

Correspondence

Rat Bite Fever: Some Comments on A Recent Minireview

DOI: 10.1111/ddg.14690

Dear Editors,

I would like to make some comments on a minireview with the focus on the uncommon zoonotic infection rat bite fever (RBF) written by Kämmerer and colleagues [1].

Firstly, I agree with the authors that the literature on RBF is sparse for a zoonosis that has been recognized since ancient times. It has been described worldwide much more recently as “rat bite fever.” But by only summarizing the most representative (well described) nine articles of the 29 retrieved case reports, some points of view could have been overlooked. Moreover, a more thorough PubMed database search and performing a backward citation search, could have yielded twice as many interesting papers published in English in the last six years. So, there are several limitations to Kämmerer et al.’s minireview that are related to the breadth and depth of information, half of the cases may be missed. My research strategy retrieved 13 cases in 2020, 6 cases in 2019, 7 cases in 2018, 12 in 2017, 10 cases in 2016 and 8 cases in 2015. Further, I consulted a series of nine cases in New York State, United States (2004–2015) that was published in 2017, and a series of eleven cases on Vancouver Island, Canada (2010–2016) published in 2018 [2, 3]. I observed that most reported cases did not lack a complete description of disease onset, laboratory findings, or therapeutic intervention.

Secondly, rat bites account for approximately one percent of animal bites, with the risk of *Streptobacillus moniliformis* infection following a bite being around ten percent [4]. RBF incidence must be largely underestimated due to frequent misdiagnoses (e. g. viral illness or rheumatologic disease), specialized techniques required to recover the microorganism from cultures, and lack of obligatory reporting of RBF infections [5]. Recently, various publications suggest that *Streptobacillus* spp. might be far more common and distributed in the environment or as commensal microbiota than previously thought [6]. The recent findings of Kache et al. (2020) of all cases reported in the period 2001–2015 in the United States reinforce that rat bite fever is rare, yet suggest it occurs more frequently than previously demonstrated in the review of 65 cases by Elliott in 2007 [4, 7].

Thirdly, RBF may be a misnomer, approximately 30 % of patients do not report having been bitten or scratched by rodents [4, 8]. Transmission occurs by a rodent's bite or

scratch or by their predators, mucocutaneous contact with the saliva, urine or feces of a rat, as well as by ingestion of food or water contaminated by a rat. The infection may be acquired by handling rats, without any apparent breach of intact skin or with a portal of entry, such as varicella lesions. So, non-traumatic transmission has been reported more frequently, e. g. via mucous membranes (kissing a rat) [9]. The cases without clear bite or scratch exposure highlight the need for a thorough history before removing RBF from the differential diagnosis list [9]. Ingestion leads to the gastrointestinal form of disease known as “Haverhill fever,” characterized by pharyngitis and vomiting.

Fourthly, RBF is a diagnostic dilemma due to missing notice of a rodent bite (or contact); non-specific clinical symptoms; fastidious growth of the widely unknown microorganism and broad chemotherapeutic susceptibility; antibiotic prophylaxis (especially beta-lactam antibiotics) after rat bites; its status as a non-notifiable disease; broad extensive spectrum of differential diagnoses but with RBF low on the differential; unsuitable diagnostic tools, and its isolation and identification is not straightforward [4, 6]. Additionally, only very severe clinical cases will be diagnostically worked up and few laboratories and physicians are experienced with RBF or are even aware of this disease [6].

Finally, the domestication of rodents has led to a broadening of the epidemiology of RBF to include pet rodent owners and pet store employees [10]. With the increase of rodent handling, there has been a concomitant increase in rat bites. Importantly, a striking increase in the number of owners of exotic pets and wildlife that may have had close contact with rodents [7]. More and more live rats are purchased due to the popularity of the Harry Potter movies (Ron's pet rat) and also to feed snakes (live) rats, for instance, by vivarium owners [6].

RBF is an underrecognized, underdiagnosed and underreported disease. Therefore, awareness of RBF must be enhanced. RBF should occupy a more prominent place in our diagnostic thinking. The broadened demographic exposure demands close attention to this disease and its causative organism by all clinicians. Clinicians should obtain a thorough zoonotic exposure history by asking about rodent encounters in the form of wild and pet rats (and mice), and maintain a broad differential diagnosis that includes RBF with any fever or infection of unknown origin [3, 5].

Many patients experience treatment delays (mainly due to the notoriously non-specific character with variable presentation: relapsing fever, fatigue, nausea, vomiting, headache, migratory asymmetric polyarthralgias and a pustular skin rash most commonly over extremities (palms and soles)). Early recognition of the disease is important, because if left untreated, RBF carries a high mortality rate, especially if endocarditis is present.

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Acknowledgements

Open access funding enabled and organized by Projekt DEAL.

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Authors' reply

Dear Editors,

We appreciate the opportunity to respond to the letter by Mr. Van Hooste. We evaluated his comments with interest, in which he kindly summarizes our article “Rat bite fever, a diagnostic challenge: case report and review of 29 cases” [1], and we thank him for his interest in our work.

Mr. Van Hooste expresses concerns over the scope of our literature search. Here, we thank him for the time he has put into a renewed literature search for pointing out additional articles. Although we have conducted our research conscientiously, literature reviews inherently bear a risk of an unintentional lack in scope. Yet, this is not the case here. Our intent in literature selection for the reader was representativeness, not comprehensiveness. We do not believe veterinary case reports to be clinically relevant nor directly translatable to human physiology [2]; although we agree with Mr. Van Hooste that these items are interesting, by excluding them, we fail to replicate his yield of “twice as much interesting papers”. Our study’s objective was to highlight the nonspecific symptoms, complexity of diagnosis, and treatment of RBF. We believe the concerns raised by Mr. Van Hooste have minimal, if any, consequence on helping us to achieve this objective.

Regarding the remaining comments made by Mr. Van Hooste, we thank him for repeating and elaborating our statements. As already described in our article, RBF does not necessarily have to result from rodent bites. Again, we agree, RBF is likely an underrecognized and underdiagnosed clinical entity due to nonspecific symptoms and the fastidiousness of pathogens [3]. We appreciate Mr. Van Hooste’s mention of the Harry Potter novels, as we enjoyed them greatly; however, whether Scabbers (Ron Weasley’s rat) caused an increase in RBF incidence remains speculation [4]. We suggest an epidemiological study.

In summary, we see our publication strengthened in multiple points made by Mr. Van Hooste. RBF is difficult to diagnose, and a delayed treatment is associated with considerable disadvantages for affected patients. We welcome critical opinions that promote useful scientific discourse and a greater visibility of this interesting, and perhaps, not-so-rare disease [5].

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