Case report/Gevalverslag

CLINICAL AND BIOCHEMISTRY FINDINGS, AND PARATHYROID HORMONE CONCENTRATIONS IN THREE HORSES WITH SECONDARY HYPERPARATHYROIDISM

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ABSTRACT

Three cases of horses with nutritional secondary hyperparathyroidism (NSH) are described. The horses showed typical thickening of the maxillae and mandibular bones with or without lameness. Laboratory findings included elevated concentrations of parathyroid hormone (carboxy-terminal and mid-molecule fractions), alkaline phosphatase and an increase in the fractional excretion rate of serum inorganic phosphorus.

Key words: Horses, nutritional secondary hyperparathyroidism, inorganic phosphorus, fractional excretion rate, parathyroid hormone.

Calcium and phosphorus metabolism is controlled by the combined action of parathyroid hormone (PTH), calcitonin and vitamin D3. Primary hyperparathyroidism is a rare condition in which there is excessive production of PTH by the parathyroid and a lack of negative feedback control of PTH production and release. Pseudohyperparathyroidism may be caused by an ectopic production of PTH or PTH-like peptides, most commonly by neoplasms of non-parathyroid origin.

Secondary hyperparathyroidism is an excessive production of PTH due to decreased serum ionised calcium or magnesium concentrations, caused by non-parathyroid disorders. The most common cause for this condition in the horse is nutritional secondary hyperparathyroidism (NSH) also referred to as "bran disease", "bighead" and "Miller's disease". NSH may be caused by feeding a ration containing a phosphorus to calcium ratio of 3 to 1 or more, regardless of whether the calcium content is deficient. NSH is a skeletal disease that typically affects young, growing horses but may be induced by pregnancy. The first clinical sign is usually an intermittent, shifting lameness due to focal periosteal avulsion, torn or detached ligaments or tendons, or subepiphysial microfractures. Joint pain may be a result of the articular cartilage erosions due to loss of underlying trabeculae. A typical bilateral symmetrical facial swelling occurs due to the osteodystrophic changes in the maxillae and rami of the mandibles. These changes in combination with the reabsorption of the laminae durae, may result in a problem with mastication.

This paper reports on clinical and laboratory findings in 3 horses with nutritional secondary hyperparathyroidism.

CASE 1:

A 5-year-old Shetland pony stallion was referred with a history of facial swelling. The diet on which the horse had been kept over the previous few years consisted mainly of natural grazing without other feed supplementation. On clinical examination, the main abnormalities were thickening of the maxillary and mandibular rami and a mildly stiff gait. The facial swelling was not painful.

Haematological and blood chemistry parameters were within normal limits. The fractional excretion rates (FE) of serum inorganic phosphorus (SIP) were higher than normal (Table 1). Parathyroid hormone concentrations (PTH) were determined by radioimmunoassay (C-terminal PTH, Instar Corp., Stillwater, Minnesota) and were significantly higher than normal (Table 1). Histopathology of a rib biopsy showed increased amounts of fibrous tissue in the bone marrow cavities.

Based on the above, a diagnosis of NSH was made and the pony's diet changed to lucerne and teff hay ad lib, in combination with commercial horse cubes and 30 g of calcium carbonate per day. The inorganic phosphorous FE was repeated about a month later and was found to be 0.09%. About a year later the owners reported that the pony's gait was normal although the facial thickening was still present.

CASE 2:

A 7-year-old mixed breed gelding was presented for a front limb lameness examination. The horse had been purchased 3 months earlier. Prior to purchase, the horse had been maintained on a grass pasture without other food additives for a few years. During the previous 3 months, the horse's diet had consisted of grains (oats and maize meal), molasses and teff hay. On clinical examination, a shifting lameness was found to be present in both fore limbs. This lameness disappeared after administration of a low palmar digital nerve block.

Radiographs of the front feet showed a mild radiolucency and an increased trabecular pattern of the phalanges with periosteal avulsion of the third phalanx. There was a...
Table 1: Clinical chemistry findings as well as parathyroid hormone concentrations in horses with nutritional secondary hyperparathyroidism

<table>
<thead>
<tr>
<th></th>
<th>Case 1</th>
<th>Case 2</th>
<th>Case 3</th>
<th>Normal Values</th>
</tr>
</thead>
<tbody>
<tr>
<td>Calcium mmol (t^1)</td>
<td>2,73</td>
<td>2,43</td>
<td>2,54</td>
<td>2,5 - 3,3^i</td>
</tr>
<tr>
<td>Inorganic phosphorus mmol (t^1)</td>
<td>1,00</td>
<td>1,08</td>
<td>1,83</td>
<td>0,8 - 1,8^i</td>
</tr>
<tr>
<td>Alkaline phosphatase U (t^1)</td>
<td>198</td>
<td>193</td>
<td>1028</td>
<td>141 - 516^i</td>
</tr>
<tr>
<td>Fractional excretion rate of phosphorus %</td>
<td>5,63</td>
<td>6,17</td>
<td>60</td>
<td>less than 0,5^i</td>
</tr>
<tr>
<td>PTH-C* pmol (t^1)</td>
<td>188</td>
<td>139</td>
<td>1060</td>
<td>32 - 92^e</td>
</tr>
<tr>
<td>PTH-MM** pmol (t^1)</td>
<td>233</td>
<td>352</td>
<td>872</td>
<td>58-209^*</td>
</tr>
</tbody>
</table>

