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# The bite of a rat infected with *Pseudomonas aeruginosa* in laboratory conditions: An uncommon case

#### **Case Report**

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#### **ABSTRACT**

Bites of laboratory animals are treated as the bites of any other animals since the possibility of existence of pathogenic microorganisms, unfavorable for human health, in the rooms where these animals reside, is not excluded. A rare case of a laboratory rat bite, used for scientific research and previously infected with Pseudomonas aeruginosa, is presented here. The patient's wound was located on the forefinger of his hand and was 1 cm long and up to 0.2 cm deep. The antitetanus prophylaxis was administered in an ambulance, including antibiotic therapy with amoxicillin-clavulanate per os. There exists a need for checks and special guidelines for the handling and retention of laboratory animals. The patient has successfully remedied the wound, thanks to consistent antibiotic therapy and antitetanus prophylaxis, and possible inflammatory complications were prevented.

Keywords: Wound, Rattus Norvegicus, antibiotic therapy, anti-tetanic prophylaxis, bio-safety measures

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### Introduction

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Rats successfully colonized urban ecosystems globally and since then, their bites had posed a great danger, being the gateway for the emergence of infectious diseases (Syeda, et al., 2018). Together with other rodents, they are the host reservoirs for at least 60 zoonotic diseases, and their arthropod ectoparasites are significant vectors of many pathogens (Syeda et. al., 2018; Katica et.al., 2003; Chaisiri et. Al., 2015; Han et.al., 2015).

Historically, all kinds of rats have been linked with the occurrence and spread of contagious diseases such as plague, typhus, leptospirosis and hemorrhagic fever. Numerous reports however indicate that the number of rodents' bites is undoubtedly smaller compared to that of for example dogs and cats (Bregman & Slavinskka, 2012; Morosetti et. al., 2013; Rothe et. al., 2015), despite the scary widespread population of rodents in almost all parts of the planet (Asaj, 1999).

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It is estimated that 20.000 people are bitten by rats in the United States annually. Children are the most common victims, as rats have become popular pets (Abrahamian & Goldstein, 2011). Bite injuries in children are most commonly found on the face and arms (Kalra et. al., 2006; Hirschhorn & Hodge, 1999).

Rat bite is an unusual issue of the urgent medicine; the bitten patients rarely come to tertiary medical centers and such bites usually remain neglected.

There is a large number of reports that describe the adverse impact of rat bites on human health, such as the appearance of foot ulcers in people with diabetes (Kalra et. al., 2006). The rat bites can be deadly (Yanai et. al., 1999), and are associated with fever post bite (Hudsmith et. al., 2001), tetanus (Mathiasen & Rix, 1993) and rabies (Marshall et. al., 1994; Kalra et. al., 2006). Rat bite fever disease, is very seriously condition caused by Streptobacillus moniliformis or Spirillum minus and when it is untreated mortality rate is 13%. The most common signs of infection are fever, vomiting, muscle pain and rush. The essential is to recognize the infection so treatment with antibiotics can start as soon as possible (Elliot, 2007).

Bites of laboratory animals are treated as the bites of any other animals, since the possibility of existence of pathogenic microorganisms, unfavorable for human health, in rooms, cages, mats, etc., where the animals reside, is not excluded. Risks to the health of researchers and laboratory staff are unavoidably higher if all the necessary zoohygienic measures within the vivarium, as well as the bio-safety measures are not fully carried out during experimental studies when, for example, toxic compounds or zoonotic agents are being used.

Protective measures taken when handling infectious material in laboratories aim at ensuring biosafety; that is to reduce or eliminate the exposure of laboratory personnel and other persons of the outside environment to potentially dangerous causers. Pseudomonas aeruginosa belongs to the second biosafety level, which implies mandatory use of personal protective equipment (glasses, masks, white coat, gloves - two pairs if necessary), good laboratory practice and the use of laboratory space corresponding to clinical and diagnostic laboratories, educational laboratories and other laboratories in which an infectious material which represents a moderate risk of transmission is present (Hukić et. al., 2010).

Because of everything above mentioned, every bite of a laboratory animal requires attention through a strict medical treatment program (National Research Council, 1997).

In the USA, out of 198 laboratories with laboratory animals, 13 reported that staff had experienced bites caused by a laboratory rodent, most common being rat (Stave et. al., 2017). Working with laboratory rats usually does not carry the risk of serious injuries. However, minor injuries can occur; most usual being bites to the fingers if the staff is not experienced and/ or if the appropriate protective measures are not applied on the rat. Bacteria Pseudomonas aeruginosa is the cause of serious hospital infections and significantly contributes to morbidity and mortality. It is the fifth most commonly hospitalized pathogen with mortality rate of 28 to 48%. Its clinical significance is that it can be a cause of hospital pneumonia, urinary tract infection, wound infection, bone infection and bacteremia. Pseudomonas aeruginosa can also cause outbreaks of nosocomial infections such as intestinal infections, skin and soft tissue infections, otitis externa (Hukić et. al., 2010). We are presenting you with a rare case of the bite of a laboratory rat infected with Pseudomonas aeruginosa, which was used for scientific research purposes.

## Case

At the Urgent Medicine Clinic, a 48-year-old man asked for medical help. He was bitten in a laboratory by an adult rat, of breed Wistar, which was previously infected with an inoculum of *Pseudomonas aeruginosa* bacterium, of density of 106 CFU/ml (colony forming unit per milliliter). The design of an experimental study on the rat that caused the injury involved instilment of 0.25 ml of inoculum in the back incision in the subcutaneous tissue, and the bite happened five days after contamination time of rat.

