Case reports: hypovitaminosis A coupled to epilepsy in four calves

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SUMMARY

In this study, four calves were brought to clinic for a history of epileptic attacks. Throughout general clinical examination, several clinical signs characteristics of vitamin A deficiency (moving difficulties, ocular globe modifications, “beautiful blindness”, loss of palpebral and pupillary reflexes) were evidenced in the 4 animals. A high pressure (> 200 mm H2O) of the cerebrospinal fluid (whose the physical aspect, cellularity and protein concentrations were normal) was found in 2 animals. In all calves, deeply lowered serum vitamin A and β-carotene concentrations (< 70 μg/L and < 100 μg/L respectively) confirmed the diagnosis of hypovitaminosis A. Expected the case n°4 infested with ascarids, the others were not parasited. After oral treatment with vitamin preparation (Ademin® containing vitamins A, D3 and E) for 2 days, no epileptic attack occurred in any animal and the other symptoms, especially ocular signs, gradually disappeared within a week. These cases confirm that vitamin A deficiency may induce epileptic attacks in calf and that a vitamin supplementation at an early stage may totally cure affected animals.

Keywords: Calf, epilepsy, blindness, cerebrospinal fluid, hypovitaminosis A.

Introduction

Epilepsy is a functional disorder occurring as a result of paroxysmal discharge of the cortical and subcortical nerves in the brain which demonstrates episodic attacks, and motoric and sensoric courses, as well as loss of consciousness, and is characterized with tonic and clonic contractions in skeletal muscles and abnormal nerval activities [10, 13].

Epilepsies can be primary (idiopathic, genuine) or secondary (symptomatic, acquired). Primary epilepsy which is a natal and possibly genetic disease, due to an organic disorder in the brain, was observed in humans and dogs [8]. Secondary epilepsy observed in humans and all vertebrates may result from brain lesions [congenital defects such as hydrocephaly, apoplexy, brain tumours, brain hypoxia; brain parasites, callus formation in the bones of the skull due to bone fractures, meningitis, encephalitis, encephalomalacia/oedema, toxins such as lead, mercury, organic phosphorus, ethylene glycol, strichnine] as well as from extraneural causes such as metabolic and functional disorders of other organs [kidney diseases, cardiac diseases and circulation disorders, liver diseases, pancreas tumours, hypoglycaemia, uremia, hypocalcemia and electrolyte balance disorders (Na, K, Mg), rhinitis, otitis, sinusitis, parasites in the nose (Oestrus ovis), parasites such as ascariidosis, teniasis and also hypovitaminosis A in young calves] [8, 12]. Additional factors such as fear, excitement, noise, light, or blows are known to play a role in epileptic attacks [13].

This study focuses on hypovitaminosis A-induced epilepsy in calves, although it is relatively scarce, since it can be easily corrected by practitioner veterinarians.

Case reports

Four calves (3 Simental crossbred and one Montafon X Yerlikara), 40-60 days old, stemming from different family enterprises presented complaints and faints and were brought to Firat University Faculty of Veterinary, Department of Internal Diseases Clinic for examination and treatment. Epileptic attacks have occurred once or twice a day in the previous week and increased to 5-6 times in recent days.
Fainting episodes lasted few minutes, then the calves stood on their feet and continued to suck their mothers. Additionally, no vitamin A supplementation was performed on calves or on their mothers.

One calf (case n°4) exhibited 4 attacks (characterized by tonic and clonic muscle contractions, recumbency, loss of consciousness, dorsiflexion of the head and neck, rotation of eyes, mydriasis and salivation) during its stay at the clinic (figure 1). After each attack, the calf stood up after a short moment like nothing was happened. During clinical examination, the body temperature was ranged between 38.3°C and 39.1°C, the heart and respiratory frequencies were comprised between 108 and 124 beats/min and 24 and 32 cycles/min respectively (Table I). It was also observed that calves crushed into barriers in front of them; eye balls were conoid, eyes were exophthalmic and showed a green-bluish fluorescence when calf head was turned towards the sun. Furthermore, pupillary and palpebral reflexes were absent and enlargement of the retinal vessels coupled to haemorrhages were evidenced during ophthalmoscopic examination. In addition, the calf n°3 presented a slight blurriness in the right eye near the center of the cornea. It was also noticed that the umbilical cord was slightly inflamed in 2 calves (calves n°1 and 2).

