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Evaluation of vertical transmission of *Toxoplasma gondii* in *Calomys callosus* model after reinfection with heterologous and virulent strain

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ABSTRACT

Toxoplasma gondii is an obligate intracellular protozoan parasite that causes a variety of clinical syndromes, but the infection is severe in immunocompromised individuals and during pregnancy due to the possibility of transplacental transmission of the parasite causing congenital toxoplasmosis. Vertical transmission of the parasite usually occurs when females are primarily infected during pregnancy. *Calomys callosus* is resistant to *T. gondii* ME49 strain, which presents a moderate virulence and congenital disease occurs only during the acute phase of infection. The aim of this study was to determine whether vertical transmission occurs when females of *C. callosus* chronically infected with ME49 strain of *T. gondii* are reinfected with a highly virulent strain (RH, type I). Females were infected with cysts of the ME49 strain. On the 1st day of pregnancy, animals were reinfected with tachyzoites of the RH strain. In the 19th day of pregnancy, placentas and embryos were processed for morphological analysis, immunohistochemistry and for detection of the parasite by PCR and mouse bioassay. Morphological and immunohistochemical analyses revealed the presence of parasites only in placental tissues. Mouse bioassay results showed seroconversion only in mice that were inoculated with placental tissues. Also, *T. gondii* DNA was detected only in placental samples. Congenital toxoplasmosis does not occur in *C. callosus* females chronically infected with the moderately virulent ME49 strain of *T. gondii* and reinfected with the highly virulent RH strain, thus indicating that primary *T. gondii* infection before pregnancy leads to an effective long-term immunity preventing transplacental transmission to the fetus.

1. Introduction

Toxoplasma gondii is an obligate intracellular protozoan parasite and an important opportunistic pathogen for humans and animals because it infects a wide range of hosts [1]. *T. gondii* infection can cause severe life-threatening disease in immunocompromised patients and congenital toxoplasmosis in newborns [2]. Tissue pathology associated with *T. gondii* infection results from parasite-induced destruction of host cells, and it can be related to strain virulence [3]. *T. gondii* is distributed in nature as a heterogeneous population that can be defined in genetic profiles consisting of three predominant clonal lineages (I, II and III) [4]. Infection in human as well as in animals, may occur with all genotypes, although the level of virulence varies between the genotypes [3,4]. Type I strains are virulent for the mouse, and infection with a single parasite results in the death of the animals. In contrast, types II and III are relatively avirulent in mice, frequently resulting in chronic infections. Recombinant and atypical strains have also been reported [3–5], particularly in Brazil where it was recently identified a higher genetic diversity than previously recognized [6].

Vertical transmission generally occurs when a woman is primarily infected with *T. gondii* during pregnancy [7], although rare exceptions have been reported in which women were infected just before pregnancy [8]. In addition, reactivation of an infection acquired before pregnancy can lead to congenital toxoplasmosis in immunocompromised women [9], whereas the transplacental transmission of *T. gondii* after maternal reinfection during pregnancy was already reported in immunocompetent women [10]. The risk of congenital infection is lower when maternal infection takes place in the first trimester (10–15%) and higher when infection occurs during the third trimester (60–90%) of pregnancy [7]. The vertical transmission is not obligatory, being observed in 20%–50%

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of maternal primary infection by *T. gondii* during pregnancy [11], mostly by types I and II strains in humans [2].

During the acute phase of infection, fastly-replicating tachyzoites convert into the latent or chronic phase with slowly-replicating bradyzoites in tissue cysts [12]. It has been accepted for years that primary *T. gondii* infection leads to life-long immunity preventing reinfection [13,14]. This view has been questioned by several authors using immunocompetent murine models [13–15]. These studies found that protection can be breached after reinfection with parasites belonging to different genotypes.

Congenital toxoplasmosis has been described in the literature in a variety of experimental models [16,17]. *Calomys callosus*, a rodent of the family Cricetidae widely distributed in Central Brazil, has been used in our previous studies, demonstrating its high susceptibility to *T. gondii* infection [18]. Also, this rodent was shown to be a suitable experimental model to study the dynamics of congenital toxoplasmosis, due to the ability of a highly virulent strain of *T. gondii* (RH strain) to infect trophoblast cells during the early blastocyst-endometrial relationship [17]. In another study, we demonstrated the vertical transmission of *T. gondii* in *C. callosus* acutely infected with the relatively avirulent ME49 strain during pregnancy, but not in chronically infected animals [19]. Recently, we reported that vertical transmission of *T. gondii* may take place when maternal infection occurs within one month before conception, thus demonstrating the time of preconceptional seroconversion that rule out a risk of congenital toxoplasmosis [20].

