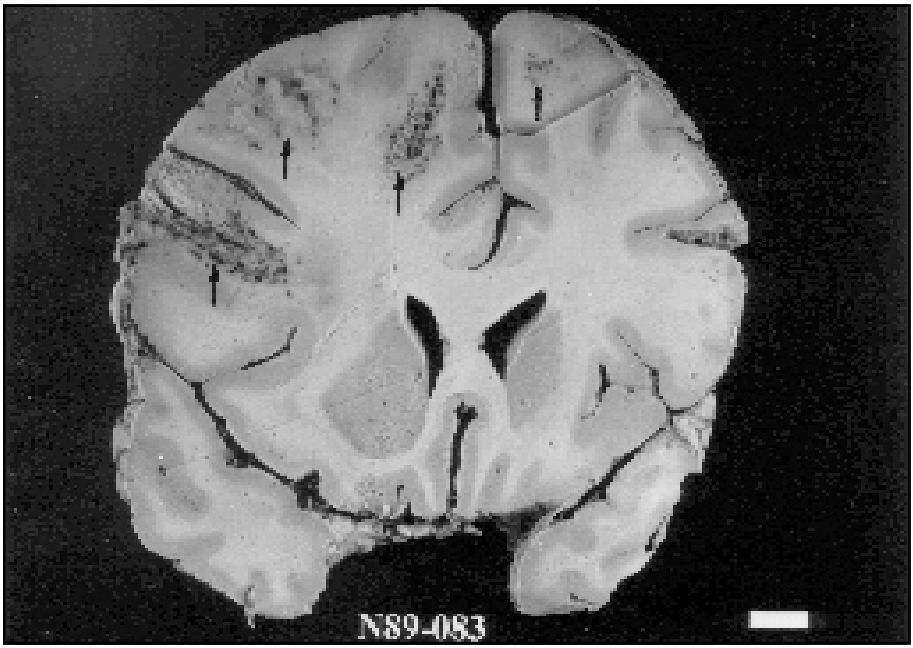

Fig 1. Frontal plane brain section showing poorly delimited necrohemorragic areas (arrows). Edema of the right cerebral hemisphere displacing the mid-line structures (bar = 1cm).

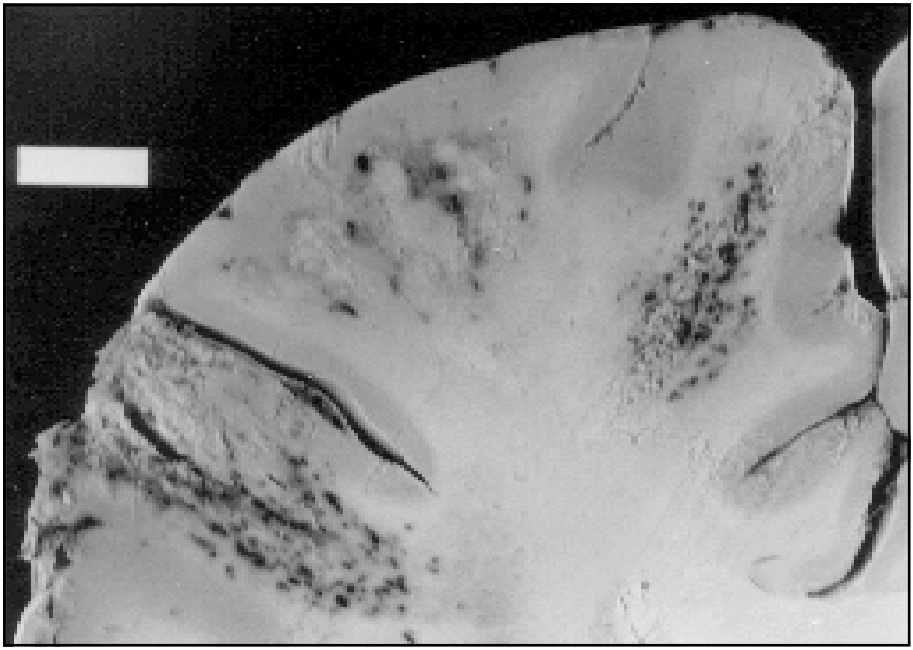

Fig 2. Detail of the Figure 1 (bar = 1cm).

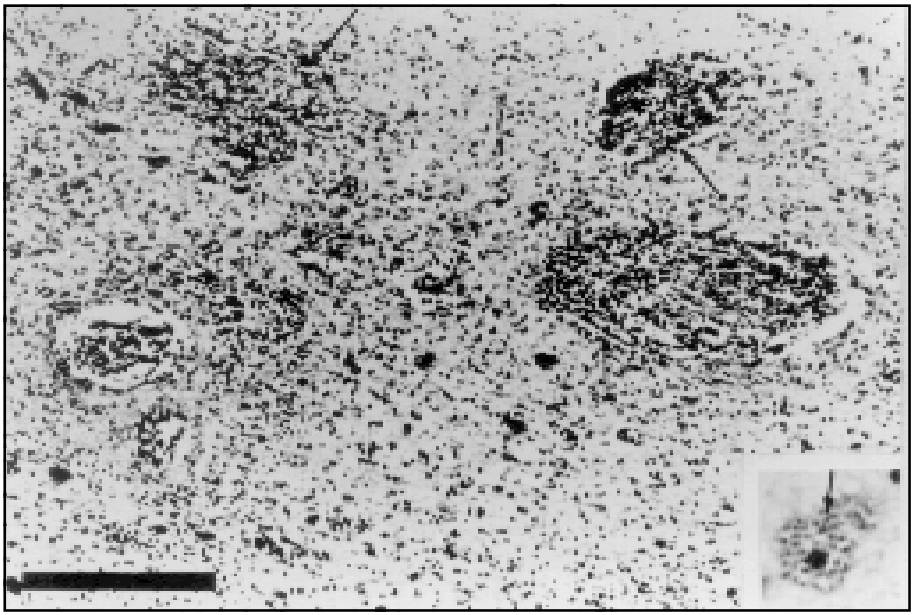

Fig 3. Histologic features of the white matter necrohemorragic lesions (arrows). Detail: T. cruzi amastigotes packed within a glial cell (H-E; bar = 122 µm).

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.[23], Navia et al.[19], Bertolli et al.[1] and Lazo[12].

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