

Treatment for active tuberculosis in giraffe (*Giraffa camelopardalis*) in a Zoo and potential consequences for public health – Case report

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Abstract

Introduction. Bovine tuberculosis (bTB) is an infectious disease that occurs in many species of both domestic and free-ranging animals, as well as animals kept in zoos. According to the Polish regulations, cattle tuberculosis are slaughtered and microbiological examinations are performed, the rest of animal species can be treated and laboratory diagnostics are not obligatory.

Case report. The presented case concerns two male giraffes which were purchased by the zoo and united with a third male. After a year, the oldest male died. *Post mortem* examinations confirmed generalized tuberculosis. After a further six months, the second male was euthanized after suffering great pain. The material for the study of drug resistance was a swab from the nose, obtained *ante mortem* from the third male. Attempted treatments did not produce the expected results. Genotyping allowed the exclusion of a common source of transmission.

Conclusions. The final effect of the anti-tuberculosis therapy in the male giraffe raises the question whether the research team should have undertaken the treatment of the animal with active tuberculosis.

Key words

tuberculosis, epidemiology, anti-tuberculosis therapy, public health, giraffe

INTRODUCTION

Mycobacterial species: *Mycobacterium bovis* (*M. bovis*) and *Mycobacterium caprae* (*M. caprae*) causing bovine tuberculosis (bTB, BTB) are members of the *Mycobacterium tuberculosis* complex (MTBC) [1]. BTB is a slow, progressive zoonotic disease, responsible for significant economic loss due to costly eradication and control programmes, and poses a threat to both to public health and endangered and protected animal species [2].

In Poland, there is a programme for the eradication of bTB: cattle aged over 6 weeks are subject to interdermal tuberculin skin test (TB skin test) at least once every 5 years, according to a European Commission Decision (209/342/EC) of 2009. Animal tuberculosis mostly proceeds without specific clinical signs; therefore, identifying individuals with a positive reaction at the TB skin test is essential. Consequently, all positive cattle are eliminated under special conditions, and suitable tissue samples are examined in the National Reference Laboratory for Bovine Tuberculosis (NRLBT), Department of Microbiology, at the National Veterinary Research Institute (NVRI) in Pulawy. NRLBT is the only laboratory in Poland for the diagnosis of animal tuberculosis [3]. The rest of animal species (except cattle) can be treated, and it is not obligatory to perform microbiological examinations.

Poland is recognized as a country officially free of bTB, despite the fact that a dozen outbreaks have been noted since

2009 [4], and the cases were not restricted to cattle. *M. bovis* and *M. caprae* infections has been reported in free-ranging animals, as well as in animals kept in zoos [5, 6].

In the world literature there are only few tuberculosis reports among large mammal species kept in captivity [7, 8]. Furthermore, neither positive nor negative trials for treatment nor total cure have been reported.

This study presents the case of bTB in giraffes in a Silesian zoo, and is the first attempt to treat bTB in the animal in Poland, using first-line anti-tuberculosis drugs for the treatment of humans. The mutual contacts between healthy and sick mammals (including human) contribute to the spread of the disease in the environment.

CASE REPORT

The giraffes originated from the zoo in Wrocław, Silesia, where tuberculosis was ascertained in giraffes and tapirs in 2002. These cases, however, were only recorded and not thoroughly investigated and described [9]. In 2010, two male giraffes from Wrocław joined a single male in the Silesian zoo. Until that time, they had not shown any signs of disease. After a year at the new location, a veterinarian caring for the animals observed such symptoms as shortness of breath, productive cough, and decreased appetite. Interview on the circumstances of the transfer of two males and epidemiological situation in the Wrocław zoo raised the suspicion of tuberculosis. In June 2010, a 17-year-old giraffe (acquisition from Wrocław) was found dead one morning in the open-air run. Six months later, the second male from Wrocław (10 years old) imported to the Silesian zoo, had to

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be euthanized due to problems with getting up and moving around. An immediate attempt was made to treat the third male (also 10 years old).

MATERIALS AND METHOD

The material for the study of drug resistance was a swab from the nose, obtained *ante mortem* from the third animal, during feeding. Microscopic examination of the smear prepared from the nasal swab revealed multiple acid-fast bacilli in each field of view. This was evidence of active tuberculosis in the giraffe. The exposed *Mycobacterium bovis* strain is presented in Figure 1. The new spoligo pattern SB2416 according to the *M. bovis* database [10] was analyzed for the resistance profile to first-line anti-tuberculosis drugs. Tests to isoniazid (INH), rifampicin (RMP), streptomycin (SM) ethambutol (EMB) were conducted with the use of Bactec MGIT 960 at the concentration limit of SM of 1.0 µg/ml, of INH of 0.1 µg/ml, of RMP of 1.0 µg/ml and of EMB of 5.0 µg/ml. Estimation of the drug resistance to pyrazinamide (PZA) was carried out using the isotopic Bactec 460-Tb system, with PZA concentration limit of 100 µg/ml [11].

