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Original contribution

Incidental secondary findings in hemorrhoidectomy specimens: a 16-year experience from a single academic center☆,☆☆

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Summary Hemorrhoidectomy specimens serve as an excellent resource for study of incidental anal pathology. Detection of most incidental findings is quite rare, although diagnosing clinically significant lesions can have profound impact on the clinical follow-ups. While there are many case reports of incidental findings in hemorrhoidectomy specimens, there are few large studies focused on this topic. The aim of this study was to describe the spectrum and likelihood of detecting incidental findings in hemorrhoidectomy specimens. We reviewed all hemorrhoidectomy specimens that showed incidental clinically significant diagnoses over a 16-year period (2003–2019) for this study. Patient's age, sex, and significant clinical history (Human Immunodeficiency Virus (HIV) status, precursor lesions, other malignancy) were recorded from clinical notes. We identified incidental clinically significant findings in 72 of 1612 (4.5%) specimens. We identified 7 incidental malignancies (squamous cell carcinoma, verrucous carcinoma, adenocarcinoma, mixed adenocarcinoma and neuroendocrine carcinoma, poorly differentiated neuroendocrine carcinoma, melanoma), 54 anal intraepithelial neoplasias (AINs), and 11 benign findings (melanocytic lesions, colorectal polyps, angiokeratoma, infectious/inflammatory). Within the AIN group, the detection of low-grade squamous intraepithelial lesions (LSILs) remained steady; there was a recent, sustained rise in detection of high-grade squamous intraepithelial lesions (HSILs), with more cases showing HSILs (2.6%) than only LSILs (0.7%). In 72.2% of patients, the incidental secondary finding represented a first diagnosis for that entity in the anal canal. Thirty seven percent of patients with anal dysplasia in the hemorrhoidectomy specimen had a prior diagnosis of squamous dysplasia in the anogenital tract. Overall, significant incidental findings were detected in 4.5% (72/1612) of hemorrhoidectomies, supporting routine histological examination of these specimens.

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1. Introduction

Hemorrhoidal disease is very common, causing morbidity in about 1 in 3 Americans in their lifetime [1]. Complications of hemorrhoidal disease account for several million ambulatory visits per year in developed countries, more than diverticular disease, colon cancer, inflammatory bowel disease, and even appendicitis [1,2]. Although the term *hemorrhoid* is used in a pathological setting, the blood vessels that constitute hemorrhoids are a normal component of the anal canal, helping to maintain continence, and are referred to as anal cushions [3]. Hemorrhoidal disease results when there is venous stasis and dilatation of the vascular spaces, which is further complicated by distal displacement and subsequently prolapses. Most patients with hemorrhoidal disease are asymptomatic unless they become thrombosed and cause pain. Other symptoms include bleeding, protrusion, and itching [4]. Management of hemorrhoidal disease is diverse. When conservative management is unsuccessful or the hemorrhoids are recurrent or higher grade, then hemorrhoidectomy or hemorrhoidopexy is sought [4].

Microscopically, hemorrhoids are characterized by dilated vascular structures, smooth muscle, and supporting connective tissue with overlying squamous or glandular mucosa [5]. Routine pathological examination of hemorrhoidal tissue has been a matter of debate, with uncertain benefits and costs varying geographically, as well as interinstitutionally [6,7]. Incidental unexpected findings have been reported in hemorrhoidectomy specimens in the past, ranging from benign findings to malignancies such as adenocarcinoma, squamous cell carcinoma, melanoma, and Kaposi sarcoma [8–15]. The institutional policy at our hospital involves examination of all hemorrhoidectomy specimens generated in the operating room, allowing us to study the spectrum of incidental findings and study the trends in detection of incidental findings over time.

2. Materials and methods

The surgical pathology archives of Beth Israel Deaconess Medical Center were queried from 2003 to 2019 for hemorrhoidectomy specimens after appropriate institutional review board approval. In our department, every hemorrhoidectomy specimen undergoes a gross evaluation for any visible lesions. If present, they are noted and sampled for microscopic evaluation. In general, if a bisected specimen can be completely submitted in one or two blocks, they are entirely submitted for microscopic examination. If not, in absence of any gross lesions or significant clinical indications, random representative sections are submitted for microscopic evaluation. Based on review of existing pathology reports, hematoxylin- and eosin-stained slides of all available cases harboring incidental clinically significant lesions were reviewed by two pathologists (P.N. and M.V.); anal skin tags often accompany hemorrhoids and were not considered clinically significant. Wherever available, existing immunohistochemically stained slides for p16 (BD Sciences, mouse antibody, 1:100 dilution), Ki67 (Dako, mouse antibody, undiluted), and any additional relevant immunohistochemical stains performed at the time of diagnosis were reviewed. Strong and diffuse (block-like) positivity for p16 and increased Ki67 labeling of cells involving the entire thickness of the lesional epithelium were considered supportive of high-grade squamous intraepithelial lesions (HSILs) [16].

