



Clinical Report

Multiple Cutaneous Inverted Papilloma in a German shepherd Dog

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Abstract

Case Description- In this clinical report, occurrence of a rare case of canine cutaneous inverted papilloma was discussed. A 4-year-old, intact, male German shepherd dog was presented with multiple skin lesions, located on the inguinal region near the root of penis, which have been progressively growing since two months ago. In close examination of the lesions multiple, firm, painful, and cup-shaped nodules in different sizes with a central pore filled with keratin were observed.

Treatment and Outcome- Surgical excision and histological evaluation was done. Histologically this tumor was characterized by endophytic projections of the epidermis extending into dermis. Cytopathic effects included ballooning degeneration of keratinocytes, koilocytosis, irregularity of keratohyalin granules, and margination of nuclear chromatin. Numerous eosinophilic intranuclear inclusions were present within keratinocytes of endophytic lesion. Immunohistochemically, the tumor cells were intensely positive for pancytokeratin. On the basis of histopathological and clinical findings, the tumor was diagnosed as multiple cutaneous inverted papilloma. There was no recurrence or any other complications in post operative monitoring.

Clinical Relevance- Inverted papillomas are relatively uncommon in dogs; whereas, the incidence of this tumor in the inguinal region is uncommon. Treatment of inverted papilloma was completed by surgical excision in ablating the tumor masses and preventing re-growth.

Key words: Inverted papilloma; dog; skin; surgery

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Case Description

A 4-year-old, intact, male German shepherd dog was presented for treatment of multiple skin lesions, located on the inguinal region near the root of penis. The owner declared that the masses have been growing up rapidly through two months prior to presentation. On clinical examination; all vital signs (heart Rate, respiratory rate and rectal temperature) were in the normal range. On dermatological examination, multiple, firm, painful, and cup-shaped nodules in different sizes with a central pore filled with keratin were observed and the masses had well-demarcated border (Fig. 1).

Treatment and Outcome

Based on the clinical examination, cutaneous neoplasia was suspected and complete surgical excision of the masses was recommended. The dog was premedicated with 0/05 mg/kg acepromazine (KELA Laboratoria) intramuscularly and anesthesia intravenously was induced with 10 mg/kg thiopental sodium (Sandoz) and was maintained with halothane 2% (Halothane BP, Nicholas Piramal). An elliptical incision was made in the skin around the lesion and the masses were dissected from subcutaneous tissues. The skin was sutured with Nylon (Monofil Polyamid, Supa) USP: 2/0 in interrupted suture pattern. Postoperative care included Cefazoline (Exir Pharmaceutical Co.) at 20 mg/kg intramuscularly, every 12 hours for 3 days. The removed masses were fixed in 10% neutral buffered formalin, processed routinely, embedded in paraffin, sectioned at 5 µm thickness, stained with hematoxylin and eosin, and studied with a routine light microscope. Immunohistochemistry of additional section was performed with Avidin–Biotin complex method by using monoclonal antibodies for pancytokeratin antibody (1/500). Microscopic examination at the nodules revealed cup-shaped epidermal proliferation with centripetal papillary projections into dermis (Fig. 2). Some of keratinocytes in hyperplastic epidermis showed ballooning degeneration of keratinocytes, koilocytosis and basophilic keratohyaline granules of various sizes (Fig. 3). Eosinophilic intranuclear inclusion bodies were observed and mitotic figures were seen mostly in the stratum basale (Fig. 4). Immunohistochemical staining revealed strongly positive staining of cytoplasm of tumoral cells for pancytokeratin (Fig. 5). On the basis of histopathological and clinical findings, the tumor was diagnosed as multiple cutaneous inverted papilloma. There was no recurrence or any other complications in post operative monitoring.



Figure 1. Well demarcated, cup-shaped nodules with a central pore filled with keratin.

