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CASE REPORT

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A Successful Vancomycin Treatment of Multidrug-Resistant MRSA-Associated Canine Pyoderma

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Case report

This report describes a case of diffuse pyoderma in a 10-year-old female dog with hypothyroidism. A previous treatment, without an early diagnosis, including cephalosporin associated with prednisolon resulted to be unsuccessfully. After clinical and microbiological examination in our laboratories, a diagnosis of methicillin-resistant *Staphylococcus aureus* (MRSA)-associated pyoderma was made. The antimicrobial susceptibility testing evidenced many resistances and susceptibility of the strain only to vancomycin and linezolid. A new therapy against hypothyroidism and associated with an appropriate antimicrobial (vancomycin) treatment, improved and resolved the infection.

Clinical Significance

To our knowledge, this is the first case of canine pyoderma caused by a strain of MRSA with a such severe multiresistant profile. MRSA infections present a serious challenge because of the emergence of resistance to numerous conventional antibiotics and the risk factors associated with the transfer of the bacteria to humans, who have a contact with infected pets.

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Introduction

Canine hypothyroidism is the most common endocrine disorders of the dog and it is characterized by cutaneous and non-cutaneous clinical signs associated with a deficiency of thyroid hormone activity.[1] Thyroid hormones play a dominant role in differentiation and maturation of mammalian skin, as well as in maintaining normal cutaneous function. They are also important for wound healing, that is weak and slow in hypothyroid dogs. Furthermore, thyroid hormones are necessary for initiation of the anagen phase of hair follicle cycle; anagen is not initiated in hypothyroid dogs, resulting in retention of hair follicles in telogen and leading to failure in growth and alopecia.[2]

Bacterial pyoderma is a common complication of canine hypothyroidism; it may be localized (pododermatitis or otitis externa), multifocal, or generalized and it may be superficial (folliculitis) or deep (furunculosis). The pathogenic mechanism of this increased susceptibility to bacterial pyoderma probably relates to an altered cutaneous barrier, immunologic hyporeactivity, or a combination of both.[2] Pyoderma is a frequent cutaneous infection of the skin in both healthy and hypothyroid dogs, and most of the cases are caused by staphylococcal strains, in particular *Staphylococcus pseudintermedius*.[3,4] However methicillin-resistant *Staphylococcus aureus* (MRSA), methicillin-resistant *Staphylococcus pseudintermedius* (MRSP), and methicillin-resistant *Staphylococcus schleiferi* (MRSS) strains have become an increasing problem and these bacteria represent risk factors for skin infections especially if they show resistance to all the conventionally used antibiotics. This communication describes a diffuse pyoderma multidrug-resistant MRSA-associated in a dog with hypothyroidism.

Case report

A 10-year-old female Fila Brasileiro dog was referred during June 2015 to the Department of Veterinary Medicine and Animal Production, University of Naples (Italy), presenting an one-year history of generalized cutaneous lesions. The owner reported that the dog had dysorexia, weight loss and depression. Physical examination revealed weight loss and depression; the mucous membranes were pale and the peripheral lymph nodes were moderately enlarged. Dermatologic disorders consisted in: multifocal alopecia, erythema, erosions and ulcers with the presence of purulent essudate on tips and interdigital level, hyperpigmentations (Figure 1). The dog had an offensive rancid odor but did not show pruritus.

Previous treatment included cephalosporin associated with prednisolon for 30 days with no improvement, on the contrary followed by an aggravation of the clinical conditions. A complete haematological, biochemical and urinary profile was performed as shown in Table 1, together with skin imprints and multiple superficial and deep skin scraping procedures. Main clinical-pathological alterations were hyporegenerative anaemia, a free 4-thyroxine reduction associated to a TSH increase. Because of lymph nodes enlargement, we also performed the immunofluorescent antibody test (IFAT) for *Leishmania*-specific antibodies

Fig.1 - 10-year-old female Fila Brasileiro with dermatologic disorders: alopecia, erythema, erosions, ulcers and hyperpigmentation.

