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CASE REPORT
Hypervitaminosis A in the cat: a case report and review of the literature

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A case of hypervitaminosis A with secondary entrapment and compression of the left brachial plexus nerve roots is described. A 9-year-old male castrated domestic shorthair, fed a home-made diet based on raw pork liver, was submitted for examination for a left forelimb lameness that evolved to paralysis over a 2-month period. Clinical examination revealed a flaccid paralysis and atrophy of all left forelimb muscles. An ipsilateral Horner's syndrome was also noted. Radiological examination of the cervical and thoracic spine showed massive new bone formation at the ventral aspect of the second cervical to sixth thoracic vertebra. The diagnosis of hypervitaminosis A was made, based on the clinical and radiographic findings, as well as the determination of serum vitamin A concentration, which was 630 µg/dl, three times above the upper normal limit for this species. Despite the unfavourable initial prognosis, the cat progressively regained function of the affected limb approximately 6 months after the diet was changed to a commercial canned food.

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A 9-year-old, male castrated, domestic shorthair was presented for examination because of left thoracic limb paralysis. According to the owner, the cat lived strictly indoors, was fed exclusively a home-made diet based on raw pork liver and had developed initially a lameness of the affected limb, that evolved to monoparesis and subsequently monoplegia progressively, over a period of 2 months. The veterinarian who initially examined the cat also noticed anisocoria and referred the case without pursuing any further diagnostic tests.

On clinical examination the cat appeared alert, was in good body condition, had a normal temperature, heart and respiratory rate, but was unable to bear weight on the left thoracic limb (Fig 1). Neurological evaluation revealed a flaccid paralysis and atrophy of all left forelimb muscles. No spinal reflexes could be elicited in the affected limb. An ipsilateral Horner's syndrome was also noted (Fig 2). Partial loss of superficial cutaneous sensation (hypoesthesia) was evident in the distal part of the extremity (below the elbow joint). Deep pain sensation remained intact. No further neurological abnormalities involving the other limbs and cranial nerves were noted. Based on the aforementioned signs, a neuroanatomical diagnosis of a left brachial plexopathy affecting the A6-T2 spinal nerve roots was made (Kitchell and Evans 1993, Dewey 2003).

Initial diagnostic investigation included a complete blood count (CBC), serum biochemistry, urinalysis and radiographic examination of the cervical and thoracic spinal column. The results of screening clinicopathological tests were normal (Table 1). Radiological evaluation revealed mild vertebral exostoses and massive new bone formation at the ventral aspect of the second

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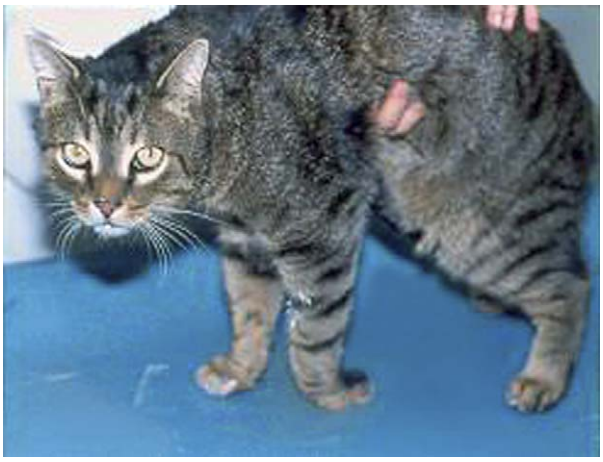

Fig 1. Clinical presentation of the cat on the day of referral. There is flaccid paralysis of the left thoracic limb.

cervical to sixth thoracic vertebra. Bone proliferation was most pronounced in the A6-T4 region, displacing the trachea and oesophagus ventrally and to the right (Fig 3a and b).

A tentative diagnosis of metabolic osteopathy resulting from hypervitaminosis A was made based on the dietary history, clinical and radiographical findings. To prove this speculation, further diagnostic investigation included the determination of serum vitamin A concentration, which was determined spectrophotometrically, using the colorimetric method described by Roels and Trout (1972), and found to be 630 μg/dl. Reported normal values for the feline species range from 50 to 200 μg/dl (Rucker and Morris 1997).

The long-term prognosis of the case was estimated as guarded to poor, because of the extensive bone lesions and the severe neurological signs inflicted by the entrapment and compression of the brachial plexus. The owner was advised to change the cat's diet to a balanced commercial canned food and the patient was discharged. Despite the grim long-term prognostic outlook, the cat adapted well to the dietary changes and improved gradually over the following 6 months. In particular, in monthly follow-up telephone calls, the owner reported a progressive regain of motor function in the affected limb while anisocoria resolved during the first month. While a re-evaluation of the animal's condition was strongly advised in order to assess the neurological status and the evolution of the radiographic findings, the owner did not comply because of the long distance of her residence from the hospital.

