Lameness in weaned pigs associated with tetracycline overdose

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Key words
Swine, medication, water supply, non-infectious, multi-factorial disease

Summary
On a piglet producing farm severe lameness was observed in pigs which had been weaned 3 weeks and longer due to severe distortions of joints and claws of fore and/or hind legs. Splaying of claws as well as flexural limb deformations particularly in the carpal joints increased in degree the older and heavier the pigs were. Because of coughing in the weaners, which had started 7–8 weeks before any lameness or limb deformation had been apparent, tetracycline was applied via water as medication. During the course of an on-site investigation, a miscalculation of dosage – 129–168 mg tetracycline per kg body weight – was revealed. It was therefore suggested to the farmer and his veterinarian to immediately stop the application of tetracycline and to use a different antibiotic against the still present coughing and sneezing. During a follow-up evaluation 4 weeks later, the farmer reported a significant decrease in affected animals. While a direct correlation between the lameness in the weaned pigs and the tetracycline dosage could not be proven, the existing evidence supports the theory that the overdosage was at least a contributing factor.

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Introduction
Tetracycline and its derivatives are commonly used as an antimicrobial drug for the treatment of infectious respiratory diseases in pigs (28). This is due to the fact that it is a so called “broad spectrum” antibiotic, effective against gram-positive and gram-negative bacteria as well as mycoplasma-species (11). Its antimicrobial characteristic is based on its inhibitory effect on the protein synthesis of the ribosomes in bacteria and its ability to form chelate-like complexes with metal ions leading to a reduced growth of bacteria (10, 13). Since pigs are usually housed in large groups, it is difficult to treat each pig individually via injection. Moreover, individual treatment is not addressing the problem that often most of the pigs within a group are infected with the same pathogens and conclusively require the same treatment. Therefore treatment either via feed or via water supply is common (21). A treatment of pigs via drinking water (where possible) is often the method of choice, as it has several advantages when compared to feeding medication:
1. The mix of medication and water is more easily homogenized (29).
2. Feed intake is usually decreased before water intake is reduced (29).
3. The bioavailability is often higher (17, 29).
4. The treatment can start without any delay and without any change in the pigs’ diet.

**Case details**

**History**

On a piglet producing farm housing 730 sows and their offspring, severe lameness was observed in pigs which had been weaned 3 weeks and longer due to severe distortions of the joints and claws of fore and/or hind legs. Two pigs, weighing 16 kg and 20 kg, were sent to necropsy with subsequent microbiological, molecular and histological examinations. A 78 kg pig was also available for examination. The farmer had kept this animal (and others like it) because he had been unable to sell it. The results of these necropsies are summarized in Table 1. Neither bacteriological nor molecular (16S-23S-rDNA-PCR identifying *M. hyopneumoniae, M. hyorhinis, M. hyosynoviae, M. hyopharyngis* and *M. flocculare*) examination of the joints could determine an infectious agent. As the findings of the necropsies and subsequent tests were insufficient to form a hypothesis as to the cause of the lameness, an on-site investigation of the farm was performed.

The farm is a two-site production system, with the sows and suckling piglets housed at the main site and a barn for the weaners situated about two kilometers away. In the half year before the first clinical signs appeared, the farm had undergone massive restructuring by increasing the number of its sows from 250 to 730 as well as by building a new barn for the weaners. Piglets are weaned at 3 weeks of age with an average body weight of 8 kg and are sold with an average body weight of 28–30 kg. The weaners are fed in three phases three different diets. The diet is a mixture of on-farm produced grains (wheat, barley and corn) and supplementary feed (including protein, minerals and vitamins). In the first week after weaning the pigs receive Diet I with 14 MJ ME/kg (incl. 30% supplementary mineral feed). After the 6th or 7th day Diet I is gradually blended with Diet II (incl. 10% supplementary mineral feed) until the animals weigh about 14 kg, after which they are only fed Diet II. The pigs receive Diet III when they weigh 21–22 kg. All diets are mixed on site. The supplementary mineral feed is delivered about once a month (1 metric ton = 40 sacks each weighing 25 kg).

