A nasopharyngeal inflammatory polyp in a cat: histopathology, immunohistochemistry, and CT scan findings

Hamid Reza MOOSAVIAN1,*, Hamideh ESMAEILZADEH2, Ramesh VAHABI2, Rana VAFAEI4, Mohammad Reza ESMAILINEJAD3

1 Department of Clinical Pathology, Faculty of Veterinary Medicine, University of Tehran, Tehran, Iran
2 Department of Pathology and Laboratory Medicine, Isfahan University of Medical Sciences, Isfahan, Iran
3 Department of Surgery and Radiology, Faculty of Veterinary Medicine, University of Tehran, Tehran, Iran

Abstract: The etiology of feline nasopharyngeal inflammatory polyps (FNIPs) has not been completely understood. To the best of our knowledge, there is no study having evaluated the immunohistochemical features of FNIPs. More studies about the histopathological characteristics of such lesions can play a pivotal role in further understanding the disease. We present the clinical manifestations, computed tomography (CT) scan, histopathology, and immunohistochemistry features of a FNIP in a 7-year-old male neutered domestic shorthair cat. CT scan examination showed nasopharyngeal space occupation with some parts of destruction in nasal cavity. Immunohistochemical study of the sections demonstrated the presence of CD3+ lymphocytes, and no reactivity was seen with CD79a. Masson's trichrome staining of the sections showed focal deposition of collagen fibers, and no goblet cells were observed in PAS staining. In conclusion, the significant neutrophilic and lymphocytic infiltration along with tissue edema and increased fibrin and collagen deposition probably point to the involvement of both innate and probably adaptive immune systems in FNIPs. Furthermore, in histopathological studies, there were no remarkable findings of allergic reactions.

Key words: Feline nasopharyngeal inflammatory polyp, computed tomography scan, histopathology, immunohistochemistry

1. Introduction
The most common diseases of the middle ear in cats are otitis media and polyps (1). Feline nasopharyngeal inflammatory polyps (FNIPs), categorized as benign, pedunculated, inflammatory, and nonneoplastic lesions, originate either from the tympanic bulla epithelial lining or from the auditory tube. The polyps that originate from the auditory tube form the middle ear or nasopharyngeal polyps (2). The etiology of FNIPs is not completely understood so far. Overall, the origin of feline nasopharyngeal polyps is either congenital or acquired (3). Response to chronic upper respiratory tract infection, ascending infection from the nasopharynx, and chronic otitis media can have an important role in nasal polyposis (4,5). Nasal polyps can be diagnosed by historical, clinical, rhinoscopic, and histopathologic findings. However, complementary techniques such as immunohistochemistry and computed tomography (CT) scanning can add valuable information. Immunohistochemistry results can help to explain the polyp's pathogenesis, which varies among different patients. Undoubtedly, in this situation, more effective therapies can be selected for each patient. CT scanning as a fast and readily accessible imaging technique can have a pivotal role in primary diagnosis, surveys of the size and location of polyps in deeper areas of the sinuses, evaluation of the extent of inflammation, monitoring, and treatment outcome. CT image analysis along with histopathologic findings can elucidate the origin of the polyp (tympanic cavity, nasopharynx, or external ear canal). On the other hand, the polyp extension and peripheral bone involvement and destruction can be detected by CT scans (6,7). In the present study, clinical signs, histopathology, immunohistochemistry, and CT findings in a cat with a FNIP are described.

2. Case history
We present the clinical, CT scan, histopathological, and immunohistochemical features of a FNIP in a cat. Four years ago, a 3-year-old male neutered domestic shorthair cat was referred for investigation of halitosis and gingivitis. The cat had a history of an accident and rear limb paralysis. Conservative therapy with antibiotics (a 1-week course of
amoxicillin/clavulanic acid as 60 mg/cat every 12 h and metronidazole as 15 mg/kg every 24 h) was indicated, and the patient was discharged.

Two years later, the cat was presented for stomatitis, rhinitis, nasal mucopurulent discharge, and conjunctivitis. CT scan findings revealed an intranasal mass with invasion of the adjacent bony structures, complete destruction of the right hard palate and the right maxillary sinus, partial destruction of the nasal sinus, severe soft tissue attenuation within the right frontal and ethmoidal sinuses, soft tissue swelling, and an abscess around the root of the right maxillary canine tooth (Figure 1A). Removal of the mass by surgery was recommended, but the owner did not consent to the surgery. Dental extraction was performed and clinical signs were relieved. In addition, conservative treatment including some short intermittent periods of antibiotic therapy, as mentioned previously, and antiinflammatory agents (prednisolone at 2 mg/kg once when rhinitis with serous discharge was detected) was transiently improving the symptoms.