Fig 2. Left-sided Horner's syndrome in the cat shown in Fig 1.

Naturally occurring hypervitaminosis A has been described in man and animals both in its acute and chronic forms and is caused by either the consumption of liver rich in vitamin A or by the excessive intake of vitamin A concentrates (Clark 1971). The chronic form is more common in cats, where it has been first reported as a debilitating metabolic osteopathy ('deforming cervical spondylosis'), associated with diets based solely on milk and raw ruminant, porcine or chicken liver, almost 50 years ago (Christi 1957, Seawright and English 1964, Armstrong and Hand 1994, Morgan 1997). The long-term effects of vitamin A on the skeleton are characterised by the formation of extensive bony osteophytes and exostoses around joints, at the site of tendon, ligament and joint capsule attachments (Hayes 1982, Armstrong and Hand 1994, Bennett 1994). The cat is particularly susceptible to vitamin A toxicity and the pathophysiological sequelae of chronic disease are quite unique and distinctive from those seen in other species (Seawright et al 1970, Clark 1971, Hough et al 1988, Franch et al 2000, Braund 2002).

Most natural cases involve adult cats ranging in age from 2 to 9 years, with no breed or sex predilection recognized (Seawright et al 1970, O'Donnell and Hayes 1987, Braund 2002). The long-term effects of vitamin A are established after months or years of excess intake and are characterised by the formation of extensive bony osteophytes and exostoses around joints at the site of tendon, ligament and joint capsule attachments. Principally affected areas include the occipital bone, cervical and thoracic vertebrae, while less commonly reported extraspinal sites are the limb joints, particularly those of the shoulder and the elbow, the sternum, thoracic

Table 1. Haematology and serum biochemistry results

Haematology	Serum biochemistry	
		Reference values
Packed cell volume: 38%	Total protein: 7 g/dl	6.2–7.8 g/dl
White blood count: 7400/μl	Blood urea nitrogen: 31 mg/dl	13.8–39.8 mg/dl
Platelets: 434,000/μl	Creatinine: 1.5 mg/dl	1.2–1.9 mg/dl
Differential white blood cell counts	Alkaline phosphatase: 111 U/l	28–158 U/l
Neutrophils: 4884/μl	Aspartate aminotransferase: 33 U/l	13–39 U/l
Lymphocytes: 1463/μl	γ-Glutamyl-transferase: 5 U/l	1–7 U/l
Monocytes: 541/μl	P: 3.7 mg/dl	2.2–6.3 mg/dl
Eosinophils: 512/μl	Ca: 9 mg/dl	6.9–9.5 mg/dl

cage and pelvis (Seawright and English 1964, Seawright et al 1970, O'Donnell and Hayes 1987, Bennett 1994, Morgan 1997). Earliest observed changes include periarticular cartilaginous and osseous hyperplasia of the first cervical vertebrae, that are not associated with signs of inflammation (Seawright and English 1964, Clark 1971). With time lesions coalesce, leading to complete joint ankylosis, initially of all cervical and cranial thoracic vertebrae (Clark 1971, Allan 2000). Less commonly, confluent exostoses form on the ventral margin of the cervicothoracic spine, than on its dorsolateral margins (Seawright et al 1970). Lesions in the forelimbs originate in the fibro-osseous insertions of ligaments and tendons in the vicinity of joints, thus initially restricting movement and ultimately producing extra-articular ankylosis. Elbow joints are commonly affected and fused completely in the flexed position (Seawright et al 1970, Bennett 1994, Braund 2002).

While the underlying pathophysiological mechanisms remain unclear, vitamin A toxicity appears to induce bone lesions via a direct effect on skeletal tissue (Braund 2002). Individual predisposition to the disturbances of vitamin A metabolism has also been suggested as an important factor in the pathogenesis of the disease (Pobisch and Onderschenka 1976, Schmidt and Geyer 1978). Periosteal trauma is one of the commonest causes of exostosis formation. In vitamin A toxicity, extensive inhibition of collagen synthesis provokes the breakdown of musculotendinous insertions in the periosteum during normal muscle activity (Clark 1971, Dickson and Walls 1985, Hough et al 1988, Franch et al 2000). Additionally, it has been suggested that vitamin A-induced increased lability of the cytomembranes renders them prone to mechanical injury (Seawright et al 1970). In cats, excessive muscular activity during grooming may explain the predisposition of the cervicothoracic spine in lesion formation (Hough et al 1988, Armstrong and Hand 1994).