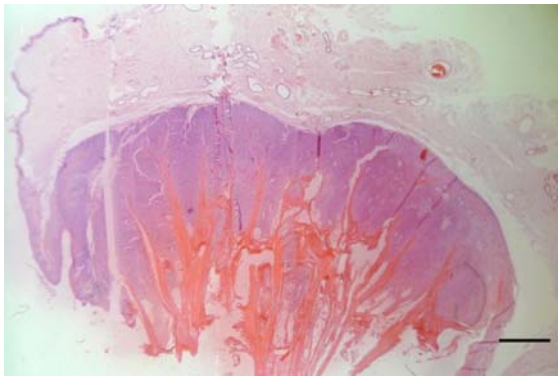


Figure 2. Endophytic projections of the epidermis extending into dermis. HE×20. Bar=1mm

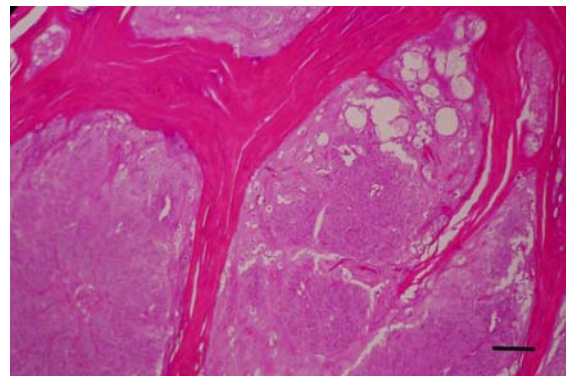


Figure 3. Hyperplastic epidermis with ballooning degeneration of keratinocytes, and koilocytosis. HE×100. Bar=100 µm

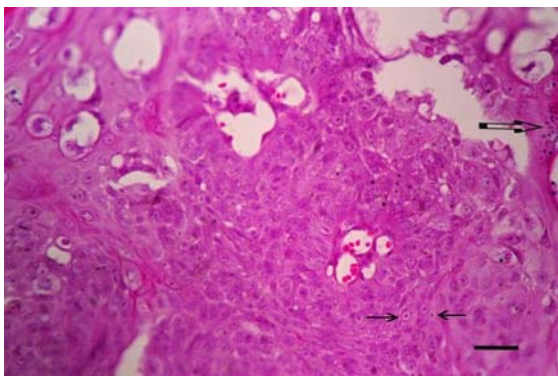


Figure 4. Eosinophilic intranuclear inclusion bodies in keratinocytes (arrow) and basophilic keratohyaline granules in stratum granulosum (open arrow). HE×400. Bar=25 µm

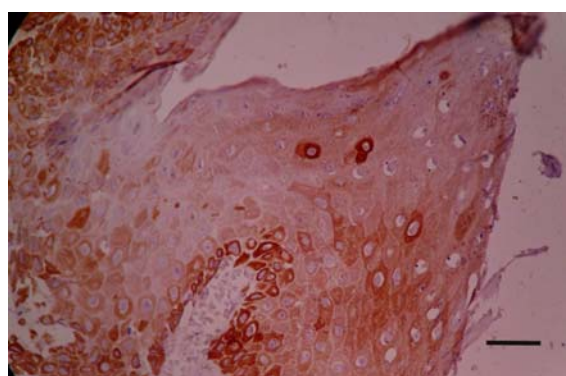


Figure 5. Strong expression of pancytokeratin by neoplastic cells. ABC×100. Bar=100 µm

Discussion

Cutaneous inverted papillomas are uncommon in dogs.¹ In human medicine, inverted papillomas commonly occur in the nasal cavity and paranasal sinuses of humans and have also been found in the urinary bladder.^{2,3,4} Human papillomavirus antigens (HPV) were found in cases of an inverted papilloma of the nasal cavity.⁵ Papillomaviruses are small, double-

stranded DNA viruses that infect a wide variety of animal species.⁶ These viruses are epitheliotropic and tissue specific, affect a wide variety of species, and can be grouped into viruses that affect cutaneous sites and viruses that affect mucosal sites.⁷ In dogs, 2 genetically distinct papillomavirus types and several variations of papillomavirus-associated syndromes have been reported.⁸ Classical viral-induced exophytic cutaneous papillomas in dogs are uncommon, usually occur on haired skin, and often spontaneously regress over time.⁴ Cutaneous inverted papilloma, first described 1988, is a rare endophytic variant that is also associated with papillomavirus but typically does not undergo spontaneous regression.⁹ Canine oral papilloma is another well-described benign lesion that occurs as single or multiple exophytic masses of the oral mucosa. Canine oral papilloma is also generally associated with papillomavirus; however, in situ hybridization suggests that these lesions are induced by a papillomavirus that is distinct from the virus that induces canine cutaneous papillomas.¹⁰ The cytopathology due to papillomavirus infection is very characteristic in paraffin sections. Swollen cells are found in the stratum granulosum. These have been called clear cells or pale cells in cutaneous fibropapillomas of cattle¹¹ and papillomas of horse¹² Affected cells have been called koilocytes in condyloma of the human cervix.¹³