Two years later, the patient was referred with unilateral nasal mucopurulent discharge. CT examination showed the presence of a soft tissue mass that elongated from the rostral part of the right nasal cavity up to the cribriform plate, associated with increased attenuation after contrast medium administration (3 mL/kg, intravenous injection of IOHEXOL 240 mg/mL) because of moderate blood supply. Furthermore, complete filling of the right frontal sinus with fluid and a soft tissue mass with several parts of active osteolysis in the right ethmoid turbinate, nasal septum, hard palate, right orbital, and frontal bones were seen. In addition, a small amount of active and irregular new bone formation and large lysis in the right maxillary and nasal bones were noticeable, causing loss of all right maxillary incisor, canine, premolar, and molar teeth (Figures 1B, 2A, and 2B). Invasions of the adjacent bony structures and especially osteolysis in the hard palate, nasal septum, right maxillary, and nasal bones were progressive and more severe in comparison to the last exam, performed about 2 years previously (Figures 1A and 1B). Moreover, some parts of destruction in the left nasal cavity, which were not seen in the previous CT scan, were present in the second CT scan.

Cytology findings showed a huge population of degenerated neutrophils, and fungal culture results were negative. For more studies, biopsy and histopathological and immunohistochemical examinations were performed (Figures 3, 4A, and 4B). Tissue samples were also studied by Masson’s trichrome and PAS staining (Figures 4C and 4D). For histopathological study, biopsy specimens were fixed in 10% neutral buffered formalin, then washed and processed through a series of graded alcohols and embedded in paraffin. Sections from well-preserved paraffin-embedded tissues were cut at 4 µm and dried in a 50 °C oven overnight. Stainings with hematoxylin and eosin, PAS, and Masson’s trichrome were done on the tissues. Rabbit monoclonal antibodies (Leica Biosystems, dilution 1:200) were used for immunohistochemical staining (CD3 and CD79a). Tissue sections were deparaffinized with xylene and rehydrated through a series of graded alcohols to distilled water. For antigen retrieval, the sections were boiled in 1 mM EDTA (pH 8.0) for 10 min, followed by washing in distilled water.

Figure 1. Comparison between first (A) and second (B) CT scans of the nasal polyp (red arrow) after 2 years. Unilateral frontal sinus discharges (asterisks), severe destruction in septa of frontal sinus (yellow arrow), and invasion to the left side are visible in B. The nasal polyp demonstrates enhancement of the peripheral rim.
and then PBS two times for 5 min each. Treatment with a blocking solution for 15 min was used to block endogenous peroxidase activity. After removing the blocking solution, the primary antibody was added, followed by washing and incubation with the secondary antibody. After washing, a suitable chromogen was added for 5 min, and finally the sections were counterstained with hematoxylin and dehydrated in 95% ethanol for 5 s. Histologically, the lesion demonstrated a respiratory mucosa with edematous and loose stroma and severe inflammatory cell infiltration. Immunohistochemical study of the sections demonstrated the presence of CD3+ lymphocytes, and no reactivity was seen with CD79a. Masson's trichrome staining of the sections showed focal deposition of collagen fibers, and no goblet cells were observed in PAS staining. Surgical removal of the polyp was indicated as the treatment of choice, but the owner did not agree.

