JOURNAL of the
AMERICAN ACADEMY OF
DERMATOLOGY
VOLUME 23 NUMBER 5 PART 2 NOVEMBER 1990

# Cutaneous horn of the penis: Its association with squamous cell carcinoma and HPV-16 infection

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Cutaneous horns of the penis are rare. Including this case, only 19 cases have been reported in the English-language literature. In 37% of the reported cases a malignant tumor was found beneath the cutaneous horn. Our case is remarkable because a stage I squamous cell carcinoma developed on the shaft of the penis of a neonatally circumcised man. Human genital carcinoma resulting from a multifactorial process in which "promoting" papillomavirus is an integral element is being increasingly reported. We review the relationship of circumcision to genital human papillomavirus infection and their synergism in the development of squamous cell carcinoma. (J AM ACAD DERMATOL 1990;23:969-72.)

Cutaneous horns are common lesions usually found in sun-exposed areas, but they can be found anywhere on the skin.[1-3] Approximately 20% are associated with malignant lesions, but when a cutaneous horn occurs on the penis the percentage is more than 33%.[4,5]

## CASE REPORT

A 57-year-old black man had a 3-month history of an "irritating growth" on the shaft of the penis. On questioning he revealed that he had had a reddish scaly lesion at the site for about 1 year before the development of a cutaneous horn. The patient was in good health otherwise and reported that he had been circumcised as a neonate.

**Physical examination.** The patient had a 5 mm, pointed, keratotic papule on the distal dorsal aspect of the penile shaft (Fig. 1). Beneath the horn was an erythematous, scaly plaque that measured about 8 mm in diameter. The lesion was freely moveable. The patient had no lymphadenopathy.

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16/4/16640

**Histopathologic findings.** The stratum corneum showed marked compact hyperkeratosis and parakeratosis. Acanthosis of the prickle cell layer with a disordered proliferation of keratinocytes was present (Fig. 2). Other prominent changes included nuclear atypia with nuclear enlargement, irregular chromatin clumping, and hyperchromasia. Focally dyskeratotic cells and multinucleated cells were also present in the dysplastic epithelium. The tumor invaded the papillary dermis focally in the form of well-differentiated squamous cell carcinoma (Fig. 3).

In situ DNA hybridization was performed for human papillomavirus (HPV) types 6, 11, 16, and 18 at the Armed Forces Institute of Pathology. A positive HPV reaction for HPV-16 was found focally in the nuclei of the squamous epithelial cells (Fig. 4). Probes for HPV-6, -11, and -18 were negative.

**Clinical course and treatment.** The lesion was excised with 1 cm clinical margins, and the resection margins were free of tumor. The patient has been examined every 3 months and after 22 months has had no recurrence of the lesion.

## DISCUSSION

The etiology of squamous cell carcinoma of the penis is multifactorial. One of the most important factors is poor hygiene together with lack of circumcision at birth. This combination produces a chronic irritation by the smegma within the preputial sac and secondary infection.[6] Under laboratory condi-