Gross descriptions and operative findings were reviewed to determine the type of specimen that harbored incidental lesions. Demographic data (age, sex) were collected. Clinical records were reviewed for each patient to determine HIV status, presence of prior or concurrent squamous intraepithelial lesions (including warts in the lower genitourinary tract), and any history of malignancy. AIN1 was classified as low-grade squamous intraepithelial lesion (LSIL), and AIN2/3 was classified as HSIL, based on Lower Anogenital Squamous Terminology (LAST) [17]. As per the LAST criteria, LSILs are defined as *Proliferation of squamous or metaplastic cells with abnormal nuclear features including increased nuclear size, irregular nuclear membranes, and increased nuclear-to-cytoplasmic ratio with little cytoplasmic maturation in the lower third of the epithelium and mitotic figures being limited to the lower one third of the epithelium or in those cases where defining features of HPV cytopathic effects are present*, whereas HSIL is defined as *Proliferation of squamous or metaplastic squamous cells with abnormal nuclear features including increased nuclear size, irregular nuclear membranes, and increased nuclear-to-cytoplasmic ratios accompanied by mitotic figures with little or no cytoplasmic differentiation in the middle third and superficial thirds of the epithelium along with mitotic figures not confined to the lower third of the epithelium and found in the middle and/or superficial thirds of the epithelium* [17].

In addition, to compare the follow-up of hemorrhoidectomy cases with and without significant incidental findings, clinical information from additional 509 hemorrhoidectomy cases without clinically significant secondary findings (from 2013 to 2019) was recorded.

3. Results

We retrospectively reviewed pathology reports from 1612 hemorrhoidectomy specimens from 2003 to 2019. On average, our department evaluated 98 hemorrhoidectomy specimens per year (range: 69–144 cases). We identified

Table 1 Incidental histopathologic findings in hemorrhoidectomy specimens.

Incidental histologic finding	Females (n = 28)	Males (n = 44)	Total (n = 72)
LSIL (AIN1/condyloma)	5	7	12 (16.7%)
HSIL (AIN2/3)	12	30	42 (58.3%)
Squamous cell carcinoma	0	1	1 (1.4%)
Verrucous carcinoma	0	1	1 (1.4%)
Adenocarcinoma	1	1	2 (2.7%)
Poorly differentiated neuroendocrine carcinoma	0	1	1 (1.4%)
Poorly differentiated adenocarcinoma with neuroendocrine features (mixed adeno and neuroendocrine carcinoma [MANEC])	1	0	1 (1.4%)
Melanoma	1	0	1 (1.4%)
Melanocytic nevi	2	2	4 (5.5%)
Genital lentiginosis	1	0	1 (1.4%)
Sessile serrated adenoma	1	0	1 (1.4%)
Tubular adenoma	1	0	1 (1.4%)
Angiokeratoma	1	0	1 (1.4%)
Granulomata	1	0	1 (1.4%)
Sexually transmitted infectious colitis (chlamydia associated)	0	1	1 (1.4%)
Hypersensitivity reaction	1	0	1 (1.4%)

LSIL, low-grade squamous intraepithelial lesion; HSIL, high-grade squamous intraepithelial lesion.

incidental clinically significant findings in 72 of 1612 (4.5%) specimens, from 44 men and 28 women (average age 44 years, range 25−76).

In 10 cases, one or more parts of the case had been representatively sampled in one tissue block. In the remaining 62 cases, all the parts of the specimen had been entirely submitted, of which 30 cases had been entirely submitted in one block, while in the remaining 32 cases, >1 block had been submitted (range − 2−10, average 3 blocks per case).

H&E stained slides were available for review in 59 cases. In the remaining 13 cases where slides were not available, information from pathology reports and clinical records was used. Two previously diagnosed LSIL cases were excluded from the study due to lack of classic features up on review.