**On-farm investigation**

The on-farm investigation showed that although 8–10% of the suckling piglets (first to second week of life) had swollen joints

<table>
<thead>
<tr>
<th>Pig No.</th>
<th>Weight (kg)</th>
<th>Morphology</th>
<th>Histology</th>
<th>Culture</th>
<th>PCR</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>16</td>
<td>lesions (ca. 1 mm in depth) on the soles and claws of all four legs (Abb. 1)</td>
<td>femur: proximal and distal epiphysis unevenly wide with a few necrotic areas; talus: pronounced cortical, appositional bone growth with reversal lines; tarsal joint: minimal lympho-histiocellular and plasmacellular infection</td>
<td>negative</td>
<td>negative</td>
</tr>
<tr>
<td>2</td>
<td>20</td>
<td>shortening of the left femur by 2 cm, lesions (ca. 1 mm in depth) on the soles and claws of all four legs</td>
<td>femur and talus: proximal epiphysis unevenly wide; tarsal joint: minimal lympho-histiocellular and plasmacellular infection</td>
<td>negative</td>
<td>negative</td>
</tr>
<tr>
<td>3</td>
<td>78</td>
<td>vertical rotation of the carpal joints, lesions (ca. 1 mm in depth) on the soles and claws of all four legs, rotation of the dew claws</td>
<td>tarsal joint: chronic purulent and proliferative synovitis</td>
<td>negative</td>
<td>negative</td>
</tr>
</tbody>
</table>

PCR: ITS-PCR identifying *M. hyopneumoniae, M. hyorhinis, M. hyosynoviae, M. hyopharyngis* and *M. flocculare*

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Fig. 1 Lesions on the front claws in the 78 kg pig.
Abb. 1 Läsionen an den Vorderklauen des 78 kg schweren Schweines
Because of a coughing problem in the weaners, which had started at the end of June, tetracycline was added to the drinking water as medication with an intended dosage of 40 mg/kg body weight (BW). This had been 7–8 weeks before any lameness or limb deformation had been apparent.

During the course of the on-site investigation, the farmer explained how the water medication worked: at 8 am half of the daily dosage was added to the water (not more than 500 g of medication per 1000 L) in one of two steel tubs, each measuring 0.75 × 0.90 × 1.50 m. At 5 pm the second dosage was added. The farmer explained that at least once in a 24-hour period the tub would be empty and would be automatically refilled with clear water. However, recalculations revealed a miscalculation of the dosage. As seen during the on-site investigation, the tub was usually not filled to the brim, but to about 10 cm below it. Therefore the animals often stepped in between the slats of the plastic flooring.

The splaying of the claws as well as flexural limb deformations particularly in the carpal joints increased in degree the older and heavier the pigs were (Fig. 3). The animals showed abnormal laying positions (ventral position with limbs tucked in rather than on the side), as well as an increasing unwillingness to stand up and move about. A few pigs over 25 kg, which the farmer had been unable to sell, displayed severe swelling of the joints as well as hyperflexion of the limbs, indicating deformations of humerus, radius, ulna, tibia and/or fibula (Fig. 4). None of the examined animals showed neurological deficiencies during clinical examination.

The on-farm produced diet was deemed adequate for the weaners by the Institute of Animal Nutrition of the University of Veterinary Medicine Hannover (Table 2). Nevertheless, in order to be certain, the farmer had changed Diets I and II to a commercial complete diet in the week previous to the investigation.

In response to the farmer’s query, the breeding organization admitted to previous knowledge of the problem, saying it was a combination of genetics and reclining habits. An increase of the room temperature by 2 °C was suggested in order to change resting habits (from a ventral-position to a lateral-position) of the pigs. This measure was immediately implemented by the farmer.