Histopathologically the proliferative lesions are subperiosteal in origin, with apposition of new woven bone around the affected sites. Cartilaginous hyperplasia originating at the margin of the articular hyaline cartilage overgrows the joint and replaces synovial membrane. At the reactive edge of the exostosis spreading of the osteogenic field into adjacent soft tissues results in atrophy and replacement of muscle fibres with new woven bone (Seawright and English 1964, Seawright et al 1970, Braund 2002). In older lesions the growing bony mass is remodeled in a process resembling fracture healing or craniomandibular osteopathy (Seawright et al 1970, Franch et al 1998a, 1998b). Contrary to the suggestion that the development of exostoses in hypervitaminosis A may be dependent on low calcium and high phosphorus ratios, amounts and relative proportions of these elements in the diet had little or no influence on the development of lesions (Seawright and Hrdlicka 1974, Cho et al 1975).

A different form of the disease has been described in kittens and is characterised by some unique features that are not seen in adult cats (Seawright and Hrdlicka 1974). These include oedema and inflammation of the gingivae, loosening or retention of incisor teeth and damage to the epiphyseal long bone plates. In the latter, vitamin A inhibits chondrocyte multiplication, rendering them thinner than normal and with severe matrix defects due to a loss of mucopolysaccharide ground substance (Clark and Seawright 1968, Clark 1971, Clark 1973, Seawright and Hrdlicka 1974). Suppression of osteoblast activity and degenerative changes in

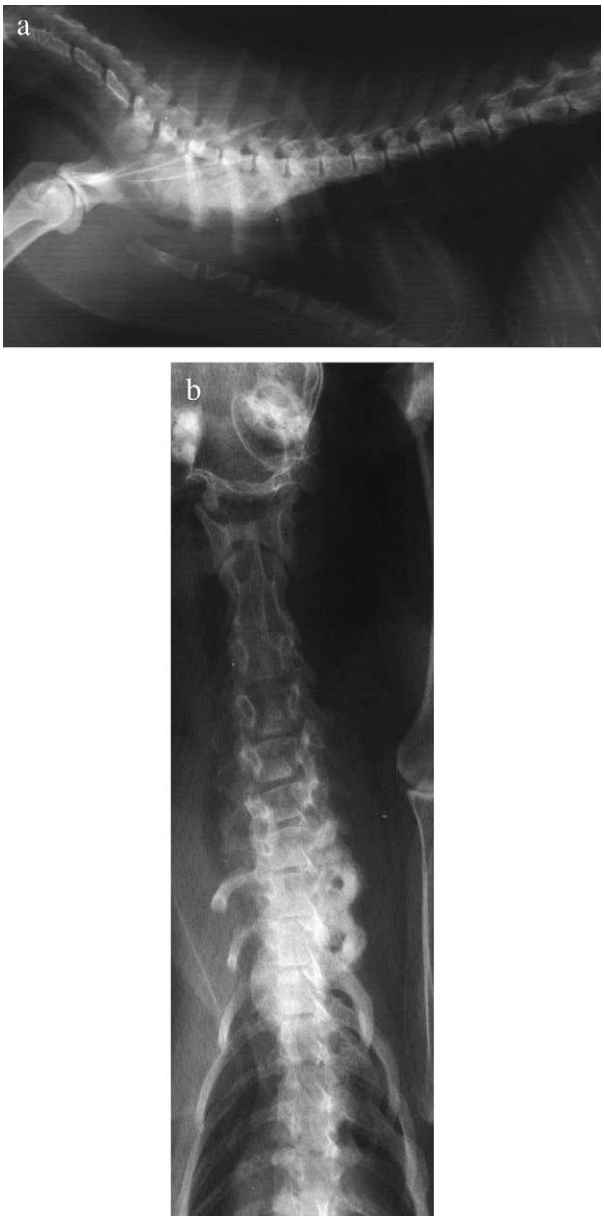

Fig 3. Lateral (a) and ventrodorsal (b) radiographs of the spinal column of the cat. There is massive new bone formation at the ventral aspect of the caudal cervical and cranial thoracic vertebrae, displacing the trachea ventrally and laterally to the right. Vertebral exostoses reduce the normal radiolucency of the cervical and cranial thoracic vertebral column.

the cartilaginous epiphyseal plates reduces the longitudinal growth, which is irreversible even with cessation of excess vitamin A intake. On the contrary to the latter, osteoblastic activity and appositional bone formation resume and thus the long bones regain normal shaft thickness but not normal proportions (Clark 1971). There is a consequent limb shortening and a distortion of some epiphyses, due to the uneven growth of irregularly damaged growth plates similar to the clinical syndrome of 'hyena disease' that is seen in calves and hypervitaminosis A of dogs (Clark and Seawright 1968, Cho et al 1975, Bennett 1994; Yamamoto et al 2003). Retardation of tooth growth is probably attributed to the depression of odontoblast activity and the subsequent reduction of dentine formation after prolonged exposure to vitamin A (Seawright and Hrdlicka 1974).