After general clinical examination of all animals including eye checks [17], blood samples were taken from jugular venipuncture into sterile tube without anticoagulant. After clotting for 2 hours at 37°C and centrifugation (1 500g, 10 minutes, 4°C), sera were carefully harvested and stored at -20°C until analysis. Serum vitamin A and β-carotene concentrations were determined by spectrophotometry (Shimadzu UV-1208, UV-VIS spectrophotometer) according to the method of SUZUKI and KATOH [19]. These 2 parameters were markedly depressed in all cases as compared with normal values (> 120 μg/L for vitamin A concentrations and > 300 μg/L for β-carotene concentration) (Table II). Furthermore, microscopic examination of faeces from all animals for parasite investigation revealed that only one case (case n°4) faeces contained ascarid eggs although all cases experienced epileptic attacks.

Cerebrospinal fluid (CSF) was sampled in 2 animals: calves were sedated with intramuscular injection of 1 mL/100 kg xylazine hydrochloride (Rompun 5%, Bayer) and after shaving and disinfection of the area, puncture of the lumbo-sacrale foramen using cannula (7 mm length, 1.1 mm calibre) was performed according to the canalis spinalis technique in animal in right lateral position [5, 8, 9]. After pressure measurement with a lumbal manometer (Hako, Germany), a CSF sample was taken into a sterile tube without anticoagulant until the pressure decreased below 200 mm water pressure. In addition to physical examination (colour, distinctness and coagulation), total cell counts (by Fuchs-Rosenthal couting chamber) and protein concentrations (by a modified biuret method) were measured [5, 8]. In these 2 cases (calves n°3 and 4), the CSF pressure was high (Table II) and the CSF aspect was quite normal. Cell counts in CSF samples were within usual ranges

![Figure 1: Epileptic attack in a calf (case n°4). Note the tonic and clonic muscle contractions, recumbency, dorsiflexion of the head and neck, rotation of eyes, mydriasis and salivation.](image)

<table>
<thead>
<tr>
<th>Parameters</th>
<th>Case n°1</th>
<th>Case n°2</th>
<th>Case n°3</th>
<th>Case n°4</th>
<th>Usual values Reference</th>
</tr>
</thead>
<tbody>
<tr>
<td>Temperature (°C)</td>
<td>39.1</td>
<td>38.3</td>
<td>38.7</td>
<td>38.9</td>
<td>38.5-39.5</td>
</tr>
<tr>
<td>Heart frequency</td>
<td>112</td>
<td>108</td>
<td>116</td>
<td>124</td>
<td>90-110</td>
</tr>
<tr>
<td>Respiratory frequency</td>
<td>30</td>
<td>24</td>
<td>32</td>
<td>32</td>
<td>30-45</td>
</tr>
</tbody>
</table>

**Table I:** Clinical parameters observed in the 4 calves presenting for epileptic attack.

<table>
<thead>
<tr>
<th>Parameters</th>
<th>Case n°1</th>
<th>Case n°2</th>
<th>Case n°3</th>
<th>Case n°4</th>
<th>Usual values Reference</th>
</tr>
</thead>
<tbody>
<tr>
<td>Serum vitamin A (μg/L)</td>
<td>42.5</td>
<td>35.6</td>
<td>27.4</td>
<td>22.3</td>
<td>&gt; 120 [18]</td>
</tr>
<tr>
<td>Serum β-carotene (μg/L)</td>
<td>37.7</td>
<td>31.0</td>
<td>15.5</td>
<td>8.7</td>
<td>&gt; 300 [18]</td>
</tr>
<tr>
<td>CSF pressure (mm H2O)</td>
<td>ND</td>
<td>ND</td>
<td>380</td>
<td>420</td>
<td>&lt; 200 [17]</td>
</tr>
<tr>
<td>CSF Protein (g/L)</td>
<td>ND</td>
<td>ND</td>
<td>0.24</td>
<td>0.30</td>
<td>0.10-0.40 [17]</td>
</tr>
<tr>
<td>CSF Cell count (10⁶/μL)</td>
<td>ND</td>
<td>ND</td>
<td>18/3</td>
<td>21/3</td>
<td>0-20/3 [9]</td>
</tr>
</tbody>
</table>

CSF: Cerebrospinal fluid; ND: not determined.