The standard bacterial strain of (*Pseudomonas aeruginosa* ATCC® - American Type Culture Collection -  $10145^{\text{TM}}$ ) was used to prepare the inoculum. The rat that caused the bite was taken out of the cage, in which two rats from the same experimental study were located and infected with the inoculum of the same concentration.

The patient's non-sterile glove was perforated. The wound was located at the top of the forefinger of patient's left hand and was 1 cm long and up to 0.2 cm deep. The wound was thoroughly rinsed with 0.9% NaCl solution, afterwards with 3% Hydrogen Peroxide solution, and later treated with solution of povidone-iodine (Isobetadine®) (Philipsen et. al., 2006). It has been superficial abrasive wound, so it was estimated that it is contraindicated to suture the wound, and reducing the potential risk of tetanus.

The first dose of 250 units of human anti-tetanus immunoglobulin was ordinated intramuscularly (i.m.) in ambulance. Antibiotic therapy was started; amoxicillinclavulanate *per os* (Xiclav 2 x 1000 mg) (Philipsen et. al., 2006). As part of anti-tetanus prophylaxis i.m. the second dose of 0.5 ml of tetanus toxoid was applied i.m. after 30 days and third dose of 0.5 ml of tetanus toxoid i.m. after 365 days.

During antibiotic therapy, and later during antitetanus prophylaxis, the patient reported feeling good, without any clinically manifested changes. The treatment was completed routinely and successfully.

### **Discussion and Conclusion**

Laboratory rodents do not like changes in their environment and do not work with unknown people (Zimmerman et. al., 2015). Laboratory rats are exceptionally fast animals and if moving, they are usually trying to escape or defend themselves if they can. It is therefore extremely important to manipulate them gently, safely placing thumb and fingers around their chests, making sure that the respiratory movements do not stop. In addition, in order to achieve the utmost safety of researchers during the experiment, the use of special grips is recommended to completely fix the rat and there lays the possibility to apply the desired substance. This would reduce the risk of bite to a minimum (Katica & Delibegović, 2019).

Immediate cleansing and early disinfection is the first step in preventing infection. It is necessary to check the vaccine status of the patient to determine the risk of tetanus. If the adult has never received three doses of vaccine before, or the information is unknown, it is necessary for the patient to receive 250 units of human anti-tetanus immunoglobulin intramuscularly or 0.5 ml of tetanus toxoid in another location intramuscularly or subcutaneously, depending on manufacturer's recommendation. One month after the first dose it is necessary to administer a second dose of tetanus toxoid, and after a period of 6 to 12 months a third one too. If the person is regularly vaccinated, and the period of the injury is within five years from the last dose, no prophylaxis is required. If the period from the last dose is 5 to 10 years long, a booster dose of 0.5 ml of tetanus toxoid is to be given, and if more than 10 years have passed since the last dose, one dose of 0.5 ml of tetanus toxoid and 250 units of human anti-tetanus immunoglobulin are needed. Although there are no clear guidelines or protocols on antibiotic prophylaxis for similar injuries, on the basis of clinical presentation of injury and anamnestic data doctor ordinarius determines the need for antibiotic ordination (Chapman et. al., 2008).

It is considered that all interruptions of skin continuity pose a risk of infection development, where agents can be introduced from the skin or from the object which caused the wound. In similar situations, when it comes to animal bites, it should be borne in mind that the risk of transmission of microorganisms residing in the oral cavity of the animal is very large. When it comes to an uninfected rat, the Staphylococcus epidermidis bacterium is present in the first place in almost 50% cases, followed by Bacillus subtilis, diphtheroids and alpha hemolytic streptococci (Abrahamian & Goldstein, 2011; Ordog et. al., 1985). Recognized as a particular clinical entity, rat bite feveris caused by bacterium Streptobacillus moniliformis, and was found in less than 10% of patients suffering a bite. In Asia, the disease is known as sodoku, and is caused by Spirillum minus (Hagelskjaer et. al., 1998).

Treating Pseudomonas infection, especially in immunocompromised patients, is uncertain and sometimes impossible. The bacteria is sensitive to a small number of antibiotics, but can also develop resistance to those during the therapy itself (Hukić et. al., 2005). Various injuries, trauma, surgery, burns make the host susceptible to colonization of P. aeruginosa (Gužvinec et. al., 2012; Kovačić et. al., 2018). Amoxicillin + clavulanic acid is most commonly used in antibiotic prophylaxis, and in the case of patients allergic to betalactam antibiotics, macrolide, aminoglycoside or quinolone antibiotics are to be used. Although the case study presented faced a case of a rat experimentally infected with bacterium P. aeruginosa, it is necessary to think about other potential agents, and so ordinated was the adequate therapy.

This is the first such report in Bosnia and Herzegovina that described the rat bite, i.e. the first such case at the emergency medicine clinic, university clinical center Sarajevo, in the post-war period. Antibiotic therapy based on amoxicillin-clavulanate and consistent antitetanus prophylaxis is a key to success in treatment of a rat bite, in patients who tolerate betalactam antibiotics and immuno-uncompromised patients. It is a priority to ensure prompt treatment in the case of bites.

Laboratory staff must have appropriate theoretical and practical training on the protection against the potential hazards to which they are exposed and must take necessary precautionary measures and procedures for assessing exposure, where continuous education is of utmost importance. Responsible researchers should be thinking in this direction both before and during the experiment.

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