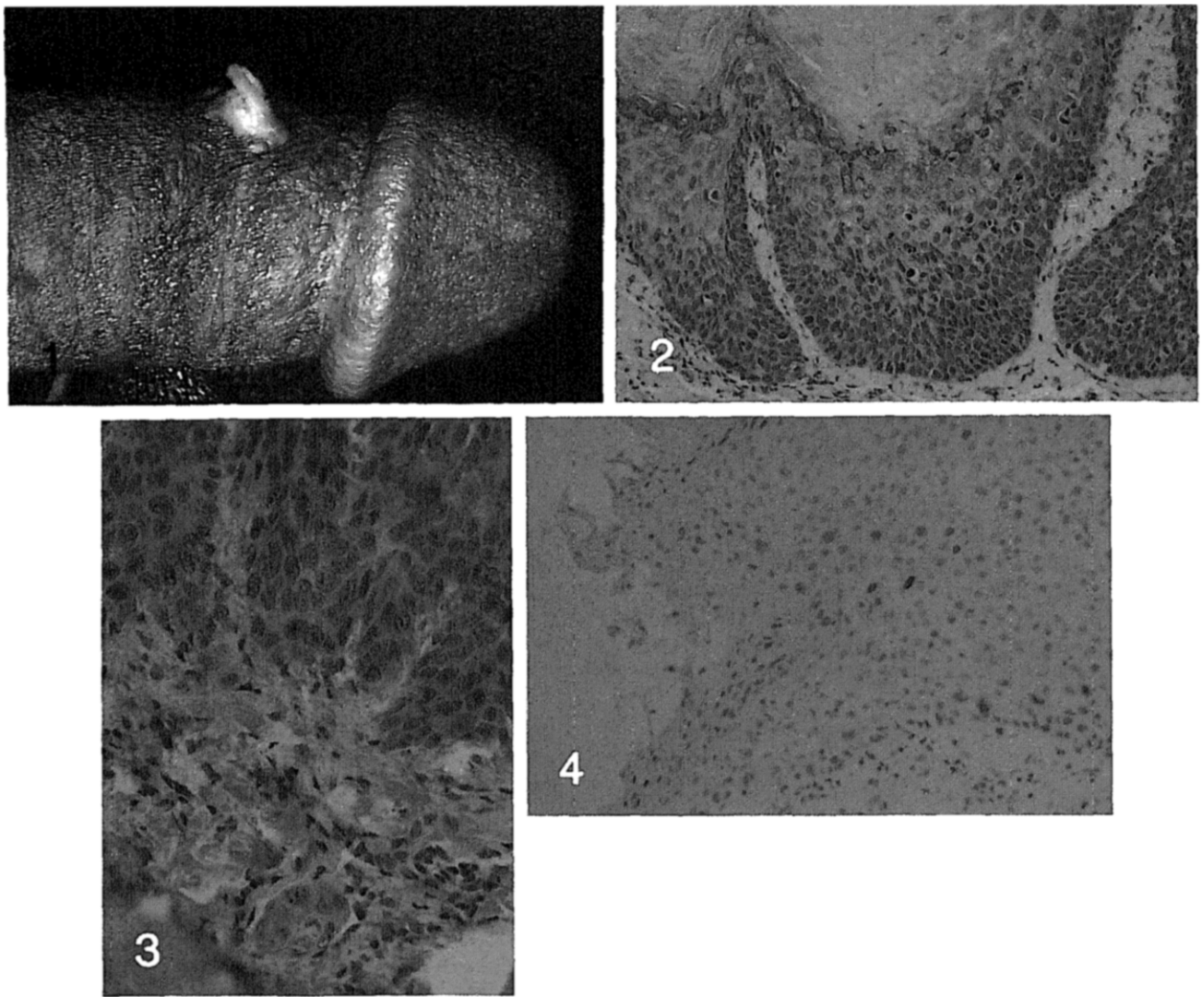


**Fig. 1.** Cutaneous horn overlying squamous cell carcinoma.

**Fig. 2.** Disordered epithelial proliferation with cytologic atypia. (Hematoxylin-eosin stain; ×100.)

**Fig. 3.** Well-differentiated squamous cell carcinoma with microinvasion. (Hematoxylin-eosin stain; ×240.)

**Fig. 4.** Positive immunoperoxidase staining for HPV-16. (Immunoperoxidase stain and 3,3′-diaminobenzidine tetrahydrochloride with hematoxylin counterstain; ×150.)

tions skin tumors, including squamous cell carcinoma, have been induced in rats by the action of long-term exposure to horse smegma.[7] Indirect evidence that this phenomenon occurs in nature can be gathered from the urologic literature. In the two largest clinicopathologic studies, with a combined patient population of 1090, the percentage of penile carcinoma in areas of possible chronic smegma exposure and irritation (i.e., glans, inner mucosa of prepuce, and coronal sulcus) is close to 99% of total penile carcinomas.[8,9]

Penile carcinoma is rare in the Jewish population, who practice neonatal circumcision.[10] When two population groups in India that share the same race but practice different religions, Hinduism and Muhammedanism, are compared, the incidences of penile carcinoma are different. Muhammedans perform circumcision between the fourth and ninth years of life in contrast to Hindus, who do not practice circumcision. In a report by Wolbrast,[11] of a total of 1193 cases of penile carcinoma in India, only 0.02% were Muhammedans. The incidence of penile

carcinoma in this country, where circumcision is commonly performed in infancy, is also relatively low. When performed after puberty, however, circumcision seems to have little advantage in preventing carcinoma.[6] This may be related to the onset of sebaceous secretion. The subsequent smegma production may produce changes in local microbial flora. This, in combination with poor hygiene and the resulting inflammatory reaction, may induce changes that potentiate the development of carcinoma.