**Table II:** Biochemical and cytological parameters observed in the 4 calves presenting for epileptic attack.
and the protein concentrations remained low, within usual values (Table II).

A vitamin preparation including vitamins A, D₃ and E (Ademin®, Sanofi-Dif, vitamin A: 500,000 I.U; vitamin D₃: 75,000 I.U and vitamin E: 50 mg) was intramuscularly administered at the dose of 2 mL once in 2 days at least 3 times and then at week intervals for a month to all cases experienced epileptic attacks. Additionally, the calf n°4 was orally treated by 7.5 mg/kg levamisole (Tetratab, Eczacıbaşı., 150 mg levamisole in each tablette) 2 times at 21 days of interval. No attack occurred in any calf between 12 hours-2 days after the treatment and all animals healed approximately within a week.

Discussion

Diagnosis of the vitamin A deficiency was based on clinical (anorexia, ill-thrift, night blindness, beautiful blindness, loss of pupillary light reflexes, enlargement of the retinal vessels coupled to haemorrhages, nystagmus, strabismus, exophthalmus, intermittent tonic-clonic convulsions, diarrhoea, pneumonia) and necropsy findings (not characteristic gross changes, compression and injury of cranial and spinal nerve roots especially on the optic nerve, squamous metaplasia of the interlobular ducts of the parotid saliva gland, focal necrotic hepatitis), as well as on vitamin A and β-carotene concentrations measured in blood serum and in liver, determination of the CSF pressure, evidence of low content of vitamin A in food and healing after vitamin A treatment [1, 14, 18]. In the 4 cases reported here, eye symptoms, high CSF pressure and low serum vitamin A and β-carotene concentrations have ascertained the diagnosis of hypovitaminosis A.

It was stated that the most obvious symptom for vitamin A deficiency in calves and maturing cows is the decrease of the adaptation to darkness [1, 10, 14, 18]; animals cannot determine their way in the dark or half-darkness, and when the disease worsens, they see no more even in light and become blind. Furthermore, these animals poorly move even when they are untied, lose the sense of direction, crash into things, swing and lose their balance when walking. The owners rarely recognise these symptoms, and often the blindness is evidenced only throughout clinical examination. A meticulous eye examination reveals several specific anomalies in mature vitamin A deficient cows: exophthalmic conditions and conical swelling in the cornea occur, the pupillary reflex is partially or completely lost with an expanded pupilla becoming as a circle and when the animal is in the dark, the light traits reflecting in the eye forms a blue-greenish flourescence also named “Schönblindheit” or “beautiful blindness”. In addition, the conjunctiva is inflamed and using ophthalmoscope the retinal vessels appear enlarged and haemorrhages occurred in some parts [1, 3, 7, 14, 18, 20]. Other eye symptoms characteristics of vitamin A deficiency such as keratitis, cornea ulcers and xerophthalmia [1, 7] slowly developed [11] and are not always present, especially when animals were brought to the clinic at an early stage. In the 4 cases reported here, eye symptoms including loss of visual perceptions and inherent moving difficulties, exophthalm and eye globe modifications, loss of palpebral and pupillary reflexes and beautiful blindness were encountered and strongly supported the hypovitaminosis A deficiency. Additionally, a cornea ulcer was even noticed in one calf (case n°3).

