

Auricular Chondritis Associated with Systemic Joint and Cartilage Inflammation in a Cat

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ABSTRACT. An adult, Japanese domestic cat presented with bilateral swelling, distortion, and erythema of ears and deformation of the limbs. Biopsy of the pinnae confirmed auricular chondritis. These lesions and the cat's general condition subsequently deteriorated, and the cat died. At necropsy, chondral changes were present in the pinnae, costae, larynx, trachea, and limbs. Histopathologically, these chondral tissues showed marked deformation with lymphocytic inflammation. The limb joint inflammation was associated with chondral erosion, deformation of subchondral bones with pannus, and thinning of cancellous bones. These lesions were consistent with the diagnostic criteria for human relapsing polychondritis. However, the cat had erosive arthritis, which appeared to be different from human relapsing polychondritis.

KEY WORDS: auricular chondritis, feline, relapsing polychondritis.

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Relapsing polychondritis (RPC) is a rare, systemic disease characterized by inflammation and destruction involving both articular and nonarticular cartilaginous structures with subsequent replacement by connective tissue [10]. In cats, a similar rare condition has been recognized as an auricular chondritis, characterized by inflammation and destruction of auricular cartilage. Gerber *et al.* [5] reported that there were only 11 cases of feline RPC reported in the literature, and they described two additional cases of feline RPC. However, only the auricular cartilage was affected in 11 cases, and the disease condition has not been reported to have a relapsing nature. Hence, in cats, the term relapsing polychondritis may be inappropriate [11]. The present report describes a cat with typical auricular chondritis associated with articular and nonarticular chondritis involving multiple sites.

A three-year-old, castrated, male, Japanese domestic cat presented with a gait abnormality. Before the gait abnormality had developed, the cat had uveitis and received treatment. Eight months later, the cat developed bilateral alopecia, as well as swelling, distortion, and erythema of the ears (Fig. 1). Biopsies of the ear edges were performed to confirm the diagnosis of auricular chondritis. Histopathological examination of the biopsy specimens revealed thinning, curling, and rupture of the auricular cartilage, and severe neutrophil infiltration destroyed the cartilage which was surrounded by granulation tissue (Fig. 2). These histologic lesions were consistent with those seen in auricular chondritis. One month later, the cat developed deformations of the carpal and tarsal joints. Then, the cat was given 5.0

mg/kg/day of oral cyclosporine (Neoral; Novartis pharma, Tokyo, Japan). Three months later, the limb joints developed severe instability and luxation. Radiographic examination showed luxation, periosteal proliferation, and osteolysis of the carpus and tarsus. The blood tests were within normal limits, except for an elevated white blood cell count (44,000/ μ l) and an increased plasma glucose level (216 mg/dl). The blood test was negative for feline immunodeficiency virus and feline infectious peritonitis virus, but the test for feline leukemia virus and the direct Coombs' test were positive. Ear swabs were negative for parasites. The dose of cyclosporine was increased to 7.5 mg/kg/day and the cat was given another treatment with oral dapsone (Lectisol, diaphenylsulfone (JAN); Mitsubishi Tanabe Pharma, Osaka, Japan) at a dose of 1.0 mg/kg/day. Subsequently, the cat's general condition deteriorated and the cat died.

At necropsy, the pinnae were firm, deformed, and thickened. The costal cartilages were swollen (Fig. 3), and the laryngeal cartilages were thickened. The articular cartilages of most peripheral joints were severely eroded. The right knee lesion was so severe that the meniscus and the ligaments had disappeared, and the tibial cartilages were deformed (Fig. 4). Other findings included swelling and hemorrhage of the mandibular, superficial cervical and other internal lymph nodes. The spleen was swollen and discolored due to marked swelling of the lymphoid structure, with yellowish necrotic foci on the surface. The liver was fragile, with multifocal white to yellow nodules, some of which had a concave surface. The thoracic and abdominal cavities contained a large amount of fluid with fibrin deposition on the visceral surfaces.

Histologically, the pinnae showed severe cartilage destruction with extensive fibroplasia, lymphocytic infiltration, and focal chondral regeneration. Periadnexal infiltration of

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mononuclear cells was also noted (Fig. 5). The subchondral bones of the limb joints were destroyed, and the cancellous bones showed marked thinning. There was partial disappearance and erosion of the articular cartilages, with inflammation, fibroplasia, and periosteal proliferation. The trachea and larynx showed submucosal lymphocytic inflammation. There was chondrolysis of the thyroid cartilage, with lymphocytic inflammation and fibroplasia. The costal cartilages were irregularly hypertrophic, and there was associated bone formation. Lymphocytes, macrophages, and neutrophils infiltrated around the cartilage (Fig. 6).