Another factor that is important as an etiologic agent in penile carcinoma is HPV. The carcinogenic potential of papillomaviruses was first recognized by Rous and Beard,[12] who observed squamous cell carcinoma arising from Shope papillomavirus–induced warts of domestic rabbits. Malignant conversion rates depended on a number of factors, including the viral strain, the host species, and the animal's immunologic response. The frequency with which malignant conversion occurs and the speed of the transition increase greatly by concomitant exposure to other cocarcinogens.[13] Rous and Beard concluded that malignant transition of papillomas induced by the Shope papillomavirus occurred as the result of a multifactorial process in which the viral infection represented an ongoing risk factor.

During the past few years the development of molecular probes for new types of HPV DNA has established the consistent association between papillomaviruses and anogenital cancer, including cervical, vulvar, and perianal tumors, as well as penile carcinoma.[14-18] Most of these tumors and tumor-derived cell lines contain HPV DNA, and in the majority the HPV DNA is actively transcribed.[19] With the further development of probes the association is likely to be increasingly common.

The development of carcinoma is a multistage process. Exposure for a limited period of time to carcinogens that are classified as initiating agents results in rapid and irreversible change. Usually no clinical or pathologic change after this exposure is present without exposure to other cocarcinogens. At a molecular level, however, the changes are present and irreversible. Other carcinogens that have been classified as promoting agents produce changes that are reversible until transformation occurs. Papillomavirus is a known promoting agent.[20] As with initiating agents, a single promoting agent seldom results in malignant transformation, but, unlike initiating agents, promoting agents, through either repeated contact or latency, may produce benign tumors without malignant transformation. Benign tumors that result from promoting agents have a variable risk of conversion into a malignant tumor. This risk may be high (e.g., HPV-16 or -18) or relatively low (HPV-6 or -11).[21] Additionally, the risk of conversion of a benign tumor to a malignant tumor is increased by exposure to other cocarcinogens.

The data suggesting that the lack of circumcision before puberty and the action of smegma have a lasting effect on the development of penile cancer are consistent with lack of circumcision as an initiating event. Thus, after a limited exposure in an adult environment in which smegma is present, an irreversible change may be present that permanently increases the risk for penile carcinoma. Other related factors are the microbial flora and its metabolites, which may act as cocarcinogens. The microbial flora are also affected by the degree of hygiene and the immune status of the host. These factors, in addition to specific agents such as cigarette smoke and herpes simplex infections, have been implicated in the development of genital malignancies.[19,20]

Our patient had a uncommon clinical lesion, a cutaneous horn of the penis, without the usual predisposing factor, that is, lack of prepubertal circumcision. However, we were able to identify an associated HPV-16 infection, which is being increasingly recognized as one of the main oncogenic agents in genital carcinomas. Other known cocarcinogens were not identified in our patient.

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# Traumatic asphyxia

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Traumatic asphyxia is a distinctive clinical syndrome characterized by cervicofacial cyanosis and edema, multiple petechiae, and subconjunctival hemorrhage after a severe crush injury of the thorax or of the upper part of the abdomen. A case of traumatic asphyxia is reported, and its clinical and pathophysiologic features are discussed. (J AM ACAD DERMATOL 1990;23:972-4.)

Traumatic asphyxia is a clinical syndrome characterized by cervicofacial cyanosis and edema, bilateral subconjunctival hemorrhage, and multiple petechiae of the face, neck, and upper part of the chest. It was first described in 1837 by Ollivier,[1] who noted these distinct features in victims trampled to death in mob violence in Paris. He coined the descriptive term "masque ecchymotique." Traumatic asphyxia is caused by a severe prolonged crushing injury of the thorax or of the upper part of the abdomen that reverses the flow of blood in the superior vena cava and in its tributaries.[2-4] The clinical findings are related either directly to the crush injury itself or to the blood flow reversal. Perthes[5] is credited with giving the first complete description of traumatic asphyxia in 1900.

Traumatic asphyxia is rare. The majority of reported cases are due to accidents in which a victim was either pinned or crushed by an automobile or by a piece of heavy machinery.[2] It also has occurred in a deep sea diver[6] and in persons who were hanged unsuccessfully.[7] Less pronounced manifestations of traumatic asphyxia have appeared in patients with epileptic seizures, whooping cough, violent vomiting, or bronchial asthma.[2] The forceful contraction of the thoracoabdominal muscles against a closed glottis, as occurs in these conditions, can simulate clinically and pathophysiologically a compression injury leading to traumatic asphyxia.

Traumatic asphyxia has prominent cutaneous manifestations. We were unable to find any reports of this disorder in the dermatologic literature. We report a case of traumatic asphyxia and briefly review its clinical features.

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