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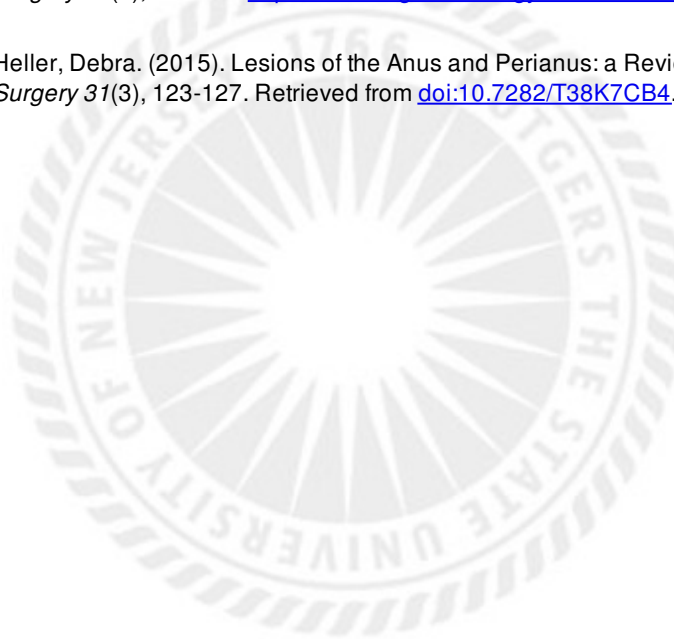
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Article begins on next page

Lesions of the Anus and Perianus: a Review

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Precis: Lesions of the female anus and perianus are reviewed.

Key words: Female, anal neoplasms, anal lesions

Abstract:

The anus and perianus may become involved by a variety of conditions. As providers of gynecological healthcare branch out into the evaluation of anal neoplasia, a familiarity with other anal and perianal lesions will be helpful if a patient with such a lesion is encountered.

Introduction:

The anus and perianus may become involved by a variety of conditions. As providers of gynecological healthcare branch out into the evaluation of anal neoplasia, including the performance of anal cytology and high resolution anoscopy, a familiarity with other anal and perianal lesions will be helpful if a patient with such a lesion is encountered, and facilitate communication and consultation as necessary. The more commonly encountered lesions are discussed. Additional rare conditions may be seen in Table 1.

Anatomy and histology:

The anal canal starts just above the perianal skin, which is a keratinized stratified squamous epithelium with dermal appendages. The lowermost aspect of the canal is lined by a nonkeratinized squamous epithelium without dermal appendages. Above that is a transitional zone containing a mix of epithelial types, usually squamous and columnar, and then more superior, a colorectal zone lined by colonic-type glandular epithelium, as the anal canal merges into the rectum(1). The transitional zone is somewhat analogous to the transformation zone in the cervix, in that this is the area of interest in HPV-related neoplasia. The anal transitional zone can have a variety of histologic appearances, including squamous, transitional and columnar. Anal glands are present in the submucosa and sphincter, and drain into the transitional zone. The presence of glandular cells on an anal cytology specimen is indicative that this transitional zone has been sampled. The dentate line is a gross landmark, between the squamous and transitional zones, and comprised of anal sinuses, valves, papillae and columns. The transitional zone may extend in some points up to 10 mm above the dentate line(1).

Anogenital mammary-like glands can be detected in the perianal skin. A more detailed review of the anatomy and histology is available(1). The terminology for the anatomy of the anal canal has been somewhat controversial over time.

Inflammatory Lesions:

Condyloma Accuminatum:

Condyloma accuminatum of the anus is common, and although patients who have anal intercourse have anal warts with greater frequency, most cases occur in patients who have not engaged in anal intercourse(2). Treatment of external anal warts is similar to treatment of vulvar warts. Although anoscopy may be deferred until the lesions resolve over fear of proximal spread, follow-up anoscopy is important due to the frequency of intraanal warts, which are associated with recurrence(2). The differential of external genital condyloma accuminatum includes verrucous carcinoma, and condyloma latum.