Fig. 2 Six-week-old pig (weaned at 3 weeks of age) showing the typical splaying of the claws.
Abb. 2 Sechs Wochen altes Schwein (im Alter von 3 Wochen abgesetzt), das das typische Spreizen der Klauen zeigt

Fig. 3 Nine-week-old pig (weaned for 6 weeks) showing a splaying of the claws and beginning distortion in the forelegs
Abb. 3 Neun Wochen altes Schwein (seit 6 Wochen abgesetzt) mit dem typischen Spreizen der Klauen sowie einer beginnenden Verbiegung der Vorderbeine

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Fig. 4 An older pig with extreme distortions and deformations.
Abb. 4 Ein älteres Schwein mit extremen Verbiegungen bzw. Deformationen

1 A summary of the individual findings is shown in an additional table (Table 4) which is available online for free download (www.tieraerztlche-praxis.de, see contents of issue 1/2013).
true amount of water in the tub was 900 L instead of 1012.5 L. Adding 500 g of tetracycline to the water equaled a concentration of 0.56 g tetracycline per liter. Assuming, for example, that a 16 kg weaner drinks 0.15 L per kg body weight (35), it would have ingested 2.4 L of water and therefore 1.344 g of tetracycline resulting in a dosage of 84 mg/kg BW instead of the recommended 40 mg/kg BW. Considering the increased room temperature as well and assuming that a weaner under such conditions drinks 1.5 to 2-times more water than usual, the recalculated amount of tetracycline is 126–168 mg/kg BW, which is 3.2 to 4.2-times the recommended dosage. According to the farmer, the pigs had received this medication continuously for 7–8 weeks. It was therefore suggested to the farmer and his veterinarian to stop the use of tetracycline immediately and switch to a different antibiotic for treatment of the still present coughing and sneezing.

Based on the findings of the on-site investigation and the previous results of the necropsies, a tetracycline-overdosage was supposed. Therefore the bones of the two lighter animals, which had previously been sent to necropsy, were analyzed with respect to calcium-phosphorus ratio and tetracycline. The obtained results are listed in Table 3.

As a follow-up evaluation, the farmer was questioned via telephone about 4 weeks later. He reported a significant decrease in affected animals, although about 1–2% of the pigs which had never received tetracycline still showed an abnormal flexibility in the joints, particularly in the fore limbs.2

### Discussion

Lameness is a common clinical problem in pigs and is caused by a multitude of factors, both infectious (Mycoplasma hyosynoviae [24], Streptococcus suis [3], Erysipelothrix rhusiopathiae [12] and Haemophilus parasuis [12] being the most common) and non-infectious (genetics [4], malnutrition [26, 34], floor type [33]).

When considering infectious causes of lameness, the age of the affected animals can help to minimize the number of possible agents. Streptococcus suis, for example, mainly infects pigs at the

### Table 2

Results of the feed analysis of Diet II.

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Unit</th>
<th>Analysis</th>
<th>Calculation</th>
<th>Requirement (25)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Dry matter</td>
<td>g/kg wet weight</td>
<td>892</td>
<td>903</td>
<td>—</td>
</tr>
<tr>
<td>Ash</td>
<td>g/kg wet weight</td>
<td>60.8</td>
<td>51.8</td>
<td>—</td>
</tr>
<tr>
<td>Protein</td>
<td>g/kg wet weight</td>
<td>224</td>
<td>179</td>
<td>210</td>
</tr>
<tr>
<td>Fat</td>
<td>g/kg wet weight</td>
<td>68.7</td>
<td>50.1</td>
<td>—</td>
</tr>
<tr>
<td>Fibre</td>
<td>g/kg wet weight</td>
<td>44.2</td>
<td>37.5</td>
<td>30–50</td>
</tr>
<tr>
<td>Energy</td>
<td>MJ ME/kg wet weight</td>
<td>13.9</td>
<td>13.9</td>
<td>14.2</td>
</tr>
<tr>
<td>Calcium</td>
<td>g/kg wet weight</td>
<td>12.8</td>
<td>7.80</td>
<td>9–10</td>
</tr>
<tr>
<td>Phosphorus</td>
<td>g/kg wet weight</td>
<td>5.93</td>
<td>5.60</td>
<td>5–6</td>
</tr>
<tr>
<td>Copper</td>
<td>mg/kg wet weight</td>
<td>176</td>
<td>n. d.</td>
<td>5–10</td>
</tr>
<tr>
<td>Zinc</td>
<td>mg/kg wet weight</td>
<td>108</td>
<td>n. d.</td>
<td>50–60</td>
</tr>
<tr>
<td>Manganese</td>
<td>mg/kg wet weight</td>
<td>145</td>
<td>n. d.</td>
<td>20–25</td>
</tr>
<tr>
<td>Vitamin D</td>
<td>IE/kg wet weight</td>
<td>2480</td>
<td>2000</td>
<td>500</td>
</tr>
<tr>
<td>Vitamin A</td>
<td>FTU/kg wet weight</td>
<td>20,038</td>
<td>n. d.</td>
<td>20,000</td>
</tr>
<tr>
<td>Phytase</td>
<td>FTU/kg wet weight</td>
<td>1150</td>
<td>750</td>
<td>—</td>
</tr>
</tbody>
</table>