Most lesions (56, 78%) were squamous (54 anal intraepithelial neoplasia [AIN], 1 invasive squamous cell carcinoma, 1 verrucous carcinoma). The rest included 5 nonsquamous malignancies (adenocarcinoma [n = 3], including one poorly differentiated adenocarcinoma with neuroendocrine carcinoma component [mixed adeno and neuroendocrine carcinoma]; poorly differentiated neuroendocrine carcinoma [n = 1]; melanoma [n = 1]) and 11 benign findings (Table 1; Figs. 1−3). Gross abnormalities were described in 7 of 72 (9.7%) cases (3 AINs, 2 malignant and 2 benign) and are described in the following sections. In 19 of 72 (26.3%) cases, no definitive histological features of hemorrhoids were present. These include 5 cases with malignancies, 3 melanocytic nevi, 1 with granulomata, 1 with adenoma, and 9 cases with AIN.

Anal intraepithelial lesions were seen in 54 of 1612 (3.3%) cases. There were 12 cases of LSILs (0.7%, 7 men and 5 women, Fig. 1A and B) and 42 cases of HSILs (2.6% of total, 30 men and 12 women, Fig. 1C and D). Of the 56 patients with squamous lesions (including squamous cell carcinoma), 22 (21 men, 1 women) were known to be HIV positive, while 14 (11 men, 3 women) were HIV negative; HIV status was unknown in 20. Two men with anal squamous lesions had a history of penile warts, and 5 women had a history of gynecologic squamous lesions. Thirty-nine of 54 (72.2%) patients had a first-time diagnosis of an anal squamous lesion on a hemorrhoidectomy specimen while 20 of 54 (37%) patients had a prior history of squamous lesions (either anal or other genitourinary and perineal sites). Gross abnormalities were present in 3 of 54 cases (2 HSIL and one condyloma) in the form of poly/polypoid lesion (0.7−1.9 cm) in the hemorrhoidal skin. P16 and/or Ki67 immunohistochemistry aided in the diagnosis of incidental AIN in 17 of 56 cases (30%), all except one were recent cases (post-2014). Analyzing trends over time, while the detection of LSIL (including AIN1 and condyloma) remained steady, there was a recent increase in detection of HSIL (Fig. 4). A diagnosis of incidental LSIL was seen in <2.5% of all the specimens per year (range: 0−2.4%). The rate of incidental detection of HSIL before 2015 was <2.6% per year (with the exception of two years, 2004 and 2007, when it was 3.3% and 3.8%, respectively); however,

