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RESEARCH ARTICLE

A HISTOPATHOLOGICAL OVERVIEW OF LESIONS OF ANAL CANAL

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ABSTRACT

Background: A wide variety of lesions of anal canal commonly presenting with bleeding per rectum are increasing in incidence nowadays. While majority of them are of non-neoplastic in nature, diagnosis and treatment of neoplastic lesions are of paramount importance. Histo-pathological examination is helpful in categorization of lesions of anal canal along with staging and grading of malignant lesionsto improvise the therapeutic decisions.

Aims: to study distribution and prevalence of lesions of anal canal in the community and comparison with other studies.

Methods: A study of 171 patients presenting with C/O abdominal pain and bleeding per rectum at B.J. Medical College, Civil Hospital, Ahmedabad over a period of three years from 2014 to 2016 was undertaken. All specimens of resected intestine (anal canal) as well as small biopsies were received and over-night fixation in 10% formalin was done. Gross examination findings were noted followed by routine paraffin embedding and tissue sectioning. Slides were stained using H&E stain, examined microscopically and staging was done followed by comparison with other studies.

Results: In the present study, out of 171 cases of lesion of anal canal, 149(93%) cases were non-neoplastic while remaining 22(7%) are neoplastic. Major distribution of the lesions was seen in the age group of 30-50 years with male: female ratio of 7:1. The most common non neoplastic lesion of anal canal is anal fistula(62.5%). Among all neoplastic lesions, Fibro-epithelial polyps(33.34%) were the commonest benign lesions and squamous cell carcinoma(16.8%) was the commonest malignant lesion.

Conclusion: Prevalence of lesions of anal canal is increasing among males of middle age. In respect to rarity of neoplastic lesions, most of the lesions of anal canal are highly curable. Thus histopathology is useful in therapeutic decisions to provide better outcome.

INTRODUCTION

While Intestinal lesions are very common in day to day practice, the lesions involving the anal canal, a part of large intestine are increasing in its incidence during the recent times. It functions as an exit-point of the large intestine for excretion of the waste products of the intestine (Turner, 2010). A wide variety of lesions including non- neoplastic as well as neoplastic lesions affect the anal canal commonly presenting with bleeding per rectum. Most commonly encountered non neoplastic lesions of anal canal are anal fistula, fissures, hemorrhoids etc. mean while various malignant lesions lead by squamous cell carcinoma are also very common (Rosai and Ackermann, 2010). Small biopsies as well as resection biopsies are used for diagnostic and/ or therapeutic purposes. Histopathology is the gold standard for the final confirmation of the diagnosis of lesions of anal canal (Dr Lavanya, *et al.,* 2010).

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Categorization of lesions of anal canal along with staging and grading of malignant lesions are an important part of the diagnostic workup and the therapeutic decisions to provide the better outcome for the patients. In the present study, 171 cases of lesions of anal canal were studied retrospectively.

Aims and Objectives

The present study was done with a view:

- To classify various lesions of anal canal into non neoplastic and neoplastic categories with appropriate sub-categorization.
- To study distribution of various lesions of anal canal according to age and to compare with other studies.
- To study sex distribution of various lesions of anal canal and to compare with other studies.
- To study the prevalence of various non-neoplastic and neoplastic (benign and malignant) lesions of intestine as well as to compare with other studies.

Review of literature

Anal canal derives from the hindgut portion of the GUT TUBE during embryogenesis. Failure of normal development leads to various congenital lesion of anal canal (web.duke.edu).The Anal Canal is the terminal 3-4 cm of the gastrointestinal Tract extending from the lower end of the rectum to perianal skin (Rosai and Ackermann, 2010), (Fenger *et al.,* 1978).

Normal Histology

The anal canal is lined by columnar epithelium in its proximal portion and by keratinized or non-keratinized squamous epithelium in its distal portion. At the interphase between the two, there is a circular zone, 0.3–1.1 cm in width, with a glistening, wrinkled appearance made discontinuous by the presence of anal papillae (Fenger C *et al.,* 1978). This zone is lined by epithelium known as *transitional*, *intermediate*, or *cloacogenic*. It expresses keratins 7 and 19 but not keratin 20 (Ramalingam P, 2001), (Williams GR, 1995).