n. d. = no data

### Table 3

Results of the bone analysis.

<table>
<thead>
<tr>
<th>Pig No.</th>
<th>Calcium-phosphorus ratio</th>
<th>Chlortetracycline (mg/kg ww)</th>
<th>Doxycycline (mg/kg ww)</th>
<th>Oxytetracycline (mg/kg ww)</th>
<th>Tetracycline (mg/kg ww)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>normal</td>
<td>&lt; 0,5</td>
<td>4,7</td>
<td>&lt; 0,5</td>
<td>1,9</td>
</tr>
<tr>
<td>2</td>
<td>normal</td>
<td>&lt; 0,5</td>
<td>&lt; 0,5</td>
<td>&lt; 0,5</td>
<td>7,6</td>
</tr>
</tbody>
</table>

ww: wet weight

1 A timeline of the events in this case is given in an additional figure (Fig. 5) which is available online for free download (www.tieraerztliche-praxis.de, see contents of issue 1/2013)
age of 1–6 weeks (3), whereas *Mycoplasma hyosynoviae* is usually considered to only affect animals of 10 weeks and older (24), although younger pigs were infected experimentally (20). Pathomorphological findings during necropsy may also hint at the etiological agent, for example a fibrinous arthritis (*Mycoplasma hyosynoviae*) versus a purulent arthritis (*Streptococcus suis*) (12). Due to the lack of pathological findings of the joints during necropsy, the authors opted to rule out all of the most common possible agents either via microbiological culture or PCR. Since no infectious agent could be identified by examining three typically diseased animals, a non-infectious cause had to be considered.

Genetics are one of the basic reasons to be considered when dealing with non-infectious lameness in pigs. Leg conformation as well as skin thickness may be predisposing factors (9). As mentioned above, the farm had undergone an extensive restructuring by increasing the number of sows from 250 to 730 as well as building a new barn for the weaners. Due to the fact, however, that the offspring of sows of all parities as well as of several different boars was affected by the limb deformations, a genetic component, although not totally excluded, was not seen as the major factor.

Osteochondrosis is also a cause for lameness in growing pigs (8). In this case, neither gross pathomorphology nor histology of the joints and bones supported the theory of osteochondrosis.

Malnutrition must always be considered when dealing with skeletal health in young animals. The phosphorus content as well as the calcium-phosphorus ratio are considered to be of utmost importance, since they play a vital role in bone development (26, 34). The amount of calcium within the feed was slightly higher than normally required, however, this does not explain the clinical problems. The other parameters were within the boundaries of requirement as well and were thus inconspicuous. Likewise, an excess of vitamin A may lead to skeletal malformation (30, 31). While the content of vitamin A within the feed was indeed marginally higher than the recommendation given for piglets (20,038 IU/kg vs. 20,000 IU/kg), it was not high enough to explain the severe clinical symptoms of the animals. A deleterious effect of hypervitaminosis A has only been described for levels exceeding a dose of 10 to 50 times the required dose over a period of three months (5, 16).

Therefore a causal relationship between the feed and the clinical problems on the farm may be disregarded.