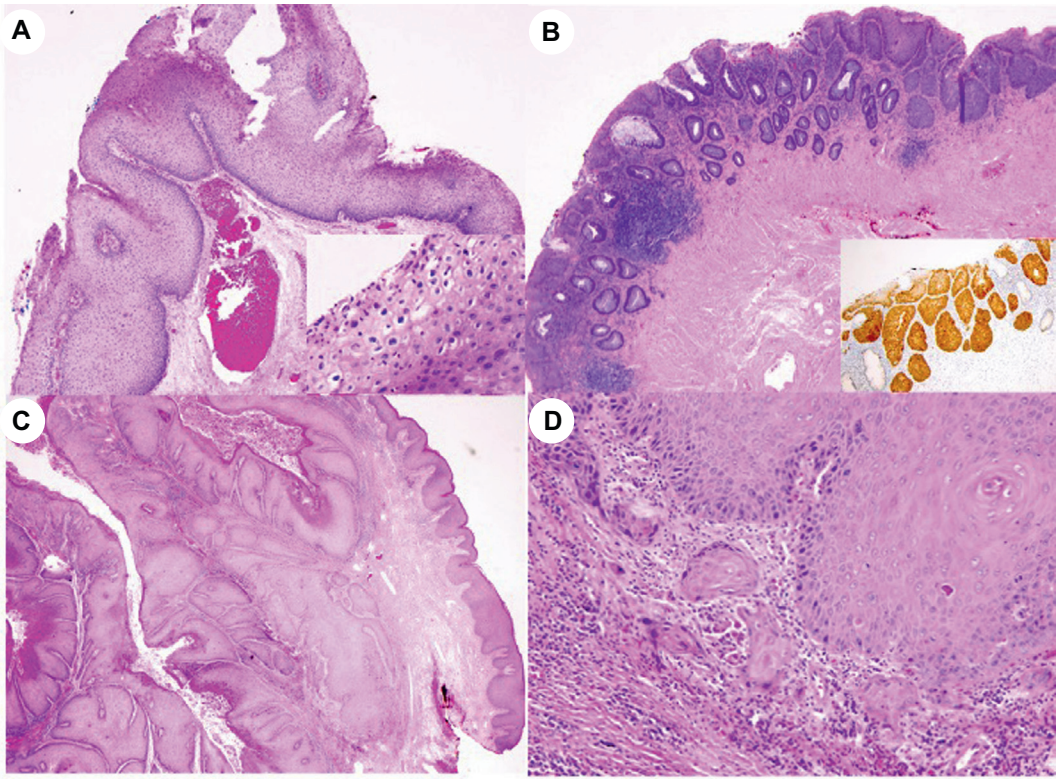

Fig. 1 Incidental squamous lesions in hemorrhoidectomy specimens: A, Portion of a hemorrhoid demonstrating low-grade squamous intraepithelial lesion (H&E, original magnification ×40). Inset image showing nuclear enlargement with hyperchromasia, perinuclear halos, and rare multinucleation in the squamous epithelium (H&E, ×400). B, High-grade squamous intraepithelial lesion overlying a hemorrhoid with strong and diffuse expression of p16 (inset) (H&E, ×40). C, A well-differentiated keratinizing squamous cell carcinoma overlying a hemorrhoid (H&E, ×40). D, Foci of stromal invasion associated with squamous cell carcinoma (H&E, ×400).

in the last four years (2015−2019), we noticed a sustained increase, with an average rate of 4.8% (range: 3.8−5.9%) per year. Follow-up data were available in 23 of 54 (42.5%) patients with AIN (average follow-up: 47.57 months, range 2−185 months). Twenty-one of 54 (38.8%) patients were followed up at our institution with subsequent anal Pap smears, 2 patients had repeat anal biopsies; none of these patients developed invasive squamous cell carcinoma. Details of cases with incidental malignancies are highlighted in Table 2; all 7 cases had no documented history of malignancy elsewhere at the time of hemorrhoidectomy excision. On review of the operative notes, there was little/no suspicion of malignancy in these cases. The lesions were clinically described as necrotic hemorrhoids (n = 2), thrombosed hemorrhoids (n = 2, Fig. 3), bleeding hemorrhoid (n = 1) and hemorrhoid with verrucous surface (n = 1), and hemorrhoid associated with fissure and skin tag (n = 1). Visible gross abnormalities were noticed in 2 cases, a squamous cell carcinoma and a verrucous carcinoma, which were described as a polypoidal skin fragment with ulceration and an ulcerated exophytic friable mass, respectively. In two other cases, cross sections were noted to be congested and edematous (n = 1) and firm and tan (n = 1). The average size of the excised specimens was 2.3 cm (range 4.9−1.2 cm, n = 6).

The eleven benign findings included a spectrum of dermatologic findings including melanocytic nevi (n = 4), genital lentiginosis (n = 1), angiokeratoma (n = 1), and hypersensitivity reaction (n = 1). In addition, tubular adenoma (n = 1), sessile serrated adenoma (n = 1), granulomatous inflammation, and sexually transmitted infectious (STI) colitis (n = 1) were also identified. Gross abnormalities were present in 2 of these benign cases (1.5 cm polypoidal projection in case of angiokeratoma and a cutaneous dimple in a specimen harboring a compound melanocytic nevus). The case with granulomatous inflammation was further worked up for acid fast bacilli (AFB) and fungal organisms using special stains (AFB, Fite and Grocott methanamine silver) which were all negative. The case with STI colitis showed a predominant infiltrate of subepithelial and perivascular plasma cells, in addition to ulceration and granulation tissue, in the hemorrhoidal tissue (Fig. 3). An immunohistochemical stain for *Treponema pallidum* was negative, and the available history revealed that serologic test for *Chlamydia trachomatis* (L2 serovar) was positive.