In the spleen and regional lymph nodes, there were many large follicular structures that had replaced the specific structure of the organs. The predominant cells in the follicular structures were large blastic cells, which had vesicular nuclei with thick nuclear membranes and a finely branched chromatin pattern. Mitotic figures were common. These blastic cells were BLA-36 (BioGenex, San Ramon, CA, U.S.A.)-positive, indicating a diagnosis of B-cell lymphoma.

The hepatic nodular lesions showed extensive fibrosis that divided the hepatocyte plates into small clusters of individual hepatocytes with lymphocytic infiltration. Other areas showed diffuse centrilobular lipidosis and bile duct proliferation with lymphocytic infiltration.

In humans, RPC is an inflammatory connective tissue disease that may affect multiple organ systems, including auricular and nasal cartilages, the vestibuloauditory apparatus, the central nervous system, eyes, cardiac valves, blood vessels, multiple joints, and tracheal cartilage [2]. It is often classified into the connective tissue immune-mediated diseases because of similarities to rheumatoid arthritis and lupus erythematosus, as well as its favorable response to corticosteroid therapy [10]. The immune-mediated destruction is directed against tissues containing type II collagen [2]. McAdam *et al.* [6] proposed that the diagnosis is based primarily on six clinical features (bilateral auricular chondritis, nonerosive sero-negative inflammatory polyarthritis, nasal chondritis, ocular inflammation, respiratory tract chondritis, and audiovestibular damage), and it is quite likely that three or more criteria are present along with histological confirmation. To the best of our knowledge, only 13 cases of feline RPC have been reported in the literature [5]. The clinical and histopathological features of the auricular lesions seen in these cases are similar to those seen in human RPC. However, in cats, only the auricular cartilage is affected, and the condition has not been reported to have a relapsing nature [11]. In the present case, the lesions affecting the auricular cartilages were similar to those described previously [2, 4, 5, 10, 11]. In addition, this case had uveitis, similar to that described in 2 feline cases [2, 5]. Damiani and Levine [3] modified McAdam's diagnostic criteria for human RPC as follows: 1. at least three or more diagnostic criteria, histologic conformation not necessary; 2. one or more of McAdam's signs with positive histological confirmation; or 3. chondritis in two or more separate anatomic locations with response to steroid and/or dapsone

treatment. According to their criteria, this case fulfilled the diagnostic criteria of human RPC. Furthermore, this case fulfilled McAdam's diagnostic criteria of human RPC and was histologically confirmed to have chondritis of the respiratory tract and costal cartilage, which has never been described in cats. Therefore, this case may be consistent with human RPC.

In the biopsy specimen, the inflammatory cells in pinnae were mainly neutrophils. However, at necropsy, pinnae showed severe lymphocytic infiltration, fibroplasia and focal chondral regeneration. Some feline RPC cases showed a neutrophilic infiltration around the auricular cartilage [2, 4, 5] as seen in the biopsy specimen of our case. In human RPC, there was perichondral inflammation mainly composed of lymphocytes, but neutrophils may be predominant in early lesions [9]. McCune *et al.* [7] reported the experimental model of auricular chondritis developed in Sprague-Dawley rats after the onset of type II collagen-induced arthritis. They observed infiltration of neutrophils and mononuclear cells around the cartilage in early stage. In the latter stage, infiltration of epithelioid histiocytes and proliferation of fibroblasts and blood vessels developed in association with the destroyed cartilage. Finally, regenerating nodules of immature elastic cartilage and small aggregates of plasma cells appeared in the pinna lesions. Therefore, we suspect that the type of the inflammatory cells represents the stage of the disease.

This case had been given cyclosporine and dapsone. A variety of drugs including corticosteroids, nonsteroidal anti-inflammatory drugs, immunosuppressive and cytotoxic drugs have been used for the treatment of human RPC [9]. Corticosteroids reliably lead to resolution of chondritis [9, 12]. In contrast, various dosages of glucocorticoids were not effective in cats with RPC [5]. However, dapsone appeared to result in some clinical improvement, and its mechanism of action has been proposed to be an effect on the immune system or inhibition of lysosomal enzymes [5]. This case was given a dose of diaphenylsulfone for two months but the lesions were not improved.

Polyarthritis, which is commonly diagnosed with auricular chondritis in human RPC, was observed in this case. However, the present case's lesions were erosive and differed from the lesions of human RPC. The polyarthritis in the present case was similar to that seen in chronic progressive polyarthritis (CPP) of cats with respect to age, sex, and histopathological changes [8]. Therefore, the arthritis in the present case was diagnosed as the deforming type of CPP.

The present case had malignant lymphoma. In humans, some chronic inflammatory conditions, such as rheumatoid arthritis, are associated with malignant lymphoma [1]. CPP [8] and PRC [10] are both cartilage-deforming diseases that are considered to be associated with autoimmune abnormalities. In the present case, the systemic lesions of the joints and cartilages may have been associated with the lymphoma, or the tumor might have aggravated these conditions.



