

Latent and Reactivated Toxoplasma Gondii Infection in HIV-Infected Patients in Albania

Ermira Muco¹, Pellumb Pipero², Arjan Harxhi³, Najada Como⁴, Arben Pilaca⁵, Tritan Kalo⁶,
Edmond Puca⁷, Klodiana Shkurti⁸, Loreta Kuneshka⁹, Dhimiter Kraja¹⁰

1, 2, 3, 4, 5, 6, 7, 8, 10 Infectious Diseases Service. Outpatient Clinic of HIV/AIDS and sexually transmitted diseases. UHC "Mother Teresa" Tirana

⁹Department of Public Health, Albania

Abstract: *Toxoplasmosis, which is caused by Toxoplasma gondii, is one of the most common parasitic infections of humans and warm blooded animals. The Toxoplasma Encephalitis (TE) is one of the most frequent opportunist infections and as a consequence the most important cause of cerebral focal lesions in HIV/AIDS patients, because of the reactivation of the latent infection. Purpose: To provide data on the prevalence of Toxoplasmosis in HIV/AIDS patients hospitalized and followed in our outpatient clinic and Infectious Diseases Service and to recognize the clinical, preclinical, therapeutic features of cases. Materials and methods: From 157 subjects with HIV/AIDS who were filled with ELISA IgM/IgG T.gondii antibodies, we studied 92 cases which had the presence of anti-T. gondii IgG. Results: The seroprevalence of Toxoplasmosis in HIV patients in our study resulted 58.59%. In 92 positive cases for IgG antibodies, 33.69% were females and 66.30% were males. We found that the most number of patients (44.56%) had finished elementary school. Most of cases belonged to age group 35-45 years old (40.21%). We found higher positivity for IgG antibodies (39.13%) in the emigrated patients. Toxoplasmic encephalitis found in 23 subjects with AIDS. T. gondii IgG antibodies were positive in 23 cases. The mean CD4 cell count was 51.73 cells/ μ L. Lesions were located in 13 cerebral areas. We recognised 15 clinical signs. Mortality resulted 56.52%. Conclusions: Considering its high rate of reactivation, all the HIV patients must be tested for the presence of Toxoplasma gondii antibodies and that should receive prophylactic treatment are the ones with AIDS and IgG positive antibodies.*

Keywords: Toxoplasma Encephalitis, HIV/AIDS, Toxoplasma gondii, Seroprevalence.

1. Introduction

Toxoplasmosis, a disease caused by Toxoplasma gondii, is one of the most common parasitic infections in humans and mammals. It is encountered in whole world, from Alaska to Australia. Seroprevalence of anti-Toxoplasma antibody varies substantially among different geographic regions, with a prevalence of approximately 11% in the United States, versus 50 -80% in certain European, Latin American, and African countries (1,2) We can be infested by this parasite through ingestion route: from contaminated water and food, from oocysts excreted by cats or infected meat, not properly cooked (3,4,5); respiratory route: responsible for so called Toxoplasma pneumonia; transplacental route, responsible for abortion and neonatal pathologies; nosocomial through blood transfusion, organ transplant and laboratory accidents (6,7,8). Living with HIV/AIDS or different type of neoplasia, therapy with immunosuppressors or pregnancy are also risk factors. So, the Toxoplasma Encephalitis is one of the most frequent opportunist infections and as a consequence the most important cause of cerebral focal lesions in HIV/AIDS patients, because of the reactivation of the latent infection (9-12). Cerebral Toxoplasmosis is typically observed in the later stages of human immunodeficiency virus infection (10,13,14). CNS disease occurs when CD4⁺ counts are less than 200 cells/ μ L. The greatest risk is in patients with CD4⁺ counts below 50 cells/ μ L (15,16,17). Patients with cerebral toxoplasmosis presented higher titers of anti-T. gondii IgG antibodies than patients with other diseases (18). In patients with CD4 cell counts below 200/ μ L, an antibody titer of \geq 150 IU/mL was found to be predictive of TE (19). There are no data related to CNS toxoplasmosis in Albania, while the prevalence of toxoplasmosis in pregnant women in Albania is 48.6% (21).

2. Aim

- To provide data on the prevalence of Toxoplasmosis in HIV/AIDS patients hospitalized and followed in our outpatient clinic and Infectious Disease Service from 2000 to 2014.
- To recognize the clinical, preclinical, therapeutic features of our cases.