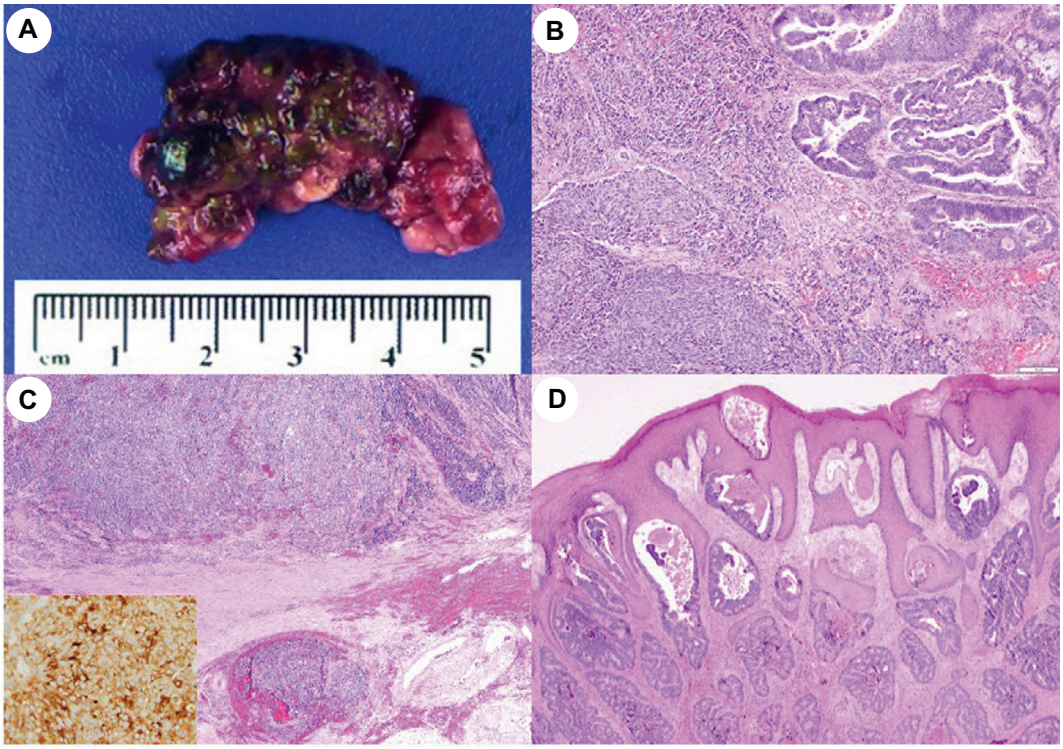

Fig. 2 Incidental carcinoma in hemorrhoidectomy specimens: A, Gross image of a specimen submitted as a thrombosed hemorrhoid, which subsequently showed carcinoma (B&C). B, Microscopic section of specimen in A showing poorly differentiated carcinoma adjacent to a focus of adenoma with high-grade dysplasia (H&E, ×200). C, The poorly differentiated component exhibits neuroendocrine differentiation (inset: synaptophysin) and is present in vascular spaces (H&E, ×100). D, Invasive adenocarcinoma in a specimen resected as a hemorrhoid (H&E, ×200).

Between 2013 and 2019, we received 536 hemorrhoidectomy cases at our institution (including 27 cases in the cohort described previously) of which in 509 cases, no significant secondary findings were noted. Of these 509 cases, one patient developed squamous cell carcinoma (human papillomavirus [HPV] associated), 4 years after hemorrhoidectomy (which was representatively sampled and did not reveal any squamous intraepithelial lesions or carcinoma) and was treated with chemoradiation.

4. Discussion

The practice of surgical pathology has evolved over the last century, from the times when surgical specimens were not routinely examined under the microscope to the present day, when stringent standardization is being implemented. While examination of all excised tissue for pathological diagnosis to rule out unsuspecting lesions was recommended as a part of minimum standards for hospitals by the American College of Surgeons in 1927, the cost effectiveness of such an approach has been questioned over the years [18–20]. The College of American Pathologists has issued guidelines regarding types of specimens that can be exempted from submission to pathology or may qualify for exemption from microscopic examination; the onus is on the institutions to formulate their own policies in this regard [19,21]. Hemorrhoidectomies and hemorroidopexies have often been the target of this debate, and these specimens are handled differently at institutions throughout the world. For instance, the French Society of Coloproctology guidelines do not mandate systematic histological examinations on hemorrhoidectomy specimens [22]. Supporting the French guidelines, Lemarchand et al. [7] concluded that systematic pathological evaluation of hemorrhoidectomy specimens was not necessary, with a caution that any grossly suspicious areas should be carefully selected for pathological examination. They observed a relatively low percentage of incidental lesions: 0.69% of 8153 hemorrhoidectomy specimens over a period of 16 years, including just 7 cases of AIN. However, not all of their specimens underwent pathological examination because their study also included cases after the French guidelines were published in 2001 [7].

