The liver as an organ at risk for *Toxoplasma* transmission during transplantation : myth or reality ?

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BACKGROUND

The parasite *Toxoplasma gondii* can be transmitted through solid organ transplantation, by the introduction of a cyst-containing organ from a donor with chronic infection into the recipient. Few cases of toxoplasmosis consecutive to liver transplantation are described, but they are usually severe because of the host immunosuppression following the allograft. Actually, the prevalence of cysts in the liver of seropositive donors is poorly documented in humans, thus prophylaxis guidelines to prevent toxoplasmosis during liver transplantation are not consensual. As hepatic *Toxoplasma* infection is difficult to explore in humans, this study aimed at characterizing hepatic cyst carriage in a murine model and at potentially defining a preferential hepatic localization.

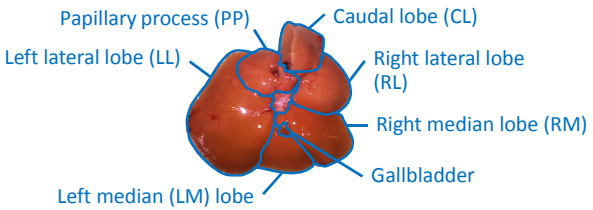


Figure 1. Anatomy of the mouse liver

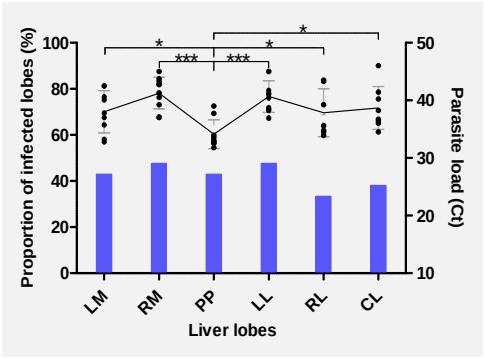
MATERIALS and METHODS

The study was conducted on 21 female Swiss mice used for routine diagnosis of congenital toxoplasmosis at the University Hospital of Rennes. Mice were infected by intraperitoneal injection of placenta from 5 mothers with a history of toxoplasma primary infection during pregnancy. Once toxoplasmosis was confirmed by a positive serology at least 5 weeks after infection, mice were sacrificed, and organs (brain, heart and liver) were collected. Liver was divided into lobes (right median, left median, right lateral, left lateral, papillary process and caudal lobe) before DNA extraction. DNA was extracted by the phenol-chloroform method, and quantitative PCR was realized using an in-house method targeting the rep529 sequence (1).

Table 1 and Figure 2. Results by hepatic anatomical piece

Anatomical piece	% of positive mice (N)
Liver (N = 21)	90,5% (19)
Left median lobe LM	42,9% (9)
Right median lobe RM	47,6% (10)
Papillary process PP	42,9% (9)
Left lateral lobe LL	47,6% (10)
Right lateral lobe RL	33,3% (7)
Caudal lobe CL	38,1% (8)
Heart (N = 15)	100% (15)
Brain (N = 17)*	100% (17)

**4 brains were missing because send to the National Reference Center (NRC) for genotyping*



The frequency of liver infection was surprisingly high (90,5%), but parasite loads were far lower (Ct ≥ 31) than in heart (data not shown) and brain (Table 2). No preferential localization was identified but the parasite loads in papillary process were higher than in any other lobe (Figure 2)(Newman-Keuls Multiple comparison test, *p* from < *0.001* to <*0.05)*.

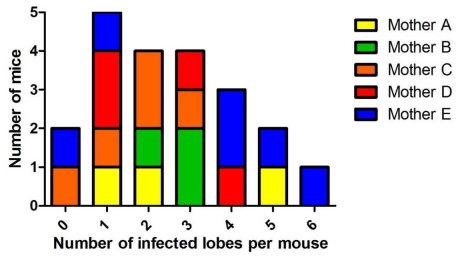


Figure 3. Distribution of the number of infected lobes per mouse

The various strains isolated from the 5 patients were distributed similarly regarding the number of infected lobes per mice, thus the distribution to many lobes cannot be attributed to a particularly virulent strain. Additionally, all isolates were genotyped by the National Reference Center and were all identified as type II strains.

Table 2. Results by number of infected lobes per mouse

Number of infected lobes / mouse	N	Liver weight (mg) Mean ±SE	Brain parasite load (Ct) Mean ±SE
0	2	2289 ± 350	NA*
1	5	2145 ± 587	24,0 ± 0,9*
2	4	1878 ± 263	24,1 ± 1,2
3	4	1953 ± 464	23,8 ± 1,6
4	3	1831 ± 419	23,0 ± 1,7
≥ 5	3	1674 ± 337	23,4 ± 0,6

**4 brains were missing because send to the National Reference Center (NRC) for genotyping*

The number of infected lobes per mouse was not correlated to brain parasite loads or to delay between infection and sacrifice (data not shown) but was correlated to liver weight (*p < 0.01*)

CONCLUSIONS

Despite the fact that the heart is well-known as the main organ at risk for *Toxoplasma* transmission during transplantation, it appears clearly that the liver is a main target organ for the parasite. This hepatotropism is not restricted to a given anatomical site, as parasite DNA could be detected in any lobe. This absence of preferential anatomical location challenges the possibility to localize cysts by guided liver biopsy in humans, to verify the frequency of cyst carriage. However, in view of this finding, liver recipients with *Toxoplasma*-mismatch transplantation should benefit from systematic chemoprophylaxis, which is not the rule in all countries.

1. Robert-Gangneux et al., Ped Infect Dis J 2010.