Anal Fissure:

Anal fissures may be due to straining or constipation, however may be associated with an underlying condition such as inflammatory bowel disease, human immunodeficiency virus(HIV), herpes, syphilis, tuberculosis, or malignancy(2). Fissures are painful, and tender to the touch. Spasm of the underlying internal sphincter adds to the pain and delay in healing. Stool softeners, and topical creams or suppositories containing a steroid and a local anesthetic are first line therapy(2). Botulinum toxin has been used for sphincter relaxation, and nitroglycerin topical for analgesia(3). More chronic fissures may require surgical excision.

Abscess and Fistula-in-ano

Infection of intersphincteric anal glands can result in abscess or fistula formation. Up to half of patients with a first time perianal abscess go on to develop an anal fistula or recurrent perianal sepsis. This risk was increased in one study with age under 40 years(4). Anal fistulas may occur de novo, but may be associated with Crohn's disease as well, which must be ruled out. Occasionally fistulas may be the presentation of anal tuberculosis, particularly in immigrants and immunosuppressed individuals(5). Fistulas are classified by location and relationship to the internal and external anal sphincters, and usually require surgical therapy, performed by those with expertise. Focus is on maintaining continence while treating the fistula and preventing recurrence. Interested readers are referred to a review of procedures described by Shawki et al(6).

While small perianal abscesses may be drained in-office, larger ischiorectal abscesses may require operating room drainage(2). More complicated intramuscular and supralelevator abscesses may also occur.

Solitary Rectal Ulcer

A lesion of unknown etiology, this lesion requires histologic evaluation to rule out cancer, which it can clinically mimic. Clinically, solitary rectal ulcer may not always be an ulcerative lesion, but may be a hyperemic or polypoid protrusion. The patients may complain of pain, bleeding, passing mucus and straining, and there may be mucosal prolapse. Histologically, there is fibrosis of the lamina propria, with extension of smooth muscle fibers from the muscularis mucosae into the mucosal lumen(7). Conservative

therapy is aimed at increasing bulk and decreasing straining, including with education and biofeedback, however surgery may become necessary in some cases(7).

Pruritus ani

The causes of pruritus ani, itching of the perianal skin, are numerous. Hygiene, avoidance of irritants that may cause contact dermatitis are among the initial mainstays. Etiologies include fecal leakage, dermatologic diseases such as psoriasis, eczema, contact dermatitis, etc, infections with fungi, parasites such as pinworms, or bacteria, hemorrhoids, tight clothing and perspiration, poor hygiene, psychogenic etiologies, and idiopathic pruritus(3). Sexually transmitted diseases may also present with pruritus. Therapy must be aimed at the underlying etiology to break the itch scratch cycle.

Crohn's Disease:

Perianal involvement by Crohn's disease is common, and may precede the development of the disease in the gastrointestinal tract. Findings include abscesses, fistulas, and skin tags. Fistulas are more common with disease lower in the bowel. Magnetic Resonance Imaging(MRI) is particularly helpful in delineating the extent of fistulization(8).

Fournier's gangrene(necrotizing fasciitis):

Perianal abscess is associated with the risk of developing Fournier's gangrene(necrotizing fasciitis) of the perineal area, a slow starting condition that rapidly

becomes life-threatening. This is a particular risk in diabetics and immunosuppressed patients. Debridement and antibiotics are used along with hemodynamic support, and skin grafting, but morbidity and mortality are high. A biopsy may serve for culture, and reveal the characteristic obliterative endarteritis, subcutaneous thrombosis, fascial necrosis and acute inflammation(9).

Benign neoplasms and tumor like lesions

Hemorrhoids:

External hemorrhoids occurring below the dentate line may be treated by local measures, although if they thrombose, will require surgical intervention, possibly in-office. Rubber band ligation and infrared coagulation are modalities that have been used to treat internal hemorrhoids, those above the dentate line(2). Old burnt out thrombosed hemorrhoids may appear as skin tags. Although hemorrhoids are considered as falling into the pathology category casually known as “ditzels”, it must be remembered than unsuspected squamous intraepithelial neoplasia(Figure 1) or other significant lesions may lurk in these specimens, and should be sought.

Prolapse

Anorectal mucosal prolapse, or full thickness rectal prolapse can occur, and require surgical repair.