The most important argument in support of routine evaluation of any tissue is detection of incidental malignant lesions. Anal cancers are often diagnosed in later stages, partly because of their uncommon location and partly because symptoms are masked by more common benign anorectal lesions [23]. As such, it is not unusual to find unexpected malignancies in hemorrhoidectomy specimens [11,13,24]. Grodsky [8] reported 7 cases of incidental

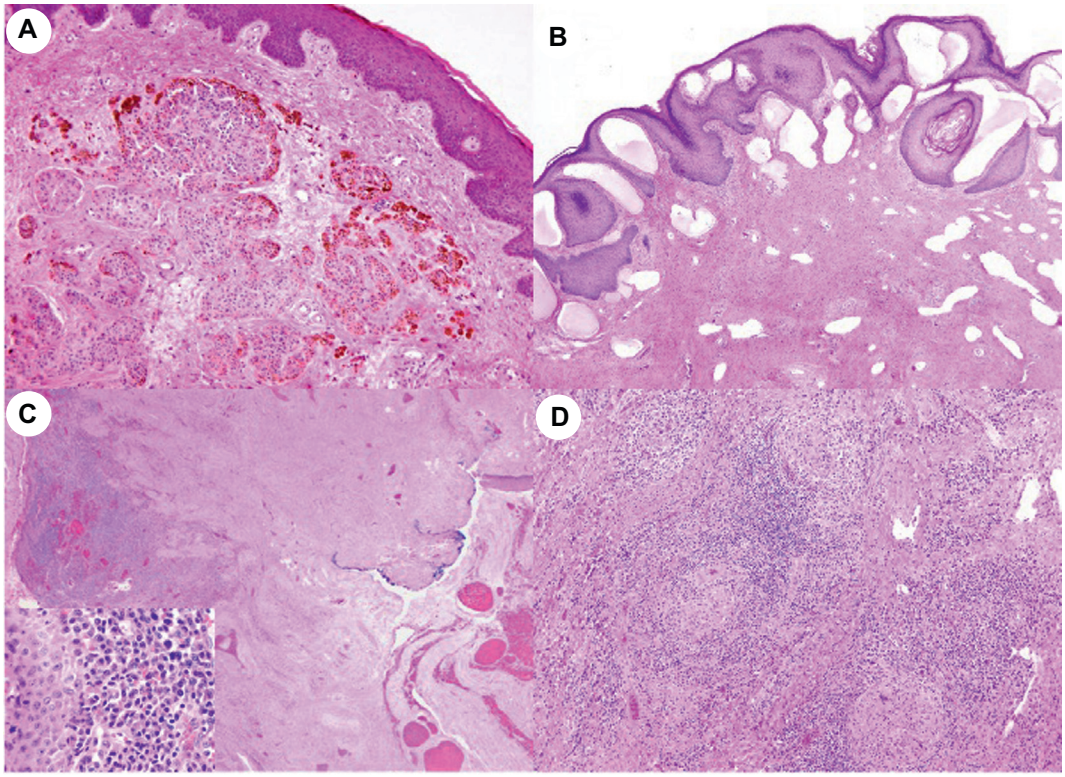

Fig. 3 A, Incidental intradermal nevus associated with a hemorrhoid (H&E, ×200). B, Angiokeratoma overlying hemorrhoids (H&E, ×200). C, A patient with *Chlamydia trachomatis* infection with dense lymphoplasmacytic infiltrate (inset) in the hemorrhoidectomy specimen (H&E, ×40). D, Non-necrotizing granulomatous inflammation in a hemorrhoidectomy specimen.

cancers in 526 hemorrhoidectomy specimens over a 10-year period. Similarly, neuroendocrine tumors, adenocarcinomas, melanomas, Kaposi sarcoma, and even metastatic carcinoma masquerading as hemorrhoidal tissue have been described [9–13]. Our study identified 7 malignancies and echoes the previously published literature that cancers can present as polypoidal protrusions, clinically masquerading as (or masked by) hemorrhoids. In 6 of 7 cases in our series, there was no clinical suspicion of cancer, and in one case, the clinical differential diagnoses included thrombosed hemorrhoid versus malignancy. Our findings indicate that gross abnormalities may not always be evident even in

