Multiple cartilaginous exostosis in a Golden Retriever cross-bred puppy

Clinical, radiographic and backscattered scanning microscopy findings

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Summary
Multiple cartilaginous exostosis was diagnosed in a six-month-old Golden Retriever cross-bred male with a history of forelimb lameness and isolated, but very painful, acute episodes. Physical examination revealed a right forelimb lameness with a firm, painful palpable mass on the cranial aspect of the forearm. The radiological examination showed the presence of bony masses at the humerus and radius as well as several masses in the ribs and spinous processes of the thoracic vertebrae. Based on the history and radiographic findings, multiple cartilaginous exostosis was diagnosed. Treatment with non-steroidal anti-inflammatory drugs was commenced for two weeks without any effect. Due to the lack of a response to the treatment as well as to the progressive physical deterioration of the animal, the owners requested euthanasia of the dog. Histology of the different exostoses demonstrated the presence of a hyaline cartilage cup surrounding a central area, formed mainly by bone and cartilage trabeculae. Signs of malignancy were not observed. Back-scattered scanning electron microscopy (BEI-SEM) study revealed well-ordered and progressively calcified cartilage trabeculae present underneath the non-calcified cartilage cap. At a greater depth, those cartilage trabeculae became osteochondral trabeculae, and the innermost were formed exclusively by woven and lamellar bone. The histological and back-scattered electron scanning microscopy results conclude that it was a well-arranged normal endochondral ossification process that followed a centripetal pattern inside the bony mass, confirming the diagnoses of multiple cartilaginous exostoses.

Keywords
Multiple cartilaginous exostoses, dog


Introduction

Multiple cartilaginous exostosis (MCE) is a bone disease of uncertain origin characterized by multiple, cartilage-capped bony protuberances that arise from the surfaces of bones formed by endochondral ossification (9). The condition is a relatively common syndrome in man (15) and it has also been documented in dogs (6), horses (17) and cats (13), although feline MCE has significant differences in comparison with the rest of the species affected (2, 14).

Historically, the condition has been designated by various descriptive terms (chondroma, diaphyseal aclasis, dyschondroplasia, enchondromatosis, hereditary deform- ing chondrodysplasia, hereditary multiple exostoses, multiple osteochondromatosis). However, a certain degree of nomenclature has currently been achieved whereby a solitary lesion is referred to as osteochondroma, and the presence of multiple lesions in an individual is defined as multiple cartilaginous exostosis (1, 8).

Both solitary osteochondromas and multiple cartilaginous exostoses are histologically identical, although multiple cartilaginous exostoses have been shown to be hereditary in dogs (7). The vertebrae, ribs and long bones are most frequently affected (6). The growth of osteochondromas continues until skeletal maturity (14) and they may remain subclinical unless enlargement causes dysfunction by compression of a vital structure typically the spinal cord (2, 15) or interference with joint function (1). This paper describes a clinical case of MCE in a puppy without any spinal cord compression, but with acute painful crises and with a complete lack of response to treatment leading to the consequent euthanasia of the patient. The histological and back-scattered scanning electron microscopy descriptions of the bony masses are also presented.

Case history

A six-month-old male cross-bred Golden Retriever was referred to our clinic because of forelimb lameness with abnormal gait and acute episodes of pain. The dog had been with the owners since it was 1.5 months old. It had been regularly vaccinated and de-wormed. Painless swellings of the left forelimb were noted by the owners at four months of age, but they were attributed to minor trauma. From the initial observation, the nodules had increased in size.

On admission, the dog was alert and had a non-weight-bearing lameness of the left forelimb. On physical examination, two compacted and well defined bone enlargements, situated at the proximal humerus and proximal radius of the left forelimb, were observed. Pain was elicited on deep palpation of the masses. Neurological examination suggested a mild proprioceptive deficit of the affected limb, although the examination was difficult due to the presence of the masses and the reluctance of the dog to be manipulated. Mild muscular atrophy was observed in the left forelimb. Muscle atrophy, to a lesser degree in the other limbs was also present. The rest of the physical examination, including the thoracic wall, was unremarkable except for poor body condition.

A complete radiographic examination was performed with the dog under general anaesthesia. Radiographs showed several...
radio-dense bony masses on the spinous processes of the thoracic vertebrae (Fig. 1) and three radio-dense bony masses on the ribs proximal to the costochondral junction (Fig. 2A, B). Two similar lesions were also detected in the left forelimb, coinciding with the protuberances observed at physical examination. One mass was located in the caudal aspect of the humeral diaphysis and the other in the cranio proximal aspect of the radius (Fig. 3). The masses associated with the vertebrae and ribs were round, whereas those affecting the limbs showed a more elongated shape, well delimited and apparently continuous with the bone cortex. Other radiological lesions were not detected. Haematology, serum biochemistry and urinalysis were performed with all values within the normal range.

