Dr Tim Nuttall and Dr Ana Mafalda Lourenco Martins invite companion readers to consider a case of alopecia, crusts and pruritus in a young Great Dane

Case presentation
A 1-year-old female neutered Great Dane was presented with alopecia, crusts and pruritus. She was otherwise well. The dog was fed a balanced commercial diet and some treats, was properly vaccinated and dewormed. She lived with two other dogs, which were healthy and had lived her whole life in Portugal.

The dog had orthopaedic surgery 6 months previously. Following this, she was hospitalised for several days and received two courses of antibiotics (enrofloxacin and amoxicillin/clavulanate), although the dose and duration of treatment was unknown. Otherwise she recovered well from the surgery.

Physical examination
The dog was in good body condition and abnormalities were limited to mild generalised lymphadenopathy and skin lesions (Figure 1). There was severe erythema with pustules, papules and scaling of the ventral abdomen. There were also multifocal areas of alopecia, erythema and scaling over the dorsal trunk.

Problem list
- Pustules, scaling and pruritus.
- Mild generalised lymphadenopathy.

Which of the following conditions are most likely?
1. Superficial spreading pyoderma.
2. Superficial pustular dermatophytosis.
3. Pemphigus foliaceus.
4. Subcorneal pustular dermatosis.
5. Superficial pustular drug reaction.
7. Lymphoma.

What would you do next?
We first performed hair plucks, skin scrapes and skin cytology to look for...
Clinical conundrum

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infection. Lymph node cytology and serology for *Leishmania infantum* was also done because of the mild lymphadenopathy and high prevalence of this disease in Portugal.

**Findings**

Skin cytology revealed degenerate neutrophils with intracellular cocci consistent with pyoderma caused by *Staphylococcus pseudintermedius* (Figure 2). Bacterial culture and antibiotic sensitivity testing were considered, but as there were no rods on cytology or recent antibiotic therapy, an empirical antibiotic choice was considered appropriate. Lymph node cytology and *Leishmania* serology were positive for leishmaniosis.

**What are your plans for management of this case?**

**For pyoderma**

Antibiotics may be empirically chosen without culture and antibiotic sensitivity testing in uncomplicated superficial skin infections without risk factors for resistance. As *Staphylococcus pseudintermedius* is the most frequent organism isolated in canine skin infections, the chosen antibiotics should be active against *Staphylococcus* spp. Topical antimicrobials are also recommended as they will help improve the skin lesions and decrease the time to clinical resolution. We therefore started treatment with a 3% chlorhexidine shampoo twice weekly and cefalexin at 30 mg/kg po twice daily.

**For leishmaniosis**

A pre-treatment complete blood count and biochemistry profile were unremarkable and we started treatment with allopurinol (10 mg/kg po twice daily for life) and meglumine antimonate (75 mg/kg s.c. twice daily for 4 weeks). Most animals will have a favourable response within 1 month and a significant clinical improvement by 3 months, after which a steady phase is reached.

**Follow-up: 1 month after treatment**

- Pustules have not resolved.
- The dog is highly pruritic.

**How would you approach this case now? Either:**

a. Consider the possibility of drug-resistant *Leishmania infantum* strains and choose an alternative protocol.

b. Continue with the same treatment and re-evaluate in a further month.

c. Repeat skin cytology.

d. Perform bacterial culture and antibiotic sensitivity testing.

e. Consider new problem (e.g. drug reaction?).

**Thoughts, further investigation and new diagnostic plan**

Skin cytology again revealed degenerate neutrophils with intracellular cocci consistent with a staphylococcal pyoderma. The leishmaniosis appeared to be under control, and resistance to treatment is very rare. We therefore concluded that the pyoderma had not cleared despite treatment with cefalexin and chlorhexidine, suggesting an antibiotic-resistant infection. Bacterial culture and antibiotic sensitivity testing were performed. We informed the laboratory of our suspicion, and they screened for meticillin-resistant organisms by plating enrichment cultures on a selective medium. PCR was used to assess whether suspect colonies had the mecA gene, which confers resistance to beta-lactam antibiotics. Culture revealed a meticillin-resistant *Staphylococcus pseudintermedius* (MRSP) sensitive to amikacin, vancomycin, linezolid, chloramphenicol and quinupristin/dalfopristin only.

**Management**

We discussed the most suitable antibiotic with the microbiologists and the owners, considering efficacy, costs, adverse effects, ethical dilemmas and availability for veterinary use. We decided to start treatment with florphenicol (35 mg/kg s.c. three times daily), which should have the same activity as chloramphenicol. Unlike chloramphenicol, florphenicol is approved for use in animals (in cattle for respiratory infections) and is not associated with aplastic anaemia. Reported adverse effects include injection site pain, anorexia and decreased water intake. We continued twice weekly bathing with 3% chlorhexidine, but this was done in our veterinary hospital by trained staff to improve efficacy and reduce potential zoonotic risks.