* Carboxy terminal of parathyroid hormone  
** Mid-molecule part of parathyroid hormone  
+ 13 adult Thoroughbred horses in full training; concentrations of PTH-MM was determined by using the PTH-MM™I25 I RIA kit (Incstar Corporation, Stillwater, Minnesota, 55082). The method has not been validated for use in horses.

Blood chemistry showed a slightly lowered blood calcium concentration and the inorganic phosphorus FE and PTH concentration was higher than normal (Table 1). A diagnosis of NSH was made and similar dietary changes were made as in Case 1. Fifty grams of calcium carbonate per day was given per os.

A follow-up examination about 3 months later, showed no signs of lameness and the phosphorus FE was normal.

CASE 3: 
An adult female Shetland pony was presented with severe enlargement of the maxillae, severe gait impairment and with severely overgrown hooves. The condition was of unknown duration and the pony had been fed on sorghum-residue for a prolonged period. The pony had had limited access to pastures. The pony moved with great difficulty. Blood chemistry findings and results of parathyroid hormone assays are presented in Table 1. The pony’s diet was changed to almost exclusively lucerne and 30 g of calcium carbonate was supplemented daily. The gait abnormality gradually improved.

Forty-two days later, a further PTH serum assay revealed concentrations of 71 and 104,9 pmol \(t^1\) of PTH-C and PTH-mm respectively.

DISCUSSION
The pathophysiology of NSH is associated with a low ratio of calcium to phosphorus in the diet which results in increased PTH secretion. This leads to increased calcium absorption from bone, the intestinal tract and the kidneys and increased excretion of phosphorus by the kidneys. The diagnosis of NSH should be made based on history, clinical signs, serum chemistries and food mineral analysis. Inorganic phosphorus FE has been shown to be a sensitive parameter in indicating dietary imbalances of calcium and phosphorus, and has been a useful indicator of NSH. In Cases 1 and 2 the inorganic phosphorus FE was measured a few days after admission of the animals to the clinic. During this period the horses were fed a teff and lucerne hay mixture. It is probable that an earlier determination of these fractional excretion rates would have yielded higher values. FE determinations are of special importance in cases where feed analysis cannot be performed and in subclinical cases of NSH as was reported in race horses in Hong Kong. Mason et al. found a high incidence of vertebral compression fractures as the only manifestation in these horses.

Carboxy-terminal PTH concentrations in horses can be determined by radio immunoassay. In the cases reported here, concentrations were significantly higher than normal (Table 1).

The main differential diagnosis for high PTH concentrations are primary, secondary and pseudo-hyperparathyroidism. In primary or pseudo-hyperparathyroidism, PTH concentrations could be very similar to the PTH concentrations reported here. The main difference between these conditions is that serum calcium concentrations are elevated in primary hyperparathyroidism and are low or normal in secondary hyperparathyroidism. Renal failure may also be accompanied by abnormal PTH concentrations.

The calcium to phosphorus ratio in the diet of horses is extremely important, especially in high performance horses. Caple et al. concluded that about 40% of the race horses in Australia receive an inadequate calcium to phosphorus ratio in their high-grain diets during racing. These authors speculated...
that much of the lameness, tendinitis and spontaneous fractures in that country could be attributable to NSH. Denny studied the racing performance in relation to different diet regimens that resulted in different serum inorganic phosphorus (SIP) concentrations. He concluded that SIP concentrations lower than an accepted mean of 1,032 mmol L\(^{-1}\) resulted in better performance during races.

Correction of NSH is usually possible by increasing the dietary calcium to phosphorus ratio to higher than 1.5 to 1, preferably up to 2.5 to 1\(^{11}\). This will usually result in the improvement of the clinical signs, but the "big head" appearance may remain unchanged\(^{17}\). Prevention of NSH is possible by keeping the calcium to phosphorus ratio not lower than 1.5 to 1.

It is interesting to note that the historical data of all 3 cases did not indicate diets which might ordinarily be thought to be high in phosphate and/or lower in calcium. The name "bran disease" may be misleading, due to the fact that feeds which apparently do not contain very low calcium or very high phosphorus levels, may also cause NSH.

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REFERENCES