Lacout A and Perronne C., Arch Microbiol Immunology 2024
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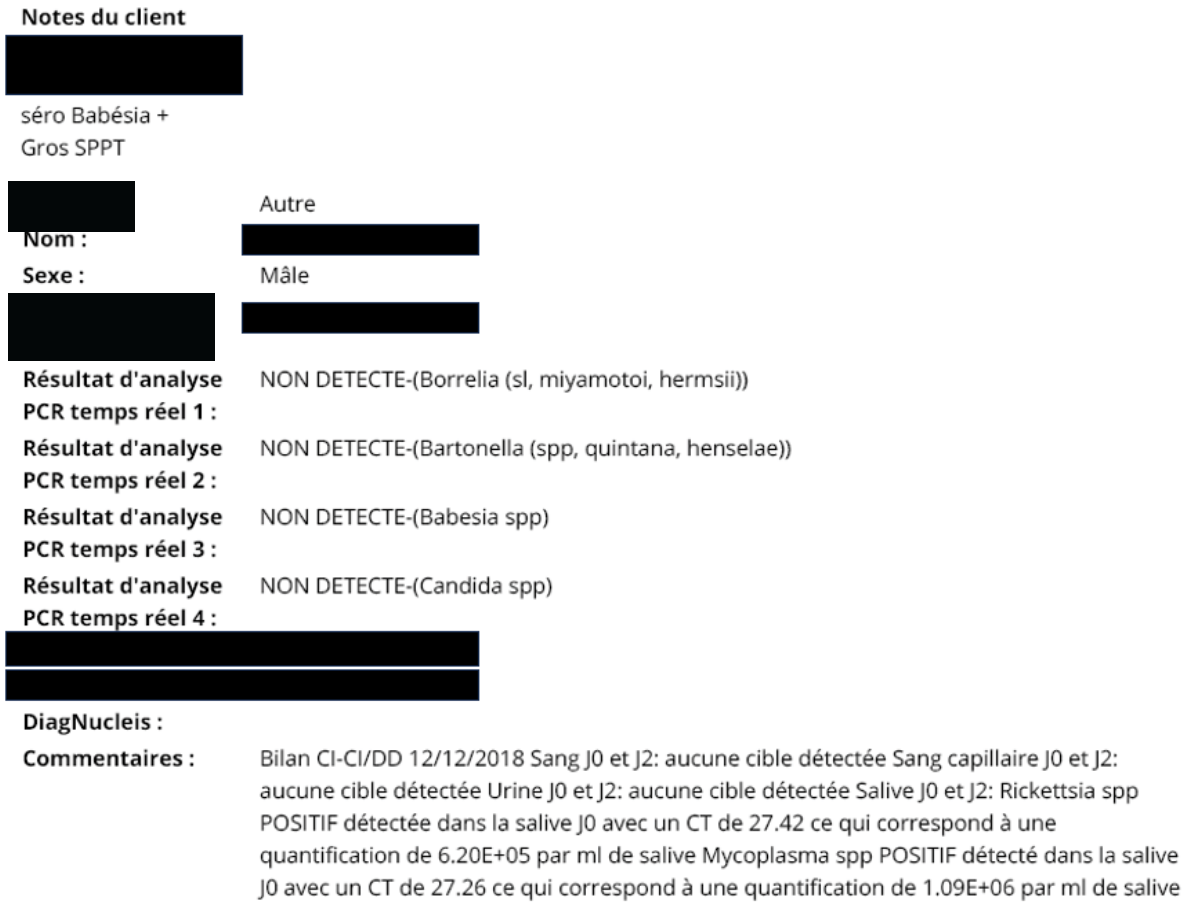
Notes du client
[redacted]
séro Babésia +
Gros SPPT
[redacted] Autre
Nom : [redacted]
Sexe : Mâle
[redacted] [redacted]
Résultat d'analyse PCR temps réel 1 : NON DETECTE-(Borrelia (sl, miyamotoi, hermsii))
Résultat d'analyse PCR temps réel 2 : NON DETECTE-(Bartonella (spp, quintana, henselae))
Résultat d'analyse PCR temps réel 3 : NON DETECTE-(Babesia spp)
Résultat d'analyse PCR temps réel 4 : NON DETECTE-(Candida spp)
[redacted]
DiagNucleis :
Commentaires : Bilan CI-CI/DD 12/12/2018 Sang J0 et J2: aucune cible détectée Sang capillaire J0 et J2: aucune cible détectée Urine J0 et J2: aucune cible détectée Salive J0 et J2: Rickettsia spp POSITIF détectée dans la salive J0 avec un CT de 27.42 ce qui correspond à une quantification de 6.20E+05 par ml de salive Mycoplasma spp POSITIF détecté dans la salive J0 avec un CT de 27.26 ce qui correspond à une quantification de 1.09E+06 par ml de salive

Figure 2: Blood, capillary blood, urine and saliva PCR analyses results.

and hydroxychloroquine (200 mg per day) for a few weeks, resulting in a resurgence of symptoms and, ultimately, improvement. An ampoule of 80,000 IU of vitamin D was also prescribed. At the end of this period, the patient self-administered flubendazole at a dose of 100 mg per day at the end of January 2019, which resulted in a very marked temporary recrudescence of the usual symptoms, resembling a Jarisch-Herxheimer reaction.