Fig. 1. Thickening, distortion, and erythema of the right pinna.

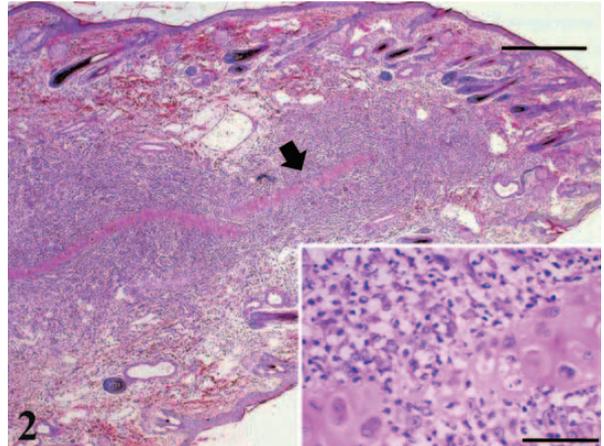


Fig. 2. Biopsy specimen of the pinna. Auricular cartilages show thinning, curling, and splitting, with severe neutrophil infiltration. Bar=500 μ m. Inset: High magnification of the lesion indicated by arrow. Note neutrophils and mononuclear cells invading the cartilage. Bar=50 μ m.



Fig. 3. Costal cartilage and sternum showing irregular swelling (*). Formalin-fixed specimen.

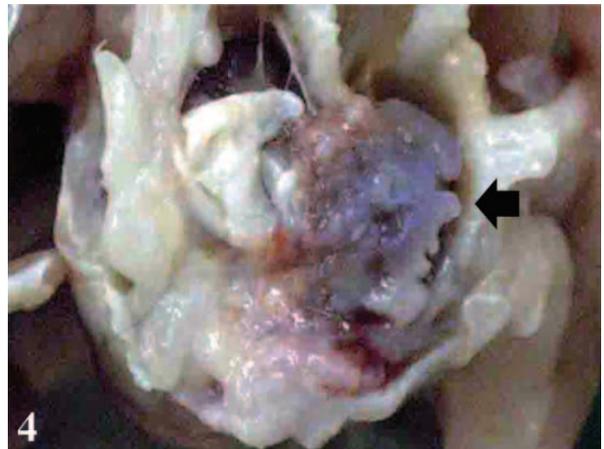


Fig. 4. Articular surface of the right knee. The tibial cartilages are deformed (arrow), and the meniscus and ligaments have disappeared. Formalin-fixed specimen.

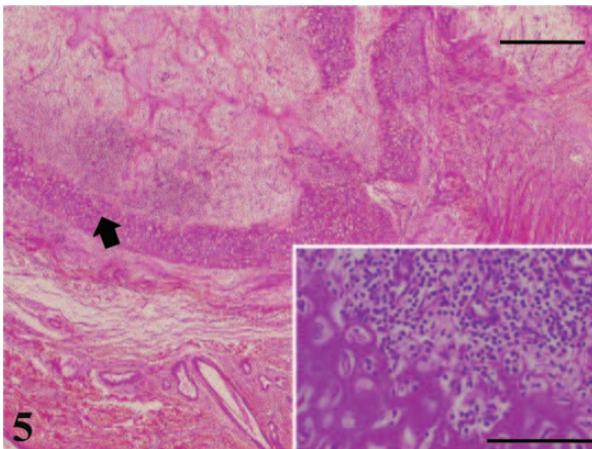


Fig. 5. The pinna at necropsy. Severe disruption of the cartilage, with extensive fibroplasia, lymphocytic infiltration, and focal chondral regeneration can be seen. Bar=500 μ m. Inset: High magnification of the lesion indicated by arrow. Note lymphocytes invading the cartilage accompanied by vascularization. Bar=100 μ m.

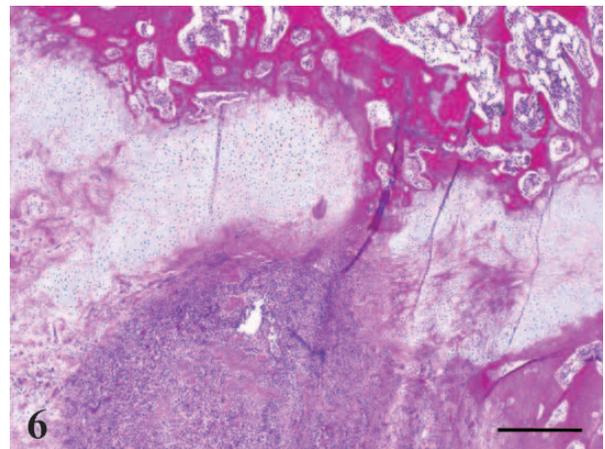


Fig. 6. Costal cartilages showing irregular hypertrophy and bone formation. Note leukocytic infiltration around the cartilages. Bar=500 μ m.

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