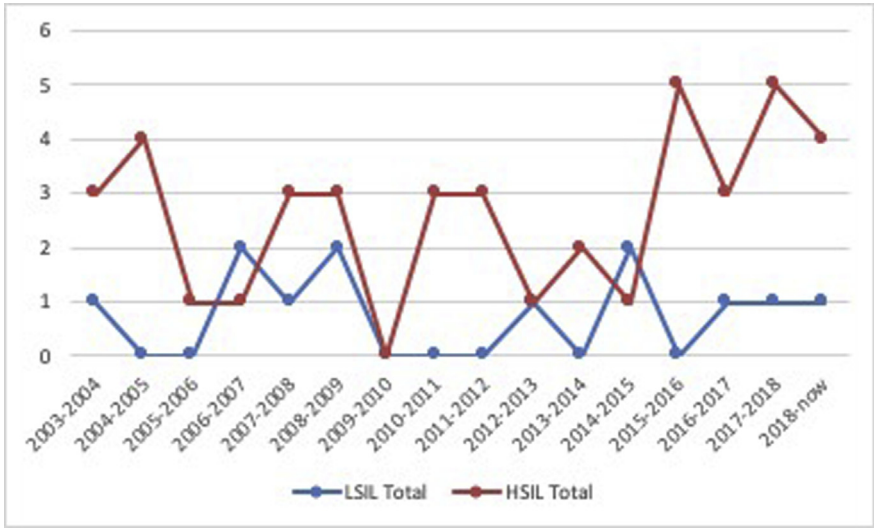

Fig. 4 Trends in incidental detection of anal intraepithelial neoplasia (AIN, LSIL vs HSIL) in hemorrhoidectomy specimens over time. LSIL, low-grade squamous intraepithelial lesion; HSIL, high-grade squamous intraepithelial lesion.

Table 2 Clinical details of incidental malignancies in hemorrhoidectomy specimens (n = 7).

Case #	Age	Sex	Gross evaluation	Diagnoses	Clinical course	Follow-up duration (months)	Status at last follow-up
1	35 y	F	No abnormal description	Poorly differentiated adenocarcinoma with neuroendocrine differentiation (mixed adeno and neuroendocrine carcinoma [MANEC])	Liver metastasis during staging evaluation	Not available/lost to follow-up	Alive with disease
2	45 y	M	Ulcerated exophytic friable mass	Verrucous carcinoma	No recurrence or metastases	48	Alive without disease
3	70 y	M	No abnormal description	High-grade poorly differentiated neuroendocrine carcinoma	Liver and lung metastases during staging evaluation	Not available/lost to follow-up	Alive with disease
4	46 y	M	Polypoidal skin fragment with ulceration	Squamous cell carcinoma	Underwent chemoradiation, no recurrence or metastases	156	Alive without disease
5	46 y	M	No abnormal description	Adenocarcinoma	Progressed with liver metastases on chemotherapy, 2 months after diagnosis and underwent right hepatic lobectomy. Local recurrences in the perineum 18 months later, followed by abdominoperineal resection. Diagnosed with brain metastases 88 months later	88	Died of disease
6	91 y	F	No abnormal description	Adenocarcinoma	No metastases during staging evaluation. No chemotherapy given.	18	Alive without disease
7	48 y	F	No abnormal description	Melanoma	Diagnosed with lung metastases 6 months later and progressed with brain metastases, while on chemotherapy.	24	Died of disease

hemorrhoidectomy specimens harboring malignancies and they may be mistaken for infarcted or thrombosed hemorrhoids, and hence, routine examination of all such specimens may be a good institutional practice.

AIN is another common incidental lesion that has been reported in hemorrhoidectomy specimens [14,15]. AIN is a dysplastic condition of the squamous lining of the anal canal arising after infection with high-risk HPV strains and is a precursor to anal squamous carcinomas. There has been a sustained rise in HPV-related anal carcinomas in Western countries in recent years [25]. Hence, the importance of diagnosing anal precancerous lesions cannot be overemphasized. Incidental AIN was recognized in 3.3% of hemorrhoidectomy specimens and constituted 75% of unsuspected clinically significant lesions in our series. Our results are in agreement with study from Bauer et al. which revealed AIN in 3.2% (2.5% HSILs, 0.7% LSILs) of their 2997 combined hemorrhoidectomies and fissurectomies