Based on the clinical and radiographic signs, a diagnosis of canine multiple cartilaginous exostoses (MCE) was made and a treatment with meloxicam (0.1 mg/kg PO, sid) for two weeks was initiated. The non-weight bearing lameness persisted and the episodes of acute pain increased in frequency and intensity. Due to the lack of a favourable response to treatment, and the progressive physical deterioration of the animal, the owners requested euthanasia.

The post-mortem examination demonstrated the presence of several bony masses, none larger than 3 cm in diameter, located on the spinous processes of ten different thoracic vertebrae. The dorsal vertebral arch of the affected vertebrae were not involved. Three large bone masses were located on the 8th and 10th left ribs and the 5th right rib. The costal masses were smoothly contoured, round-shaped, with a diameter ranging from 3 to 10.0 cm, and expanding medially from the pleural surface of the ribs into the thoracic cavity. The consistency of the masses was very firm. Despite the masses being large enough to cover several ribs, they were firmly attached to only one. Once sectioned, a hard reddish trabecular network surrounded by a hard pinkish covering could be observed.

The macroscopic aspect of the humeral and radial bone masses was similar to the costal masses, except for a more elongated shape, with a large area of contact between the mass and the affected bone. A clear continuity between the protuberance and the bone cortex was observed in both cases. The central area of the humeral mass showed a more compact bone aspect that allowed for an easy delimitation between the bony mass and the medullary cavity of the humerus.

The bony masses were sectioned and the sections were divided alternatively into two groups. One half of the sections were decalcified and processed for conventional histology (haematoxylin and eosin staining). Histopathology of the decalcified slices showed a similar pattern in all of the sections. They were composed of two components, an external cap of hyaline cartilage, which mimicked a growth plate and produced bone by orderly endochondral ossification (Fig. 4); and a central core of cartilage and immature bone with intervening marrow spaces. These spaces were filled by a haematopoietic tissue. In one rib section, islands of hyaline cartilage retained subperiosteally were seen. Evidence of malignancy was not noted in any of the masses evaluated.

The remaining bone sections were processed, without decalcification, for back-scattered scanning electron microscopy (BS-SEM). The BS-SEM study revealed a well-arranged network of calcified cartilage trabeculae placed just underneath the non-calcified cartilage cap (Fig. 5). Those trabeculae showed a centripetal calcification gradient and, more deeply, some woven bone formation appeared on the surface of those trabeculae, forming a network of osseochondral trabeculae (Fig. 6). The innermost area of the exostoses was formed exclusively by a dense network of woven and lamellar bone trabeculae. The histological and BS-SEM findings demonstrated a well-arranged normal endochondral ossification process following a centripetal pattern inside the bony mass confirming the diagnosis of MCE.

**Discussion**

Multiple cartilaginous exostosis is a skeletal disorder which primarily affects bones that develop by endochondral ossification (8). Bones of intramembranous origin are not affected (9), except in feline MCE (14). Canine MCE is regarded as a self-limiting disease in which growth ceases at the time of skeletal maturity (14).

The vertebrae, ribs and long bones are most commonly affected in the dog (6). Although all of the regions of the vertebral column may be involved, the spinous processes of the thoracic region, as in the case reported here, is the most common site (14). Posterior vertebral elements (neural arch and spinous process) are also the areas from where spinal osteochondromas originate most frequently in humans (16). Unlike the dog, the

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most frequent region affected in humans is not the thoracic segment, but the cervical region (16). Exostoses affecting the ribs can be found on both lateral and pleural rib surfaces, but those on the pleural aspect are especially prominent (17) and may compress pulmonary lobes, as in the case reported here.

Limb exostoses are located on the outer cortical surface of the metaphysis or adjacent diaphysis of long bones, whereas the epiphysis is never involved (14). In some cases, the exostoses can directly (9), or indirectly (12), involve the growth plate, leading to limb shortening or angular deformities. In the case described in this paper, the round-shaped exostoses of the ribs and vertebrae, with a sessile base and the more varied shape of the long-bone exostoses, are comparable with the pattern previously described by Watson (18). All of the exostoses observed in our case were contiguous with bone cortices. We did not observe appendicular exostoses completely separated from the underlying bone resembling tumoral calcinosis, as reported by some authors (9).