3. Results and discussion

FNIPs are one of the most common diseases of the upper respiratory tract in cats (1). The etiology of FNIPs has not yet been fully elucidated. Based on studies in humans, inflammatory cells of both the innate and the adaptive immune system may have an important role in nasal polyposis. The nasopharyngeal mucosa is an essential barrier protecting the host from exposure to foreign antigens and microbial colonization. The impairment of the barrier's integrity and innate immunity has been reported in patients with chronic inflammation, atopic dermatitis, and asthma. Reduction of important proteins in epithelial defense and repair such as S100A7 and S100A8/9 has been shown in patients with chronic rhinosinusitis with nasal polyps (8–10). Defects in this barrier have a pivotal role in dysregulation of local immune homeostasis, microbial colonization, and increased allergic sensitization and can finally lead to nasal polyposis establishment (11,12).
The significance of tissue inflammatory cells of innate immunity such as neutrophils, mast cells, and eosinophils has not been completely understood in nasal polyposis. Studies of patients from western countries have shown that nasal polyps are characterized by predominant eosinophilic inflammation, while neutrophils are usually the predominant cells in patients from eastern countries. In some human patients with nasopharyngeal polyps, especially in patients with eosinophilia, tissue mast cell infiltration has been seen (13,14). Based on a literature review, the exact pathogenesis, prevalence, and extent of eosinophilia and tissue infiltration of eosinophils and mast cells in feline nasopharyngeal polyps are not completely understood, and the exact role of these cells in nasal polyposis as a causative or bystander factor both in human patients and animals is also controversial. In the present study, many neutrophils and a few eosinophils in an edematous background were observed. On the other hand, in addition to the innate immune system, the adaptive immune system may have a pivotal role in nasal polyposis. In polyp tissues, elevated expressions of mediators such as B-cell-attracting chemokines, B-cell survival factor, and B-cell-activating factor of the TNF family are important factors in the proliferation and accumulation of B-cells in respective tissues (11). Increased local synthesis of autoantibodies such as IgG, IgE, and IgA has been documented in polyp tissues, and some of them, especially IgE, can have potential pathogenic importance (15). Polyclonal production of IgE antibodies, often initiated by *Staphylococcus aureus*-derived enterotoxins, is identified in sinonasal tissues in allergic and nonallergic rhinitis, atopic and nonatopic sinonasal polyposis, and allergic fungal rhinosinusitis. IgE can induce degranulation of mast cells and basophils and amplify the Th2 response within the mucosal tissue, resulting in the release of typical mediators in patients with allergic rhinitis and nasal polyposis.

Figure 4. Representative photomicrographs of nasal mucosa sections stained with CD3 and CD79a, Masson’s trichrome, and periodic acid–Schiff (PAS). Scattered cells of CD3 T lymphocytes (arrowhead) were present in the stroma (magnification: 400×) (A). There were no CD79a T lymphocytes (magnification: 400×) (B). Masson’s trichrome staining showed the basement membrane thickness and increased subepithelial collagen deposition (arrowhead) (magnification: 100×) (C). PAS staining showed the lack of goblet cell hyperplasia (magnification: 100×) (D).
significant lymphocytic infiltration (CD3+, CD79a–) along with tissue edema and increased fibrin and collagen deposition can point to the existence of similar mechanisms in polyp development. Although the etiology of feline nasopharyngeal polyps has not been completely elucidated, it appears that branchial arch remnant as a congenital etiology and chronic inflammation as an acquired etiology are the two important causes of FNIPs (19,20). The response to chronic inflammatory processes, such as chronic otitis media or caliciviruses, can have a major role in tissue polyposis. However, the role of caliciviruses and herpes virus in the growth of nasopharyngeal polyps remains controversial. Some studies have demonstrated that the presence of these viruses is not associated with the development of inflammatory polyps (19). Conversely, chronic inflammation can be seen after polyp development, and thus it can be a dilemma in polyp pathogenesis. In the present study, CT scanning had a key role in the primary diagnosis of the nasal polyp. The findings revealed an intranasal mass with invasion and destruction of the adjacent bony structures. A recent study showed that postcontrast CT images can be helpful in distinguishing a nasopharyngeal polyp from a collection of exudate or a neoplastic mass (6). CT scanning also had an important role in the study of the growth rate and extension of the nasal polyp over 2 years. Invasion of the adjacent bony structures and osteolysis in some bones were progressive during 2 years and also the polyp growth caused some parts of destruction in the left nasal cavity, which was not seen in the first CT scan.

In conclusion, in the present study, the presence of polyp tissues in the nasal cavity of a cat with chronic conjunctivitis, rhinitis, gingivitis, and stomatitis may help to uncover the role of chronic inflammation in polyposis. On the other hand, nasopharyngeal polyps can have a key role in chronic and recurrent rhinitis and even stomatitis because of partial or complete obstructions, which may lead to fluid and debris accumulation, bone destruction, and fractures, and finally may serve as a predisposing factor for bacterial colonization. Significant neutrophilic and lymphocytic infiltrations, along with tissue edema and increased fibrin and collagen deposition, can point to the involvement of both innate and probably adaptive immune systems in FNIPs. In the present study, CT scanning had an important role not only in primary diagnosis and location of the polyp but also in the study of the growth rate and extension of the nasal polyp over the course of 2 years.

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References