3. Material and Method

From a database of 157 subjects with HIV/AIDS who were filled with Enzyme-Linked Immunosorbent Assay/ ELISA IgM/IgG T. gondii antibodies, we studied 92 cases between age of 15 - 67 years old which had the presence of anti-T. gondii immunoglobulin G (IgG). Cerebral Toxoplasmosis defined by the Centers for Disease Control and Prevention Criteria. Diagnosis of TE was based on the association of central neurological disorders, typical lesions on CT scan or MRI and successful response to the specific treatment.

4. Results

In 92 positive cases for IgG antibodies: 31 of them (33.69%) were females and 61 cases (66.30%) were males. The male/female ratio was 1.96:1. We classified our cases were positive for IgG antibodies according to age group: 1 case (1.08%) of them belonged to age group 15-25 years old; 20 cases (21.73%) age group 25-35 years old; 37 cases (40.21%) age group 35-45 yrs old; 25 cases (27.17%) age group 45-60 yrs and 9 cases (9.78%) of cases were older than 60 years old. Our patients had performed all grades of education: 12 cases (13.04%) resulted graduated in

university; 39 cases (42.39%) with high school graduation; and 41 cases (44.56%) elementary school. Emmigrated patients was 36 (39.13%).

Toxoplasmic encephalitis found in 23 subjects with AIDS. In 23 cases, 16 of them (69.56%) were males and 7 cases (30.43%) were females. The male/female sex ratio was 2.3:1. Medium age of patients was 45.95 years old (range: 27- 60); medium age of males was 43.12 years old (range: 27- 58); medium age of females was 52.42 years old (range: 40-60). Elementary school had only 11 cases (47.82%); 10 cases (43.47 %) had high school; 2 cases (8.69%) university

degree. Married were 19 cases (82.60%). TE as a first clinical presentation was found in 18 cases (78.26%) and from these 12 cases (52.17%) were males and 6 cases (26.08%) were females. Before the first episode of TE, 5 patients (21.73%) were given antiretroviral therapy (mean: 9.8 months; range: 1-18 months). T. gondii IgG antibodies were positive in 23 cases (range: 209-2239 IU/ml). The mean CD4 cell count was 51.73/ μ l (range:16-176/ mm^3). Toxoplasmic Encephalitis appeared with fever, headaches, confusion, vomits and other clinical sings (Table 1)

Table 1: Symptoms/signs at presentation in 23 patients with TE

Symptos/Signs	No.	(%) of Patients (N=23)
Fever	16	69.56%
Headaches	21	91.30%
Confusion	13	56.52%
Nausea or vomits	15	65.21%
Lethargy	9	39.13%
Neck Stiffness	8	34.78%
Ataxia	7	30.43%
Cerebellar signs	6	26.08%
Hemiparesis	12	52.17%
Convulsion	8	34.78%
Cranial nerve disturbances	9	39.13%
Sensory deficits	9	39.13%
Aphasia	12	52.17%
Stupor	16	69.56%
Coma	13	56.52%

The head CT scan was performed on all cases, highlighting unique or multiple hypodense lesions with mass effect and edema. MRI of the head was performed in 18 cases (78.26%), noting unique loops or multiple lesions with hypersignal to reinforce after iv contrast, the hemosiderin signal in the periphery, with edema and mass effect. CT/MRI of the head identified single lesion in 4 cases (17.39%) of patients (Fig 1); two lesions in 3 cases (13.04%); three lesions in 1 case (4.34%) and multiple lesions (> 4) in 15 cases (65.21%) of them. (Fig 2). 21 cases (91.30%) had edema.



Figure 1 : Single lesion in TE.

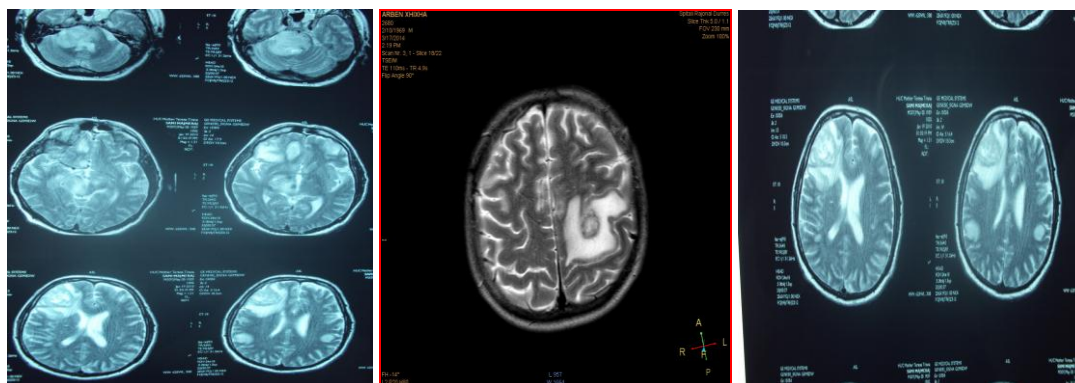


Figure 2 : Multiple lesion in TE.