Polyps

Polyps usually occurring higher up in the colon or rectum may be seen on anoscopy, including hyperplastic polyps, which have no neoplastic potential, and adenomatous polyps such as villous adenoma, tubular adenoma, or tubulovillous adenoma, which are considered cancer precursor lesions and need to be biopsied. The finding of adenomatous polyps should trigger a colonoscopy(2). Polypoid lesions may also represent pseudopolyps associated with inflammatory bowel disease.

Premalignant & Malignant lesions:**Anal intraepithelial neoplasia**

The presence of anal condyloma may be associated with either low risk or high risk human papillomavirus(HPV) types. In the presence of high risk HPV, a condyloma accuminatum of the anus may therefore represent a risk of carcinoma, even in the absence of histological dysplastic changes(10). Flat dysplastic lesions may be either low or high grade squamous intraepithelial lesions(LSIL, HSIL). This terminology is in accordance with the Lower Anogenital Squamous Terminology(LAST) terminology for HPV-related squamous neoplasia(11). Anal intraepithelial neoplasia is thought to be the precursor to anal squamous cell carcinoma, however the natural history is not known, and treatment modalities are less developed than for cervical lesions(12).

As an awareness of anal disease being part of the spectrum of HPV disease in women becomes more widespread, anal cytology specimens are being performed on greater

numbers of women, particularly those in high risk groups such as HIV positive women. Although men and women with HIV, and men who have sex with men are at higher risk for anal cancer, anyone infected with high risk HPV is potentially at risk of developing anal cancer. In one study of women with genital intraepithelial neoplasia(cervical, vaginal or vulvar), there was a 12.2% prevalence of anal intraepithelial neoplasia(13). Another study of women with genital intraepithelial neoplasia, where there was a mixture of immunocompetent(84%) and immunosuppressed women, the authors found an almost 28% prevalence of anal intraepithelial neoplasia(14). Women do not need to have practiced anal receptive sex to have preinvasive or invasive anal disease, although it does increase the risk(15).

Performance of an anal pap may be performed in the lateral or dorsal lithotomy position. A moistened dacron swab with no lubricant may be used, inserted as far as possible, about 3-4 cm, and rotated with pressure against the walls while removing it(16). A familiarity with the cytopathology criteria, which are slightly different than cervical cytology specimens, is important. There is an anorectal transitional zone, just as there is a transitional zone in the cervix. The presence of glandular cells in an anal cytology specimen, while not requisite for specimen adequacy, assures that this transitional zone has been sampled. Anucleate squames may be abundant on an anal pap, as may fecal material, and if the only materials present, this is not a diagnostic specimen. The criteria for LSIL and HSIL are similar to cervix(figure 2). Although anal screening is in its infancy compared to cervical cancer screening, but it is the best available prevention strategy currently available. More experience with anoscopy, delineation of who should be screened by anal cytology, as well more experience in interpretation of anal cytology

specimens will improve anal screening. This is critical, as many anal cancers are diagnosed with positive lymph nodes and large size(15). A detailed description of the technique of anoscopy is available(16).

Paget's disease

Paget's disease of the perianal region may be of similar skin appendage origin to vulvar Paget's disease, however may also represent a colorectal adenocarcinoma-in-situ, or even extension from a genitourinary neoplasm. Immunohistochemistry can help delineate these clinically and histologically similar lesions. Cytokeratin 7(CK 7) and Gross cystic disease fluid protein-15(GCDFP-15) positivity are seen in primary vulvar Paget's disease. Cytokeratin 20(CK 20) positivity, negative GCDFP-15 and usually negative CK 7 favor a colorectal origin, and CK 7 , CK 20 and Uroplakin II positivity and GCDFP-15 negativity favors a urothelial primary lesion(17). This distinction is important for appropriate therapy.

Invasive malignancies of the Anus

Unfortunately, anal malignancies may be diagnosed late. Presenting symptoms, when present, include mass, pain, and bleeding(18).

The lowermost aspect of the anal canal can be delineated histologically by the transition from perianal skin containing dermal appendages, to the non-hair bearing

squamous epithelium of the lowermost canal. The uppermost aspect, however, has no histologic differentiation, as upper anal canal and rectum are both lined by colonic-type epithelium. By convention, a tumor that originates no more than 2 cm above the dentate line is considered an anal canal cancer(10).