Table 1. Laboratory data: **a)** Hematology, **b)** Urinalysis

a) **Hematology**		
Analyte	Data	Reference interval*
RBC	4.13 M/µl	(5.50-8.00)
Hgb	9.0 g/dl	(12.0-18.0)
Hct	27.3%	(37.0-55.0)
MCV	66 fL	(60-76)
MCH	21.7 Pg	(20.0-27.0)
MCHC	32.8 g/dL	(32.0-38.0)
PLT	400 K/µL	(240-400)
WBC	16.4 K/µL	(6.0-16.0)
Segmented neutrophils	72%	60-77
Lymphocytes	20%	12-30
Monocytes	8%	3-10
Eosinophils	2	8%
Basophils	0	Rari
Urea	34 mg/dL	(25-35)
Creatinine	0.71 mg/dL	(< 1.8)
Glucose	84 mg/dL	(60-120)
Aspartate aminotransferase	33 UI/L	(5-45)
Alanine Aminotransferase	20 UI/L	(10-47)
Gamma Glutamiltransferase	2 UI/L	(<5)
Total bilirubin	0.2 mg/dL	(<0.5)
Alkaline phosphatase	100 UI/L	(<180)
Total protein	6.0 mg/dL	(6.0-7.7)
Albumine/Globuline ratio	0.75	(>0.6)
Triglycerides	52 mg/dL	50-100
Cholesterol	135 mg/dL	125-250
TSH	1 ng/mL	0.03-0.45
Free 4- thyroxine	<0.39 mg/dL	0.6-2.7
IFAT ***(Leishmania infantum)***	Negative	
b) Urinalysis		
Specific gravity	1030	(1025-1045)
PH	7	5,5-7,0
Leucocytes	Negative	Negative
Nitrite	Negative	Negative
Protein	Negative	Negative
Glucose	Negative	Negative
Ketone	Negative	Negative
Urobilinogen	Negative	Negative
Bilirubin	Negative	Negative
Blood	Negative	Negative
Protein/creatinine ratio	0.2	<0.2
Sediment	Normal	Less than five red blood cells, less than five white blood cells, few epithelial cells, few hyaline or granular casts, some crystals (Per high power field)

that resulted negative.

According to hormone concentration result and to clinical signs (lethargy, inactivity, dermatologic alterations, mild anemia) a diagnosis of hypothyroidism was made.[5]

Skin cytological examination revealed the presence of numerous degenerated neutrophils and some macrophages with abundant foamy cytoplasm. Many coccus-shaped bacteria were seen in the cytoplasm of neutrophils and *Malassezia pachydermatis* organism where observed on the slide. The Ziehl–Neelsen and periodic acid–Schiff stains were negative for mycobacteria. Cutaneous swab and hair sample were used for bacteriological analysis. Macroscopic observation of the colonies, Gram staining, standard laboratory methodologies (catalase, oxidase, staphylocoagulase tube test), and miniaturized biochemical tests API system (bioMérieux SA, Marcy L'Etoile, France) were in accordance with the identification of methicillin-resistant *Staphylococcus aureus* (MRSA).

The presence of the *mecA* gene was detected by growth on oxacillin-containing media (2 mg/L), agar diffusion with oxacillin disks (5 µg) and positive latex agglutination test (PBP2' Test Oxoid Ltd, UK). The isolated bacterial strain showed resistance to different antibiotics,[6] and it was susceptible only to vancomycin and linezolid, as shown in Table 2. The antimicrobial resistance pattern of the MRSA strain justifies the failure of initial therapy carried out with an inappropriate antibiotic.

Thus, based on clinical signs, skin and hair, and microbiological investigations, a diagnosis of severe pyoderma associate with multirdrug-resistant MRSA was done.