Table 2: CT/MRI findings/ location in 23 patients with Toxoplasmic Encephalitis

CT/MRI findings / location	No.	(%) of Patients (N=23)
Frontal	10	43.47
Parietal	9	39.13
Occipital	5	21.73
Temporal	6	26.08
Basal ganglia	9	39.13
Cerebellum	4	17.39
Cortical-medular junction	5	21.73
Thalamus	2	8.69
Corpus callosum	3	13.04
Peritrigonal region	2	8.69
Parahypocampus girus	1	4.34
Precentral girus	1	4.34
Parasagittal girus	1	4.34

Mortality resulted in 13 patients (56.52%), with time duration 6 days (range 3-10 days). Twenty two (95.65%) patients were treatment with Trimethoprim (10 mg/kg/day) plus Sulfamethoxazole (50 mg/kg/day) and only one case treated with Pyrimethamine (50 mg/day) plus Sulfadiazine (4 g/day) and folic acid (25 mg/day) that proved successful. Anticonvulsant agents were administered in the occurrence of convulsions. Glucocorticoids were added as adjuvant therapy in complications with a mass effect. Highly active antiretroviral therapy (HAART) began after at least 2 weeks of antiparasitic therapy. Side effect in patients treated with Cotrimoxazole: hypersensitivity reactions occurred in 2 patients (8.69%); gastrointestinal adverse events occurred in 7 patients (30.43%); mild rhabdomyolysis occurred in 1 patient (4.34%); hemolytic anemia occurred in one patient; however, no patient stopped taking therapy. In 10 cases that survive 4 of them had clinical improvement by the 9th day of treatment and 6 cases had clinical improvement by the 21th day. Imaging studies showed complete resolution of the lesions by 28-45 days.

5. Discussion

The above article highlights valuable epidemiological and clinical data about latent and reactivated *Toxoplasma gondii* infection in HIV-infected patients in Albania, because no data has been reported in our population on the TE incidence. In our study the seroprevalence of toxoplasmosis in HIV patients resulted 58.59%. Some study presented it from 20-73.7% (10). This high prevalence maybe can explain with regional area of our country. Most Toxo-IgG antibody seropositive cases were males. The sex predilection could be attributed to the higher risk of professional, consumption of meat etc (9). Studies made about the spread of toxoplasmic infection in different age groups have shown an incidence of this infection that increases with age (presence of specific antibodies from 8% for ages 2-6 years old in 53.4 % for those over 40 years old (9,22-24). We found higher positivity for IgG antibodies, 39.13% in the emigrated patients, related to their life style (most of them work as farmers).

The cerebral form was found mostly at the ages 35-55 years old, as a consequence of the reactivation of latent infection

(11,25) Also this group age has the high prevalence of adult retrovirosis in Albania (26). CNS toxoplasmosis presented 15 different semiotic signs mostly reported headaches, vomits, clinical symptoms described by other authors (10,11,25,27). We had variety of topographic cerebral lesions in our patients, mostly resulted ganglionic lesions, frontal and parietal. We evidence the fact that mostly the cases had multiple lesions, based on the literature data (20). The mortality was relatively high, related with the lately coming of these patients to us. Noticed that TE was the first AIDS manifestation in 78.26%. We know that TE is the one of the most common opportunist infections in AIDS; showed in 10-50% of them with a high mortality (28) Mostly our cases were treated with Trimethoprim/sulfamethoxazole, as a first choice for treating TE because it is unexpensive, effective and well-tolerated. This medicament is also well prescribed in literature (29). We think that our above data can contribute to the deeper recognition of TE, which as was evidenced represents a protozoosis often problematic and potentially deadly.

6. Conclusions

Toxoplasmosis is one of the most lethal opportunistic infections in AIDS patients. Therefore, new strategies to prevent Toxoplasmosis are necessary. In order to do this, we need exact data on seroprevalence of this infection in the normal population, which in our case means the positive HIV population. Considering its high rate of reactivation, all the HIV patients must be tested for the presence of *Toxoplasma gondii* antibodies, and all cases with positive toxoplasma antibodies should receive prophylaxis.

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