examined microscopically over a 15-year period. Hui et al. [15] studied unsuspected anal HSILs and squamous cell carcinomas in hemorrhoidectomy specimens and genotyped them for high-risk HPV types. They reported anal HSILs in 2.1% of cases. HPV 16 was the most common high-risk HPV type [15]. A recent study by Mascagni et al. [6] revealed mild anal dysplasia and warts in 18 of 3017 cases (0.59%), which is quite similar to our study (0.7%), and 9 squamous cell carcinomas in hemorrhoid resection cases from 2003 to 2017 and no cases of HSIL. This could be attributed to variability of high-risk populations served at different hospitals. We have observed a rise in incidental detection of HSIL in hemorrhoidectomy specimens at our institution. While this increase may be related to the increased use of p16/and or Ki67 immunohistochemical stains in recent years, it may also parallel the higher incidence of HPV-related premalignant and malignant lesions found elsewhere in recent years [25]. Making any epidemiologic conclusions is beyond the scope of this study.

In the absence of routine screening protocols for anal lesions (except in high-risk individuals), hemorrhoidectomy specimens provide an excellent resource to study the incidence of anal pathology in the general population. The possibility of diagnosing AIN should always be kept in mind while dealing with hemorrhoidectomy specimens, more so when the hospital serves a high-risk population. It is also important to note that although many patients with anal HSIL have a history of sexually transmitted infections or have risk factors for the same, a subset of the patients may lack such clinical history. Regardless, the risk of transformation of anal HSIL to anal squamous cell carcinomas is nearly 10% within 5 years of diagnosis [26]. Most AIN is treated either by ablation or excision. Lee et al. [26] concluded that those cases that are excised are more likely to recur than cases that are ablated, as excision may not be a complete treatment due to their multifocal nature. In such scenarios, hemorrhoidectomy alone may not be a sufficient treatment and additional therapies may be warranted. In our available follow-up data, re-excision was performed for one patient, while the majority were followed up with anal Pap smears.

Various nonmalignant incidental findings have also been rarely reported in hemorrhoidectomy specimens, including tuberculosis [27], Cytomegalovirus (CMV) [28], and melanocytic nevi [29]. We similarly observed 4 cases of melanocytic nevi in our study, as well as other benign lesions such as sessile serrated adenoma, tubular adenoma, angiokeratoma, granulomas, and hypersensitivity reaction.

An interesting case of sexually transmitted infection (STI) presented clinically as hemorrhoidal disease in our series. Microscopically, the lesion demonstrated ulceration, granulation tissue, prominent subepithelial plasma cell infiltrate, and perivascular plasma cell aggregates. An immunohistochemical stain for *T. pallidum* was performed and found to be negative at the time of diagnosis. Serologic testing confirmed positivity for *C. trachomatis*. While clinical history is paramount in diagnoses of sexually transmitted infection affecting the distal gastrointestinal tract, an STI can be suspected when there is predominant submucosal plasma cells, endothelial swelling, and perivascular plasma cells with minimal crypt centric damage and along with a lack of mucosal eosinophilia [30].

The follow-up data from the control group (2013−19) showing the risk for developing malignancy or clinically significant lesions in patients, who do not show any secondary significant findings on hemorrhoidectomy, are limited. Only one of 509 such patients in out cohort subsequently developed squamous cell carcinoma. It is not known if complete submission of the specimen may have revealed a precursor lesion. The data are too limited to justify any recommendation for complete submission of hemorrhoidectomy specimens.

We acknowledge certain limitations in our study. We reviewed all cases with additional significant findings in hemorrhoidectomy specimens reported at the time of primary diagnosis; however, there was no pathological review of control cases that did not harbor an additional diagnosis and their clinical features and follow-ups. As a result, we acknowledge that the incidence of incidental findings may be higher than that of our reported figures. While we do note an increasing trend in incidental detection of HPV-related lesion in hemorrhoidectomy specimens, we do not have correlating epidemiological data to make any definite assessment regarding the reason for this increase. Our assessment of gross findings was also based on the available operative notes and gross descriptions, which cannot be independently verified. Another limitation of our study is the relatively limited follow-up data for our AIN cases; some patients may have received follow-up care at more specialized institutions.

5. Conclusion

Systematic and thorough evaluation of hemorrhoidectomy specimens represents an opportunity to diagnose occult disease. Diagnosis of incidental malignancy remains the most important argument supporting routine examination of all hemorrhoidectomy specimens. Diagnosis of anal dysplasia on hemorrhoidectomy specimens can facilitate further clinical follow-up, either surgical or by cytology, depending on the clinical situation. Identification of benign findings such as STIs can help in initiating treatment and further workup of patients and their contacts.

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