These characteristic changes were evident in the present case of canine inverted papilloma. The source of viral exposure in this case is undetermined and the specific papillomavirus type in these lesions could not be identified, since frozen tissue was not available for more detailed molecular characterization. It is likely that the virus is different from the characterized canine oral papillomavirus, because the lesions affect the skin rather than the oral mucous membranes. Although these lesions resembled intracutaneous cornifying epitheliomas (keratoacanthomas), they appear to be a distinct lesion, probably with a different etiology. Although cutaneous viral papillomas are usually benign, apparent transformation into squamous cell carcinoma has been recognized in some canine cases. The use of immunohistochemistry in the small animal diagnostic routine has already become reality, allowing more accuracy and precision in both diagnosis and prognosis.

The rarity of this type of tumor precludes clinical trials in this field so there are no particular guidelines for the treatment of recurrent tumors but surgical correction can be considered for primary treatment of inverted papilloma in dogs. Accordingly, reporting of similar cases yield useful information about the diagnosis and treatment of canine cutaneous inverted papilloma.

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اولین گزارش پاپیلومای معکوس در یک قلاده سگ نژاد ژرمن شفرد در ایران

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توصیف بیمار: یک قلاده سگ نر چهار ساله، نژاد ژرمن شفرد به دلیل بروز چندین ندول فنجان‌ی شکل دردناک، دارای رشد پیش رونده در پوست ناحیه مغابنی به دانشکده دامپزشکی دانشگاه شهید باهنر کرمان ارجاع داده شد. در ملامسه، ندول‌ها دارای قوامی سفت و محتوای کراتینی بوده و در معاینات بالینی، بررسی تابلوی خونی، آنالیز بیوشیمیایی سرم و رادیوگرافی هیچ گونه علائم غیرطبیعی مشاهده نگردید و حیوان جهت برداشت ضایعات به بخش جراحی ارجاع داده شد.

درمان و نتیجه آن: جهت انجام جراحی، حیوان با رژیم بیهوشی تیوپنتال سدیم با دوز 10 mg/kg و هالوتان 2% بیهوش شد و بعد از آماده سازی ناحیه توسط برش الپتیکال توده‌ها خارج و محل برش توسط نخ نایلون $2/0$ با الگوی تکی ساده بخیه شد و ضایعات در محلول فرمالین 10% جهت تشخیص به بخش پاتولوژی ارسال شد. آنتی بیوتیک تراپی با داروی سفازولین با دوز 20 mg/kg جهت پیشگیری از عفونت اعمال گردید. در بررسی میکروسکوپی ضایعه، اثرات سایتوپاتیک از قبیل دژنراسانس کراتینوسایت‌ها، کویلوسایتوزیس، گرانول‌های کراتوهیالینی و گنجیدگی‌های ائوزینوفیلی داخل هسته‌ای در کراتینوسایت‌ها و ضایعات اندوفیتیک که تا ناحیه درم ادامه داشتند مشاهده گردید که تشخیص حضور پاپیلومای معکوس را تایید نمود.

کاربرد بالینی: حضور این نوع تومور به ویژه در ناحیه مغابنی در سگ‌ها رایج نمی‌باشد و بر اساس مطالعات انجام شده این گزارش، نخستین مورد تشخیص داده شده در ایران است که استفاده از روش جراحی به عنوان درمان اولیه این نوع تومور جهت جلوگیری از بروز حالت بدخیمی در مراحل پیشرفته بیماری توصیه می‌گردد.

کلید واژگان: پاپیلومای معکوس، سگ، برداشت جراحی