Considering that a primary *T. gondii* infection can provide protective immunity against reinfection, but the risk of congenital toxoplasmosis during pregnancy is unclear when the infection occurs among parasites with different genotypes, the present

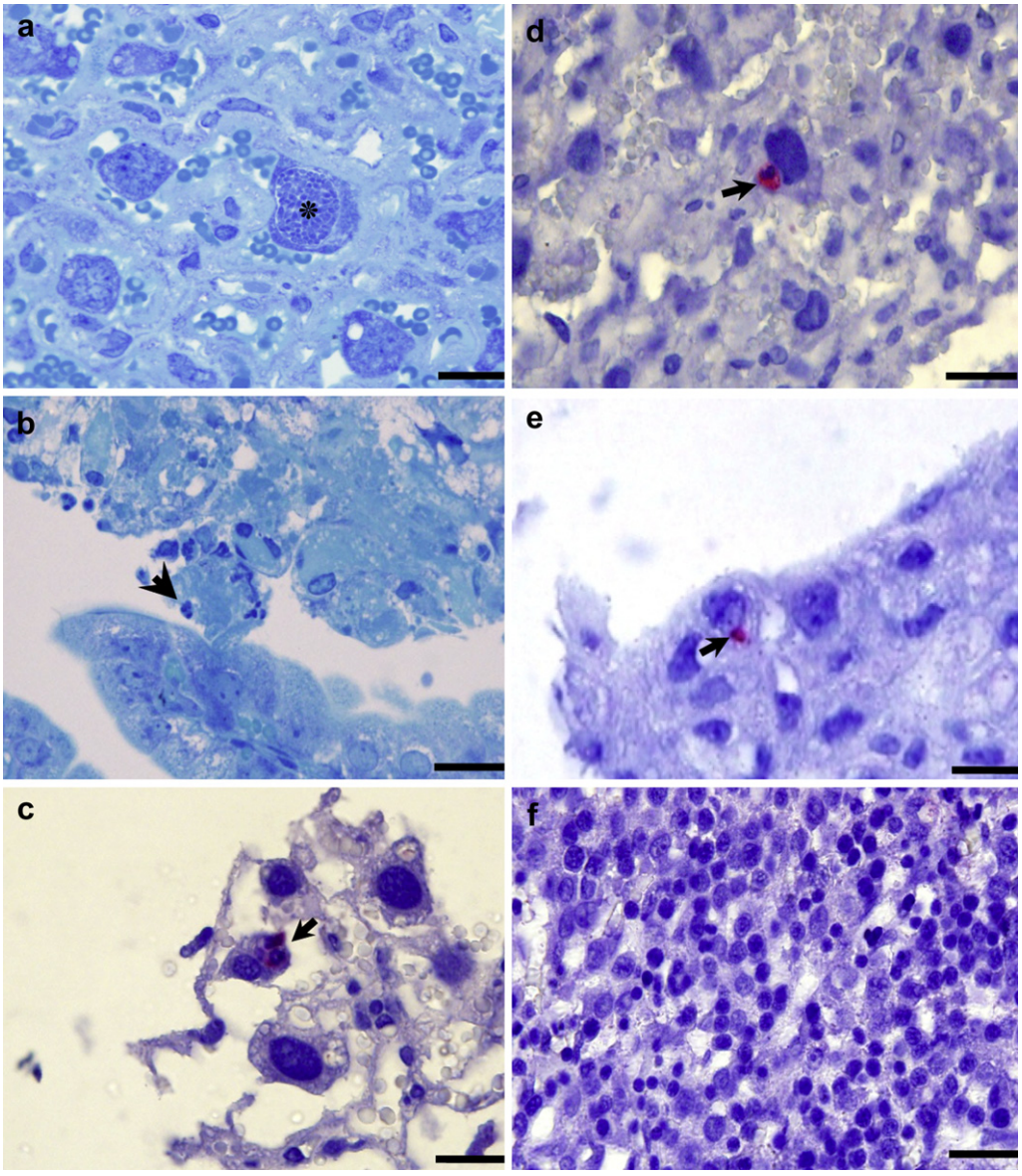

Fig. 1. Photomicrographs of placenta and embryo tissues from *Calomys callosus* chronically infected with ME49 strain of *T. gondii* and reinfected with RH strain after different days of primary infection (doi). Group I, after 48–53 doi; group II, after 58–63 doi; group III, after 73–78 doi; and group IV, after 88–93 doi. Staining by toluidine blue shows the presence of parasites in (a) placenta labyrinth cells (asterisk) from females of group II and (b) placenta decidua (arrowhead) from females of group IV. Immunohistochemical staining using alkaline phosphatase and fast red-naphthol showing the presence of parasites (arrows) in (c) placenta labyrinth zone from females of group I; (d) placenta labyrinth zone from females of group II; (e) placenta decidua from females of group III; and absence of parasites in (f) embryo liver cells from group III. Counterstaining by Mayer's haematoxylin. Bar scale: (a, c–f): 14 μm; (b): 35 μm.