Dog was treated with vancomycin 500 mg BID, intravenously, included in 250 ml of glucose 5% solution for 14 days, followed by 500 mg of vancomycin orally, BID, for 15 days. This therapeutic scheme was adapted to the owner's compliance. Vancomycin was administered associated to a topical therapy based on medicated antimycotic shampoo containing disinfectants and antifungal agents (2% chlorexidine and 2% miconazole) every three days, and with synthetic sodic levothyroxine (20 µg/kg/day orally). After one month the dog showed a good improvement of cutaneous lesions: hair growth, ulcers and erosions healing, disappearance of purulent material and bad odor, lymph node volume reduction and mental alertness and activity increase (Figure 2).

The clinical signs and clinical-pathological abnormalities associated with hypothyroidism resulted to be resolved within the first week of treatment through the appropriate thyroid hormone therapy.

Discussion

Endocrine alopecia may take several months to complete regrowth and a marked reduction in hyperpigmentation of the skin. Bacterial skin infection associated to hypothyroidism are frequent and needs a specific antibiotic treatment to avoid a spread of multidrug-resistant bacteria.

Fig. 2 - Dog improvement after one month of specific treatment.

The increasing number of community acquired and hospital acquired methicillin-resistant staphylococci (MRS) both in human and animals has been already well reported,[7-9] as well as the possible transfer of MRS from dogs to humans has been already described and this risk

Table 2. Antibiotic susceptibility testing results.

Antibiotic classes	Tested antibiotics	*S/R
Aminoglycosides	Amikacin (30 µg)	R
	Gentamycin (10 µg)	R
	Kanamycin (30 µg)	R
	Neomycin (30 µg)	R
	Streptomycin (10 µg)	R
	Tobramycin (10 µg)	R
Cephalosporins (second generation)	Cefoxitin (30 µg)	R
	Cefuroxime (30 µg)	R
Cephalosporins (third generation)	Cefoxatime (30 µg)	R
	Ceftazidime (10 µg)	R
	Ceftiofur (30 µg)	R
	Ceftriaxone (30 µg)	R
Fluoroquinolones	Ciprofloxacin (5 µg)	R
	Enrofloxacin (5 µg)	R
	Nalidixic acid (30 µg)	R
	Norfloxacin (10 µg)	R
Glycopeptides	Vancomycin (30 µg)	S
Lincosamides	Clindamycin (2 µg)	R
Macrolides	Azithromycin (15 µg)	R
	Erythromycin (15 µg)	R
Oxazolidinones	Linezolid (30 µg)	S
Penicillins	Amoxicillin-clavulanic acid (30 µg)	R
	Ampicillin (10 µg)	R
	Oxacillin (1 µg)	R
	Penicillin (10 IU)	R
Polymyxins	Colistin sulfate (10 µg)	R
Rifamycins	Rifampicin (30 µg)	R
Sulfonamides	Trimathoprim-sulfamethoxazole (25 µg)	R
Tetracyclines	Doxycycline (30 µg)	R
	Tetracycline (30 µg)	R

*S, susceptible; R, resistant

represents a serious public health issue.[10] Solutions to address this fact are required both in human and veterinary medicine because these multidrug-resistant microorganisms can survive in a wide range of potential niches and with large possibilities to be transmitted from animal to human and *viceversa*. The phenomenon of microbial resistance, which is based on genetic plasticity of bacteria, has emerged as a consequence of the selective pressure exerted by the antimicrobial usage in human medicine, veterinary medicine, animal production, agriculture and food technology.[11-13]

This report demonstrates that the application of sanitary measures as a precise diagnoses (bacterial isolation and antimicrobial susceptibility testing), before the therapy, could resolve the disease as soon as possible and, also, contain the diffusion of resistant strains. Furthermore, the increasing incidence of MRSA infections in pet animals and overall the big problem of MRSA strains difficult to treat because their resistance to many antibiotics (not just methicillin) is an emerging problem.

This case of MRSA enforces the suggestion that the vancomycin can be given to dogs as last choice antibiotic to help in control the spreading of multidrug-resistant staphylococci among the community, but it's important to remember that the use of vancomycin in animals needs to be very prudent to avoid contributing to antibiotic resistance in people. Antimicrobial resistant staphylococci cause infections that are difficult to treat and that represent an important aspect of "one health" viewpoint.

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