In hypervitaminosis A clinical signs are associated with the skeletal lesions. Early manifestations of the disease, indicating the presence of pain include lameness of one or both thoracic limbs, stiffness and reluctance to move, and precede the establishment of bone lesions (O'Donnell and Hayes 1987, Bennett 1994). Cervical immobilisation prevents self-grooming and, in severe cases, prehension of food. The head may be held in a ventroflexed position and there may be scoliosis of the cervical spine and painful reaction upon its manipulation. Affected cats often adopt a marsupial-like posture as a compensation for their inability to move their head and neck (Seawright et al 1970, Allan 2000, Braund 2002).

Foreleg lameness can be associated with compression of peripheral nerves or ankylosis of the elbow and shoulder joints, which are fixed in a flexed position (Armstrong and Hand 1994, Morgan 1997). Other signs caused by spinal nerve compression at the level of the intervertebral foramina include cutaneous hyperesthesia and atrophy of the cervical and appendicular muscles (Allan 2000, Braund 2002). Less common findings are voice change related to proliferative exostoses that compress laryngeal structures and regurgitation due to the compression of the oesophagus (Armstrong and Hand 1994, Braund 2002). Diagnosis is usually based on history and the characteristic radiographic findings, which may be detected after 10 weeks on an induction diet (Allan 2000, Braund 2002). Rarely, affected cats with typical clinical signs have minimal radiographic abnormalities in the cervical spine or develop lesions first in extraspinal sites (Vanderlip 1983, Allan 2000, Franch et al 2000).

Although in the presented case the exostoses extended as far as the cranial (C2) portion of the cervical spine (Fig 3a), its range of motion was unaffected because the majority of newly formed bone was located in the cervicothoracic region (C6-T4). Despite the size of spinal exostoses and the associated tracheal and oesophageal displacement, respiratory distress and regurgitation were

not noticed. Massive new bone formation affecting mainly the left side of the cervicothoracic spine (C6-T4) resulted in impingement of the brachial plexus nerve roots, particularly those forming the radial nerve (C7-T2), with subsequent loss of motor function of most extensor muscles in the affected limb. The ipsilateral Horner's syndrome, caused by damage to the sympathetic preganglionic nerve fibres at the level of T1–T3 spinal roots, the proximal portions of these nerves and the rami communicans, is an unusual finding in hypervitaminosis A, although the cervicothoracic spine is the most commonly affected site (DeLahunta 1983). This type of sympathetic dysfunction is most commonly associated with traumatic and/or neoplastic plexopathies (Wheeler et al 1986, Dewey 2003). Most caudal brachial plexus injuries bear a poor prognosis (Steinberg 1988, Kitchell and Evans 1993, Dewey 2003).

Despite the severe neurological signs, the cat of this report made an almost complete functional recovery upon cessation of excess vitamin A intake. As a follow-up radiological or even neurophysiological evaluation was not possible, only a speculation of a reversible peripheral nerve dysfunction can be made (Steinberg 1979). Neurapraxia refers to a transient loss of function inflicted with limited damage to the axons or their supportive connective tissue structures. The degree of motor and proprioceptive dysfunction is variable, but nociception is preserved because large diameter axons preferentially affected (Wheeler et al 1986, Dewey 2003). In this case, ischaemia and/or mild paranodal demyelination could have accounted for the temporary dysfunction. It has also been reported that in animals with extensive involvement of the spinal nerve roots, the spinal cord may show atrophy with disappearance of neurons and fibres, especially in the dorsal horns of the grey matter (English and Seawright 1964).

The vitamin A status of animals may be evaluated on the basis of clinical and biochemical procedures, such as the measurement of retinol in serum or plasma. Normal serum retinol concentrations for the cat are reported to range from 50 to 200 μg/dl, whereas in those receiving liver diets much higher concentrations (451–1281 μg/dl) are common (Seawright et al 1967, Roels and Trout 1972, O'Donnell and Hayes 1987, Rucker and Morris 1997). The estimated serum vitamin A concentration in the cat of this report was three times over the upper normal limit, therefore confirming the clinical diagnosis. Apart from the elevated serum vitamin A concentration, no other haematological abnormalities, including serum alkaline phosphatase activity, calcium and inorganic phosphorus levels, are noted in most clinical cases, as it was seen in the presented one (Seawright et al 1970).

In general, chronically and severely affected cats bear a poor prognosis in terms of functional recovery, as correction of the diet after the disease becomes established results in cessation of the progress of lesions, but no significant reversal or improvement of the debilitating clinical manifestations (Seawright et al 1970, Clark 1971). Exceptions, however, do occur with temporary or permanent spontaneous recovery (Pobisch and Onderschenka 1976). Apart from its interesting clinical features, this case shows that estimation of prognosis in hypervitaminosis A may not be always accurate, thus encouraging both the clinician and the owner to pursue symptomatic treatment of the affected cats.

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