Housing conditions, especially the flooring, also factor as a cause for lameness and abnormal limb growth (15). Plastic is often used for building in weaner and grower compartments, as it has two major advantages: its low conductance of warmth and the fact that it is easy to clean and to disinfect. A disadvantage is, however, that it is very slippery when wet, which it may often be due to contamination with feces, urine and water. The consequent slips and falls of the piglets may increase abnormal movement in joints, tendons and ligaments. Owing to the inherent gait of the pig, slipping occurs mostly in the fore limbs (37), which may be the reason for why the affected pigs were more likely to have problems there, than compared to the hind limbs. In general, trauma is a cause of lameness in pigs. Trauma may be due to inappropriate housing and/or transport conditions (18).

Another fact which has to be considered is that when a slatted floor must be appropriate for pigs from 8 kg to about 30 kg, it is always a compromise between the largest slats which can be tolerated by the youngest and the smallest slats which can be tolerated by the oldest. German legislation allows for a maximum of 11 mm in weaners (defined as 3 or 4 to 10 weeks of age) and a maximum of 14 mm for growers and finishers (defined as older than 10 weeks) (36). The greatest concessions are usually made by the youngest animals, as seen in this case, where the recently weaned piglets often stepped in between the slats. This may also have increased abnormal movement and thus caused the observed splaying of the main claws.

All the previously discussed factors may lead to lameness in pigs, but since none of these were shown to have extreme deficiencies, neither one single factor nor all put together could have produced the clinical symptoms as observed. Therefore another, non-infectious agent must have contributed significantly to the problem. The role of the calculated over-dosage of tetracycline, however, still remains to be addressed.

Bone accumulation of tetracycline and the subsequent effect has often been documented in pigs and in other species (14, 22, 32). In calves, overdosage of doxycycline has been reported to induce lethargy, dyspnea, tachycardia as well as necrosis of the myocardium, acute renal tubular necrosis and fatty degeneration or congestion of the liver (6). However, in an experimental study also in calves an overdosage of 5 times the recommended dose of doxycycline failed to reproduce these symptoms and pathological findings (6). Overdosage of tetracycline must not therefore necessarily result in detrimental effects for internal organs. In horses, for example, tetracycline is in use as a remedy for flexural limb deformations in the new born foal (2). It has been shown that oxytetracycline disturbs the normal structure of collagen fibers by inhibiting the matrix metalloproteinase-1 (MMP-1) mRNA expression (2) thus elongating the ligaments and tendons of the foals simply by their own weight (1). The concentration used is two doses of 44–70 mg/kg BW given intravenously 24 hours apart (1).

**Conclusion for practice**

While a direct correlation between the lameness in the weaned pigs and the dosage of the tetracycline could not be proven, evidence did exist to support the hypothesis that the overdosage was at least a contributing factor. Therefore, when dealing with lameness in pigs, the importance of excluding non-infectious agents as primary cause as well as considering the cumulative effect of several different factors (for example housing and genetics) should be emphasized.

Regardless of the fact whether our hypothesis concerning the tetracycline is correct or not, the authors believe that this case also demonstrates the importance of the strict supervision of the type of application and the dosage of any medication by the herd veterinarian.
However, to the authors’ knowledge, the effects of an overdosage of this magnitude (3 to 4 times) and for such a length of time (7–8 weeks) have not been reported in the literature.

While it could not be demonstrated that the amount of tetracycline in the bone itself (Table 3) was significantly increased to allow for the hyperflexion and lameness, the concentration of tetracycline may have been high enough to “weak” the tendons and ligaments of the weaned pigs. This may also explain why the other clinical and histological findings described in the literature could not be reproduced in this particular case. Therefore it may be speculated that the overdose in tetracycline exacerbated the influence of housing and genetics on the lameness. The fact that after withdrawal of the antibiotic the incidence of lameness in the weaned pigs decreased to 1–2% supports this theory. That some lame animals remained is not surprising, because good management cannot completely eliminate the influence of other factors (23).

Conflict of interest

The authors confirm that they do not have any conflict of interest.

References


