Fibrodysplasia Ossificans Progressiva in a Maine Coon Cat with Prominent Ossification in Dorsal Muscle

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ABSTRACT. A one-year and six-month-old female Maine Coon cat presented with skin problems and paravertebral induration with a history of seven months. Survey radiographs and computed tomography revealed prominent calcifications in both sides of cervical, thoracic and lumbar vertebrae and soft tissue in femoral regions, below knee regions and in brachial regions. Histopathological findings from muscle biopsy samples showed connective tissue proliferation around adjacent skeletal muscle, cartilage formation and endochondral ossification. On the basis of these findings, this feline patient was diagnosed with fibrodysplasia ossificans progressiva (FOP). The most prominent signs observed in this FOP case were significant calcifications of dorsal muscle and presentation of cutaneous signs at the early stage.

KEY WORDS: feline, fibrodysplasia ossificans progressiva.

Fibrodysplasia ossificans progressiva (FOP) is a rare connective tissue disorder in humans and is inherited in an autosomal dominant manner [8–10]. FOP in humans is characterized by congenital malformation of the great toe and progressive heterotopic ossification of tendons, ligaments, fasciae and skeletal muscles, which begins in the first decade of life [2, 5]. The ossification of skeletal muscles often shows a typical anatomical distribution pattern involving the upper back and neck [5, 7, 11].

In cats, only seven cases presenting with FOP-like conditions have been reported to date, and none of them were related by birth [6, 13, 14]. All the feline patients were diagnosed as FOP based on radiographic and histopathological findings of lesions and were euthanized because their conditions poorly responded to treatment.

The clinical signs of the above feline patients on admission included stiffness, posterior paresis and progressively altered gait, with no dermatological manifestations, in contrast to human FOP cases, which often exhibit seborrhea and baldness. We present herein the case of a Maine Coon cat admitted to our hospital due to dermatological problems without an apparently abnormal gait. She was diagnosed with FOP based on X-ray findings and computed tomography (CT) which showed vigorous multiple ossifications of dorsal muscle area. Clinical signs and histopathological findings corresponded to the diagnosis.

A one-year and six-month-old female Maine Coon cat presented with alopecia, pigmentation, crust, seborrhea and erythema on the pinna, abdomen, axilla and inner side of the femoral region (Fig. 1a). Purpura was observed in the left forearm and the inguinal region (Fig. 1b). These symptoms started when the cat was eleven months old and gradually extended to the other areas of the body. Physical examination revealed bilateral popliteal lymphadenopathy and paravertebral induration. The cat had an awkward gait without pain at physical examination, and routine neurological examination revealed no abnormal results.

Routine hematology and biochemistry revealed mild leukocytosis (19.8 x 10⁹/L) and elevated plasma alkaline phosphatase (203 U/L), but the plasma concentrations of urea nitrogen, creatinine, calcium, phosphorus, glucose, total cholesterol and total protein were within the normal limits. Malassezia yeast was detected in an impression smear from the axillary region and ventral skin.

Survey radiographs revealed multiple calcifications around vertebral and femoral regions, in soft tissue below knee regions and in brachial regions; there was also lowered transparency of bronchial tubes. CT indicated significant ossifications in both sides of cervical, thoracic and lumbar vertebrae (Fig. 2). CT numbers of the calcified lesion were 675.2 ± 44.7 Hounsfield units, mean ± SD). These significant ossifications seemed to existed in the locations of muscles.

Since the feline patient was suspected to have FOP based on the clinical signs and the CT scans, an incision biopsy under general anesthesia was performed to obtain muscle tissue from the lumber longissimus. Skin punch biopsy samples were also obtained from axilla and abdominal lesions. In muscle sections stained with hematoxylin and eosin, connective tissue proliferation around adjacent skeletal muscle was evident with cartilage formation and endochondral ossification (Fig. 3).

Proliferative connective tissue invaded into muscle fibers. Hyaline and vacuolar degeneration of muscle fibers

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were observed, with muscle fibers being replaced in a large part by the connective tissue. Infiltration of inflammatory cells was minimal in the muscle sample. In skin sections, acanthosis and vacuolar degeneration were observed in the epidermis, and a pale basophilic mucinous change was seen in the superficial dermis (Fig. 4). The mucinous materials were positive for Alcian blue (pH 2.5) staining. In Periodic acid-Schiff-stained skin sections, a few Malassezia yeast was observed in the stratum corneum. In the present case, the cat died unexpectedly 6 months after diagnosis. At necropsy, extensive edema and congestion were observed in both lungs. The histopathological findings for muscle tissue obtained at necropsy were similar to the biopsy findings except for infiltration of lymphocytes and plasma cells in muscular tissue.

FOP, a rare connective tissue disease, is an inherited disorder with an autosomal dominant trait in humans. FOP in humans is characterized by the proliferation and ossification of skeletal-muscle-associated connective tissues, primarily aponeuroses, fasciae, tendons and ligaments. Recently, a causative gene mutation was discovered in the gene of the BMP type1 receptor in human patients with FOP [10]. However, the cause of FOP in cats is not well known, and there is no evidence that the disorder is inherited [14]. As only seven feline cases of FOP have been reported so far [1, 6, 12–14], it is not obvious whether feline FOP is the counterpart of human FOP, whether it occurs in a familial fashion or whether there is a predisposed breed. The age at onset of clinical signs in the seven reported cases ranged from 10 months to 6 years old (median 2.6 years). The age at onset of clinical signs in the present case was thought to be earlier than that of the other seven feline FOP cases.

Of the 34 human FOP cases reported by Connors and Evans [2], six cases presented with skin manifestations such as baldness and seborrhea. In contrast, all the reported feline FOP cases presented with muscle swelling and progressive stiffness without skin problems at the initial admission. However, it is not surprising that this case revealed skin manifestations as a chief complaint because strong epidermal cell proliferation might be a response to undermin-
Heterotopic ossification around skeletal muscle has been observed in all the reported cases, primarily in the forelimb and thigh soft tissue in four of seven cats, cervical soft tissue in two cats, hindlimb in one cat and dorsal soft tissue in one cat. In contrast, in the present case, heterotopic ossification in perivertebral lesions was severe, whereas that in the limbs was mild. The difference of the ossified lesions may be related to the milder stiff gait and the existence of cutaneous signs at the first presentation.

The histopathological findings in the muscles in feline FOP are similar to those in human FOP [1, 6, 12–14]. In some feline cases, perivascular lymphocytic infiltration in lesional muscle tissue was regarded as the earliest histopathological finding, and this has also been noted in human patients with FOP [4]. There were no histopathological findings such as the inflammatory infiltration in the present case, although the onset of FOP in this case is thought to
The previous feline cases were treated with various drugs including vitamin E, selenium, prednisone and diphosphonate disodium etidronate [6, 13]; however, clinical improvement was not achieved, and the cats were euthanized within several months after diagnosis. The present patient was observed without therapy and died suddenly. Thoracic radiography and necropsy findings suggested that dyspnea due to ossification of bronchial tubes might have been a major cause of death.

REFERENCES