**What should we tell owners about transmission to humans?**

1. MRSP is potentially a zoonotic pathogen but transmission to humans is less common than MRSA.
2. Zoonotic staphylococcal infections are rare.
3. Groups at risks for zoonotic infection include owners with open wounds, that are immunocompromised or undergoing surgery.
4. Owners should contact their doctor if they have any doubt or worries.
5. The Worms and Germs blog is very useful for owners (www.wormsandgermsblog.com).

Follow-up
The dog started to improve after implementation of the new antimicrobial treatment protocol (Figure 3). Complete clinical resolution took 3 months, and treatment was then continued for a further 14 days. The dog has been in complete remission and has not received any medication except allopurinol for 6 months. The other two dogs in the household remained healthy throughout and there was no evidence of zoonotic transmission to the owners or veterinary staff.

Discussion
Most veterinary practitioners are used to treating staphylococcal pyodermas, as these are common in general practice. Nevertheless, clinicians should be aware of meticillin-resistant staphylococci. MRSA and MRSP infections are much less common than antibiotic-sensitive infections but the prevalence appears to be increasing. This is of great concern because of the therapeutic challenge, risks for contamination of veterinary premises and zoonotic potential. In particular, MRSP infections often have a very restricted range of antibiotic sensitivity.

The zoonotic potential of MRSP infections (Figure 4) scares owners, and there are ethical dilemmas for clinicians, including whether or not to use antibiotics with adverse effects (e.g. chloramphenicol and aminoglycosides) or those that are important for human health (e.g. vancomycin and linezolid). Currently, the absence of guidelines for the diagnosis and treatment of multidrug resistant

Figure 3: The patient’s lesions have gradually improved after 3 weeks of florphenicol

Figure 4: Schematic drawing showing the most important direction for the transmission of MRSP (blue) and MRSA (pink), both of which are potentially zoonotic diseases.
infections leaves the choice of antimicrobial to the practitioner. It is therefore important that you are prepared to deal with these cases. Discussing cases with your microbiologists can be very helpful, and you may need to refer the case for specialist care and treatment.

Empirical antimicrobials can be appropriate for first-line treatment of staphylococcal pyodermas, as most isolates have a relatively predictable sensitivity pattern. Clindamycin, cephalosporins and amoxicillin/clavulanate are suitable provided that it is a surface or superficial infection, cytology is consistent with a staphylococcal infection, it is the first treatment and there are no risk factors for resistance.

Culture and antibiotic sensitivity testing, however, should be performed for deep pyodermas, if rods are seen on cytology, after multiple antibiotic courses, after treatment failure and if there are risk factors for resistance. In hindsight, the surgery and antibiotic treatment 6 months earlier should have alerted us to the possibility of antibiotic resistance in our case, and we should have taken samples for culture from the dog on the first visit. Antibiotics to treat resistant infections should be chosen based on the results of culture and antibiotic sensitivity testing.

Topical therapy is often useful as the high local concentrations that are achieved can overcome some resistance. For example, 9 out of 10 cases of MRSP infections in dogs have been cured following treatment with topical fusidic acid, even though in vitro sensitivity testing revealed resistance to fusidic acid. In this case we elected to use systemic treatment because the extent and nature of the lesions were not suitable for topical antibiotic therapy alone. We also used chlorhexidine, as recent studies have shown that this is highly effective against MRSP; 5 out of 8 dogs with MRSP infections were cured or substantially improved following treatment with a 2% chlorhexidine shampoo. Compliance can be a problem with topical treatment, and we therefore used trained staff to ensure proper application and improve efficacy. Treatment should be continued to complete clinical resolution and beyond if it is possible that sequestered bacteria may survive (e.g. deep pyoderma, orthopaedic infections, etc.).

Why do these resistant infections occur? Risk factors in dogs have been poorly investigated, but things to watch out for include (Figure 5): previous antimicrobial therapy, particularly with fluoroquinolones and/or beta-lactams; frequent antimicrobial use; recurrent infections; prolonged hospitalisation; postoperative or nosocomial infections; and non-healing wounds.

Responsible antibiotic use will be important in preserving the clinical efficacy of these drugs. Antibiotics should not be used unless an infection has been confirmed, and bacterial cultures should be performed more frequently. We should also question whether the patient really needs systemic antibiotics, or whether topical antimicrobials and antibiotics would be more suitable. It is also vital to communicate the importance of treatment to owners in order to improve compliance, reduce therapeutic failure and decrease the risks of resistance.

Affiliation

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Figure 5: Number and nature of known risk factors for MRSA/MRSP in this patient

AMX = amoxicillin ± clavulanic acid; ENR = enrofloxacin