Squamous cell carcinoma

Squamous cell carcinoma represents about 70% of anal cancers(10), and arises from the anorectal transitional zone. Approximately 4650 incident cases were diagnosed in the United States in 2007, of which more than half were in women(19). It is thought to be highly associated with HPV 16 and 18(10). Risk factors are similar to other lower genital tract HPV disease. Histologic subtypes, such as transitional, basaloid, and cloacogenic may also occur(10).

The LAST project(11) evaluated the available literature on the subject, and has proposed that superficially invasive squamous cell carcinoma of the anus(SISSCA) be defined as squamous carcinoma with an invasive depth of ≤ 3 mm from the basement membrane of the point of origin AND has a horizontal spread of ≤ 7 mm in greatest extent, AND has been completely excised. Literature on this subject is scarce. Future studies using these criteria will provide evidence of whether or not this discriminatory point will be accurate in delineating lesions with a significantly lower risk of lymph node metastases.

Anal melanoma

Anal melanoma is a type of mucosal melanoma, unrelated to sun exposure. It may present as a pigmented lesion, however up to 29% may be amelanotic(20). It may be mistaken for thrombosed hemorrhoids. It is unfortunately often diagnosed in advanced stage, with distal metastases at diagnosis being present in up to 57% of patients(17)with concomitant poor prognosis.

Other neoplasms:

Rare cases of verrucous carcinoma, basal cell carcinoma, perianal mucinous adenocarcinoma, apocrine adenocarcinoma , neuroendocrine carcinoma and undifferentiated carcinoma and lymphoma have occurred. Verrucous carcinoma, because of the exophytic nature, may prove diagnostically difficult for the pathologist to diagnose on biopsy if the deeper endophytic portion is not biopsied.

Mesenchymal lesions such as gastrointestinal stromal tumors(GIST) and a variety of sarcomas can rarely occur in the anus, as can Kaposi's sarcoma in patients with acquired immunodeficiency syndrome(AIDS). Metastatic disease to the anus has occurred.

Conclusion:

A familiarity with anal lesions will help the gynecologic practitioner who is screening for anal neoplasia when they are encountered, and facilitate communication, and appropriate referrals if necessary.

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Table 1-Lesions of the anus and perianus that can occur in women:

Congenital and Pediatric Lesions

Stenosis/atresia

Vacterl

Rhabdomyoma

Presacral tailgut cyst

Inflammatory Lesions:

Dermatologic and gynecologic lesions affecting vulva

Condyloma accuminatum

Fissure

Abscess

Fistula-in-ano

Crohn's Disease

Solitary rectal ulcer

Pruritus ani

Sarcoid

Anogenital granulomatosis

Hidradenitis suppurativa

Post-streptococcal dermatitis

Fournier's gangrene

Traumatic and birth injuries

Benign neoplasms and tumor like lesions

Hemorrhoids

Prolapse

Gastric heterotopia

Endometriosis

Granular cell tumor

Apocrine adenoma

Adenoma of anogenital mammary-like gland

Trichoepithelioma

Leiomyoma

Premalignant & Malignant lesions:

Anal intraepithelial neoplasia

Paget's disease

Squamous cell carcinoma and subtypes

Verrucous carcinoma

Mucinous adenocarcinoma

Apocrine adenocarcinoma

Porocarcinoma

Anal melanoma

Neuroendocrine carcinoma

Undifferentiated carcinoma

Lymphoma

Metastases

Legend:

Figure 1-Hemorrhoids with HSIL-This specimen was received in the Pathology Laboratory as an excision for hemorrhoids, which consist of the dilated and thrombosed vessels seen to the left(1A), however there was also unexpected high grade squamous intraepithelial neoplasia present, involving the glands(1A right, 1 B).

Figure 2-Anal cytology. If the specimen is composed only of anucleate squames(A), the specimen is inadequate. While not requires for adequacy, the presence of glandular cells(B) indicates that the transitional zone was sampled. LSIL(C) and HSIL(D) are similar in appearance to the cervical counterpart. Note in figure 2D a binucleate cell showing LSIL in the lower left of the image, with the smaller cell showing HSIL in the center above it.