Serum vitamin A and β-carotene concentrations exceed 120 µg/L and 300 µg/L respectively in healthy calves, whereas concentrations ranged from 70 to 120 µg/L for vitamin A and from 100 to 300 µg/L for β-carotene are considered as critical and vitamin A and β-carotene concentrations below 70 µg/L and 100 µg/L respectively confirm hypovitaminosis A diagnosis and are coupled with clinical symptoms [11, 14, 15, 18, 20]. Indeed, REDDY and GANAPATHY [15] observed clinical symptoms of vitamin A deficiency when blood vitamin A concentrations were inferior to 120 µg/L and HAYES and NIELSEN [11] reported that high CSF pressure and ocular papille oedema firstly occur when plasma vitamin A concentrations are below 50 µg/L. ALTINTAŞ et al. [2] have found that the average vitamin A concentration in 40 blind calves was 62.1 ± 4.9 µg/L and in blind beeves, serum vitamin A concentrations were comprised between 30.6 and 120 µg/L (mean: 66.1 µg/L) [3]. In vitamin A deficient calves, convulsions were associated with concentrations below to 90 µg/L [15] and night blindness with concentrations below 33.6 µg/L [20]. Moreover, HAYES and NIELSEN [11] have demonstrated that clinical symptoms of hypovitaminosis A appeared within 150 days in 35 day old calves not supplemented with vitamin A whereas in parallel, vitamin A concentrations decreased to 50 µg/L. In the current study, all diseased calves exhibited low serum concentrations of vitamin A (< 70 µg/L) and of β-carotene (< 100 µg/L), confirming the diagnostic of vitamin A deficiency.

Epileptic attacks can be sometimes encountered in vitamin A deficient cows [6, 7]; when animals are stimulated, they fall and convulse, lose their consciousness for 3-5 minutes and thereafter they recover and stand up. These fainting episodes were seen in the 4 cases reported here. The CSF pressure in healthy mature cows is below 200 mm water pressure [17] while an increase of the CSF pressure in vitamin A deficiency early appears [4, 11]. It is probable that the enhancement of the CSF pressure induces unconsciousness and convulsions. In this way, a high CSF pressure was found in 2 calves (380 and 420 mm H₂O, respectively). As CSF samples were not blurry, not coagulated and were clear and limpid and as CSF cellularity and protein concentrations were within usual values, an inflammatory origin for neurologic signs [4, 17] can be ruled out. On the other hand, although ascarid eggs were evidenced in faeces from the calf n°4 and that secondary infections were evidenced in faeces from the calf n°4 and that secondary epilepsy may result from parasite related diseases [10], epileptic attacks seemed to be more related to hypovitaminosis A than to parasite infestation in this particular case since serum vitamin A and β-carotene concentrations were dramatically lowered (more than in the 3 other cases), the CSF pressure was very high (420 mm H₂O) and the calf has quickly recovered after combined levamisole-vitamin treatment. Nevertheless, ascarid infestation would promote the vitamin A deficiency by impairing intestinal vitamin assimilation.

It has been reported that the clinical signs due to a high CSF pressure in vitamin A deficient beeves (ataxy, incoordination,
tremors, swingings, extreme stimulation) disappeared within 48 hours after vitamin A treatment [14], but as far as ocular injury was concerned, it was sometimes difficult to evaluate specific recovery, especially in old cases and in these cases, slaughtering was suggested [14]. However, ANTEPLIOGLU et al. [3] have emphasized that blindness in animals with hypovitaminosis can be cured using vitamin A preparations provided that the treatment was administered at the early stage of the disease. SINGH et al. [16] have reported that 4 out of 5 blind calves responded to vitamin A treatment expected if blindness was due to congenital malformations or to other causes than hypovitaminosis A. In the cases reported in the present study, epileptic attacks disappeared within a short time after vitamin treatment and calves healed relatively quickly in agreement with literature [3, 6, 16].

As a conclusion, epileptic attacks in the 4 cases studied in the present report are induced by hypovitaminosis A diagnosed from characteristic eye symptoms, increase of the CSF pressure and direct measurement of serum vitamin A and β-carotene concentrations. Successful results can be obtained from vitamin treatments in the early stage of the vitamin deficiency.

References