Subsequently, in early January 2019, an anti-*Babesia* protocol was administered due to positive serology and symptoms suggestive of parasitosis (unexplained dyspnea, hot flashes, some chills): atovaquone (250 mg) and proguanil (100 mg) 3 tablets per day, then 6 tablets per day, combined with azithromycin (250 mg) once a day, for 15 days. Treatment was well tolerated, with no Jarisch-Herxheimer-type reactions. Fatigue diminished; brain fog and concentration problems disappeared. Joint pain remained, mainly in the feet, knees and elbows. Skin lesions, on the other hand, reappeared. Because of the incomplete improvement, and the chronicity of probable Lyme disease, several courses of anti-infective treatments were implemented from early April 2019, including azithromycin, tinidazole (7), doxycycline and hydroxychloroquine, followed by ceftriaxone infusions.

Each treatment resulted in Jarisch-Herxheimer-type reactions, pointing to treatment efficacy and partial improvement in the patient's clinical condition, followed by stabilization. The skin lesions eventually disappeared. In September 2023, a relapse was effectively treated with 10 days of doxycycline (200 mg daily). Sometime later another self-administered dose of flubendazole resulted in intense return of all clinical signs, just as pronounced as at the start of treatment: pain and, above all, confusion and brain fog. A short course of corticosteroids rapidly and completely resolved these symptoms. Every dose of flubendazole since the onset of the disease produced the same reactions in the patient. The hypothesis of sequestration of bacteria, in particular *Borrelia,* inside the parasites was put forward. Other courses of low doses of flubendazole (25 to 50 mg per day for a few days) were each time followed by Jarisch-Herxheimer reactions. Finally, at the time of writing (end of 2023), the patient is in complete remission (he has stopped taking flubendazole), has been able to devote himself fully to his work once again, and has set up several companies in the forestry sector.

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Discussion

We suspected that this patient had Lyme disease (caused by infection with a bacterium of the genus *Borrelia*) despite negative serology, as it is published that seronegative cases are possible (8-10). His clinical pattern was compatible with SPTT/PTLDS, a syndrome that may be due to other factors than borreliosis, including co-infections, such as babesiosis (11, 12). The term chronic Lyme disease has long been controversial, and we might have referred to it as "persistent" Lyme disease. Nonetheless, published case reports and observations in everyday practice point to a succession of remissions and relapses when antibiotics are introduced and stopped in patients with Lyme disease. In addition, mechanisms of chronicity are known, such as biofilms and round forms, and have been observed in vivo. The Centers for Disease Control and Prevention (CDC) which is the national public health agency of the United States under the Department of Health and Human Services in Atlanta now recognizes the existence of chronic manifestations of Lyme disease (13). There should therefore no longer be any scientific controversy on this subject.

Jarisch-Herxheimer reactions are well known exacerbations of the symptoms of patients with some chronic infectious diseases, when effective treatment is initiated. These reactions, first described in the treatment of syphilis, reveal the treatment activity. They must be distinguished from possible adverse drug reactions. Jarisch-Herxheimer reactions may be severe. They result from the destruction of infectious agents, possibly through the release of endotoxins, and are mediated by TNF alpha, along with other inflammatory cytokines (14). These reactions are usually a sign of the effectiveness of the treatment. Indeed, the patient's symptoms decreased after each exacerbation observed with flubendazole, providing transient recovery and finally long-term remission. This favorable course had not been achieved with antibiotics or antiprotozoal drugs alone. Particularly striking were the severe reactions to flubendazole. These were not adverse reactions, since they vanished despite the continuation of treatment. It is unclear why flubendazole, which is an antiparasitic drug, with no known direct effect on *Borrelia*, is able to trigger such reactions and then to improve the patient's condition. The question could be raised of a possible sequestration of *Borrelia* inside undetected helminths, as it has been well described for schistosomes and *Salmonella typhi* (15, 16). The destruction of parasites could release bacteria, in particular *Borrelia*, which would explain the temporary exacerbation of clinical signs. This hypothetical mechanism could also explain some chronic forms of Lyme disease in addition to other known mechanisms such as sequestration of bacteria in biofilms or transformation of spirochetes in round bodies, allowing *Borrelia* persistence despite antibiotic therapy. Further investigations should be conducted to corroborate this hypothesis.

Conclusion

In conclusion, patients with chronic Lyme disease can sometimes be multiple-infected: with bacteria, parasites and viruses. In such patients, an exacerbation of clinical signs (Jarisch-Herxheimer reaction) on flubendazole could be indicative of an associated parasitic infection. *Borrelia* could be sequestered within the parasites that could be destroyed by flubendazole. This mechanism could explain certain chronic forms of Lyme disease.

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