Lesions of anal canal

A. Congenital lesions

Anorectal anomalies occur in approximately 1 of every 3000–5000 births. They are divided into three major types, depending on the relationship of the lower bowel to the puborectalis component of the levatorani muscle (Louw JH, 1971). High or supralevator anomalies (40%), Intermediate anomalies are rare (15%) and Low or translevator anomalies (40%)comprise the ectopic (perineal, vestibular, or vulvar) anus, anal stenosis, and covered anus.

B. Inflammatory lesions

1. ***Anal Ulcer*** is a chronic process having nonspecific microscopic appearance and is surrounded by chronic edema and fibrosis.
2. ***Anal Fissure*** is a single linear separation of the tissues of the anal canal extending through the mucosa most commonly found at posterior commissure overlying the bifurcation of the sphincter as it divides to circle the rectum. The microscopic appearance is nonspecific (Madoff *et al.,* 2003).
3. ***Anal Fistula*** is an abnormal tract having an internal opening within the anal canal, usually at the dentate line which may lead to the skin, or end blindly in the perianal soft tissues (Hanley PH *et al.,* 1978). The lining of the fistula is made of granulation tissue, although epithelium may eventually grow at either end of the tract along with nonspecific microscopic appearance (Figure 2). It can be a manifestation of the tuberculosis, crohn's disease, ulcerative colitis or actinomycosis (Logan *et al.,* 1969).
4. ***Granuloma Inguinale (Donovanosis)*** is a chronic superficial ulceration caused by *Calymmatobacterium granulomatis*, which can extend to the perianal region and which may be confused clinically with squamous cell carcinoma (O'Farrell N *et al.,* 2001). Definitive diagnosisis evident if DONOVAN BODIES are found in Warthin–Starry or Giemsa preparations.
5. ***Lymphogranuloma Venereum*** is a sexually transmitted disease caused by Chlamydia trachomatis which can cause a granulomatous proctitis. Microscopic changes are follicular lymphohistiocytic and plasmacellular infiltrate in the wall, associated with neuromatous hyperplasia and extensive fibrosis (De la Monte *et al.,* 1985).

C. Hemorrhoids

It is the result of the ectasia of the hemorrhoidal vascular plexus and divided into *external* (outside the anal verge, in the territory of the inferior rectal vessels) and *internal* (inside the rectum, in the territory of the superior rectal vessels) (Hulme-Moir *et al.,* 2001).Thrombosis of external hemorrhoids is frequent (Figure 29). The organization and recanalization of these thrombi can lead to florid papillary endothelial hyperplasia, a process that can be over-interpreted as angiosarcoma (Figure 3) (Kuo *et al.,* 1976).

D. Neoplastic lesions of anal canal

1. Condyloma and HPV related lesion

In the anal region, condylomaaccuminata is the most common HPV related lesionpresents as one or more papillary excrescences lined by hyperkeratotic squamous epithelium (Figure 6) usually exhibiting variable degrees of koilocytotic changes (Rock B et al 1992).The types of HPV most commonly encountered are 6, 11, 16, and 18. Other lesions in which HPV participation is often found include anal intraepithelial neoplasia, verrucous carcinoma/giant condylomaacuminatum of Buschke–Löwenstein, and squamous cell/basaloid carcinoma.

2. Anal Intraepithelial Neoplasia (AIN)

It embresses dysplasia, squamous cell carcinoma in situ (CIS), and Bowen disease of the anus. AIN lesions are divided into three grades (AIN 1, AIN 2, AIN 3) depending on their microscopic severity, using criteria similar to those employed in the cervix and also been classified into a *Bowenoid type* (more common) and a *differentiated type* using criteria as used for vulvar intraepithelial neoplasia (Rosai and Ackermann, 2010).