Neither did we observe the pattern described by other authors in which the limb exostoses follow a bilaterally symmetrical distribution (12, 17).

Unless enlargement causes dysfunction by compression of a vital structure such as the spinal cord (2, 15) or the trachea (1), the dogs with MCE may remain subclinical. If the lesion interferes with the movement of a joint (1) or undergoes malignant transformation (8, 4), the condition can also...
show clinical signs. About half of the dogs with MCE have a history of intermittent or progressive lameness or progressive paresis (14).

The clinical signs of the patient reported in this paper could be related to an impingement of a peripheral nerve. The fact that none of the spinal exostoses found in our study appeared to compress the spinal cord and that the exostoses by themselves are apparently non-painful (12), even when larger masses are present, seems to support this statement. A similar case to the one described here has been reported in human medicine with intermittent radial nerve palsy due to a humeral osteochondroma (19). When spinal cord compression is present, complete removal of the exostosis has been reported with good results (2). In this case, surgical removal of the limb masses was not considered due to the problem of establishing which limb exostosis was causing the clinical signs, the difficulty of removing the bony protruberances without damaging the impinged anatomical structures or compromising the functionality of the limb and finally, due to the possibility that other masses may continue growing until skeletal maturity, thus creating further clinical problems or malignant transformation.

In a review of 21 reported cases of canine MCE, eight were euthanized before one year of age, due to the progression of signs caused by MCE and five of the remaining 13 had neoplastic transformation of a single exostosis when they were seven to 10 years old (9). Radiographic signs of malignancy include loss of the smooth contour of an exostosis accompanied by bone destruction or production within the exostosis or along its base (14). Apparent enlargement of the exostoses on serial radiographs should be interpreted with caution because the enlargement may be due to progressive calcification of the cartilage cap, leading to a misdiagnosis of a malignant bone tumour (4). Chondrosarcomas and osteosarcomas are usually reported as a result of a malignant transformation of a single exostosis in the dog (8, 9), and a parosteal sarcoma has been described in the cat (14). Sequential radiographic studies and bone biopsy are necessary to confirm neoplastic transformation of an exostosis. Chondrosarcomatous transformation in humans is reported in 1%-5% of solitary osteochondromas and 10%-25% of patients with MCE (10, 16). It has been suggested that malignancy of these lesions in humans can be determined by the thickness of the cartilaginous cap as seen by magnetic resonance. A thickness greater than two to three centimeters warrants consideration of malignancy (16).

The aetiology of canine MCE is uncertain. It has been shown that a single dominant autosomal gene is responsible for MCE in human beings (16) and horses (22) and probably also in dogs (3, 7, 8). Due to its similarities with juvenile osteochondromatosis, the two main theories based on the human condition have been adopted by veterinary medicine. The first theory explores factors such as perichondrial ring defects, or physical stresses at the margin of the growth plate, which lead to a proliferation of the growth plate in an unnatural direction, developing a growth plate-like structure at right angles to the bone shaft (14). Biochemical disorders in cartilage matrix synthesis may also cause loss of chondrocyte cohesion within the growth plate, allowing redirection of endochondral growth (14). Mutation of the genes encoding glycosyltransferase, an enzyme that takes part in the heparan sulphate proteoglycan biosynthesis, is involved in human MCE (20). The second theory considers that the defect may lie with the periosteum, which due to some unknown initiating factor may regain its perichondrial potential (2, 14). Some authors believe that both theories are not mutually exclusive (14). On the other hand, the feline leukaemia virus has been implicated in feline MCE (9) and viral particles have been detected in the chondrocytes of the cartilage cap of feline patients (14).

The BS-SEM technique allows the histological study of undecalcified samples, avoiding the loss of valuable information as a consequence of the decalcification process of the samples for conventional histology (5). The BS-SEM identification of the different calcified tissues observed in our study was based on the back-scattered electron contrast and fibre arrangement of the matrix, as well as the size and shape of the cellular lacunae, as has been previously described (5). The BS-SEM findings demonstrated a well-arranged normal endochondral ossification process but placed in an incorrect site. The centripetal calcification pattern, inside the bony masses and the changes regarding composition and maturity of the trabeculae, can only be clearly identified with this technique, which, to the authors’ knowledge, is the first histological description of the disease using undecalcified samples.

Finally, the early age of onset, the metaphyseal location of the limb lesions in the majority of cases, and the characteristic radiographic and histological patterns, allow for the differentiation between MCE from other syndromes characterised by benign polyostotic exostoses, such as canine disseminated idiopathic skeletal hyperostosis (DISH) (11) or tumoural calcinosis (9).
References


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