The following drugs were used in the treatment of the surviving male: ethambutol (dose 30mg/kg body weight,

1x daily *per os*), rifampicin (10mg/kg body weight, 1x daily *per os*), pyrazinamid (30mg/kg body weight, 1x daily *per os*) and streptomycin (30g/kg body weight 2 x weekly *i.m.*). In the absence of relevant information, the treatment schedule designed for elephants was applied [12, 13, 14]. The cost of the planned treatment was about 1,750 EUR.

Disappearance of bacilli in nasal secretions after the 6-week routine treatment might prove the partial effectiveness of the therapy. Unfortunately, after a further 2 months of treatment, according to the diagram shown previously, the third male was euthanized due to cardiopulmonary failure. Tuberculosis lesions in the lung of the 10-year-old giraffe are presented in Figure 2.



Figure 2. Numerous foci of granulomatous inflammation (tuberculosis lesions) in the lung of a 10-year-old giraffe



Figure 1. *Mycobacterium bovis* growth on Stonebrink Medium

DISCUSSION

Ante mortem diagnosis of TB in giraffes is related to their immobilization. Giraffes are the tallest and the largest living terrestrial ruminants in the world and anaesthesia carries particular risks of mortality because of their physical characteristics, e.g. large body, long legs, long neck and heavy head [15]. The most common cause of death of this species is injury to the spinal cord during awakening from anaesthesia [16]. These animals also did not show any signs of disease and for these reasons they were not included in the planned research tuberculin tests, prepared in accordance with applicable regulations. In the absence of these data, it cannot be stated whether the animals became infected in the original location or in the new zoo. The nature and extent of the tuberculous lesions observed in the 3 giraffes indicated the presence of old lesions. Genotyping method (spoligotyping, MIRU-VNTR) allowed the exclusion of a common source of transmission between the animals. To date, there are no reports in the available literature about the successful treatment of large mammals in zoos. The treatment and intervention in the presented case seems to have been too late, which resulted in the spread of the disease; it appears that elimination of the infected animals, as is the case in cattle, would have brought substantially more immediate benefits.

This case indicates an urgent need for regular tuberculin or other testing in all species of animals, especially in the

case of animal transfers between zoos. It is also necessary to exchange information on animal health and diseases existing in zoos, not only at national but also at international level.

During this time, the giraffe were a potential source of infection for other animals, as well as for people visiting the zoo. It could be said that everyone breathed the same air under the same roof in the enclosure, and the most common route of tuberculosis infection is the air passages. The inhaled mycobacteria reach the lungs, where the immune mechanism is triggered and the infection is limited for tuberculomas [17], the germs of which may survive for years in a latent state [18]. Additionally, the experimental treatment applied could have endangered all the staff of the zoo, primarily the veterinarian who applied the medication daily for the period of 2 months.

The giraffe is a species which adapts well to living in captivity; however, the International Union for Conservation of Nature (IUCN) granted it vulnerable status, which same subspecies being closed as endangered [19]. Giraffes tend to live longer in comparison to other ruminants [20], and their main health problems in zoos, apart from infectious diseases, concern the treatment of overgrown and misshapen hooves [16].

According to the data supplied by the European Association of Zoos and Aquaria (EAZA), there is a surplus of the species in European zoos and obtaining new animals for rebuilding the giraffes herd is not a problem [21].

CONCLUSIONS

The final effect of the anti-tuberculosis therapy in the male giraffe raises the question whether the research team should have undertaken treatment of the animal for active tuberculosis. The giraffe enclosure in which the sick giraffe was kept remained open to the public throughout the treatment period. During this period, the giraffe was a potential source of tuberculous infection for other animals, as well as people visiting the zoo.

In 2016, tuberculosis due to *M. bovis* was reported in 2 patients from the Silesia Province. Molecular diagnostics allowed the exclusion of a common source of infection in this case, and the number of confirmed *M. bovis* cases in humans decreased in the European Union (in accordance with the European Union summary report on trends and sources of zoonoses, zoonotic agents and food-borne outbreaks in 2013).

Table 1. Identification of isolates *Mycobacterium bovis* from giraffes

Gender and age of the giraffes	Clinical material	Identification		
		GenoType MTBC	Spoligotype	MIRU-VNTR
giraffe male, ca 17 years old	lymph nodes, lung	<i>M. bovis</i>	SB0856 ¹	321522243421232
giraffe male, ca 10 years old	lymph nodes, lung	<i>M. bovis</i>	SB0856 ¹	422522255421192
giraffe male, ca 10 years old	nasal swab	<i>M. bovis</i>	SB2416 ²	422622254421196

¹ Assigned by www.Mbovis.org

² Spoligotypes not previously registered in the www.Mbovis.org database.

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