3. Carcinoma

Higher incidence of anal carcinoma has been noted in old age group with female to male ratio of 3:1 and presents with bleeding per rectum (50%), pain (40%), mass(25%), and pruritus(15%)(Frisch *et al.,* 1993).HPV has been detected in anal carcinomas with HPV16 being the specific subtype in 82% of HPV+ cases (Duggan MA *et al.,* 1991).On gross examination, it presents as an exophytic or infiltrative growth with or without ulceration near the pectinate line (Figure 1).On microscopic examination, two distinct types of carcinoma arise in this area: (1) *squamous cell* carcinoma, analogous to its counterpart elsewhere in the skin (Figure 5); and (2) *cloacogenic*(transitional, basaloid) carcinoma, supposedly originating from the transitional epithelium of the region. The latter tumor identified by the presence of solid tumor nests exhibiting peripheral palisading somewhat resembling that seen in cutaneous basal cell carcinoma (hence the alternative term *basaloid*) (Grinvalsky HT *et al.,* 1956)(Figure 4). Dougherty and Evans have proposed to subdivide them into

five types: keratinizing, nonkeratinizing, basaloid, with mucous cysts, and pseudoadenoid cystic (Dougherty BG *et al.,* 1956). Immunohistochemically, anal carcinomas exhibit reactivity for all major cytokeratin classes, epithelial membrane antigen (EMA), carcinoembryonic antigen (CEA), and blood group isoantigens (Levy R *et al.,* 1991). Anal carcinomas also showhigh expression of SOX2 (an HMG-box embryonic stem cell transcription factor) but not of CDX2 (Long KB *et al.,* 2009). The prognosis of carcinoma of the anal canal depends on several parameters e.g. patients age, tumor location, size and stage, microscopic grading and staging of the lesion etc (Boman *et al.,* 1984).

OTHER MICROSCOPIC TYPES includes small cell neuroendocrine carcinoma, spindle cell carcinoma, veruccous carcinoma, adenocarcinoma, mucinous adenocarcinoma and basal cell carcinoma(Rosai and Ackermann, 2010).

Tumor, Node, Metastasis (TNM) Staging Scheme for Carcinoma of the Anal Canal (Peter A. Humphrey)

Primary Tumor (T)

TX - Primary tumor cannot be assessed
T0 - No evidence of primary tumor
Tis - Carcinoma in situ
T1 - Tumor ≤2 cm in greatest dimension
T2 - Tumor >2 cm but not >5 cm in greatest dimension
T3 - Tumor >5 cm in greatest dimension
T4 - Tumor of any size invades adjacent organ(s), e.g. vagina, urethra, bladder

Regional Lymph Nodes (N)

NX - Regional lymph nodes cannot be assessed
N0 - No regional lymph node metastasis
N1 - Metastasis in perirectal lymph node(s)
N2 - Metastasis in unilateral internal iliac and/or inguinal lymph node(s)
N3 - Metastasis in perirectal and inguinal lymph nodes and/or bilateral iliac and/or inguinal lymph nodes

Distant Metastasis (M)

MX - Distant metastasis cannot be assessed
M0 - No distant metastasis
M1 - Distant metastasis

Stage grouping

Stage 0	Tis	N0	M0
Stage I	T1	N0	M0
Stage II	T2	N0	M0
	T3	N0	M0
Stage IIIA	T1	N1	M0
	T2	N1	M0
	T3	N1	M0
	T4	N0	M0
Stage IIIB	T4	N1	M0
	Any T	N2	M0
	Any T	N3	M0
Stage IV	Any T	Any N	M1

4. Paget's disease of anal canal

It is a malignant glandular neoplasm having a predominant or exclusive intraepithelial location. Clinically, it presents as an erythematous, ulcerated lesion of eczematoid appearance. On microscopic examination, the Paget cells are predominantly located along the epithelial basal layer. Most of them are arranged individually, but occasionally there are nests and gland-like formations. These cells are large and have an abundant pale cytoplasm with occasional signet ring appearance (Goldblum *et al.,* 1998). It can be subdivided into two types depending on their pattern of differentiation, one (by far the most common) resembling apocrine glands (cutaneous type) and the other resembling colorectal adenocarcinoma (endodermal type). As a rule, the former is exclusively intraepithelial (as is its counterpart in the vulva), whereas the latter is often associated with invasive rectal adenocarcinoma (Goldblum *et al.,* 1998).

5. Malignant melanoma

Most cases occur in adults with the typical gross appearance is that of single or multiple polypoid masses covered by a smooth surface (Ellis *et al.,* 2010). On microscopic examination, the tumors are usually pigmented, and two-thirds show a 'junctional' component with a lentiginous appearance in the adjacent mucosa (Wanebo *et al.,* 1981). The overall prognosis, which in general is extremely poor, is directly related to tumor size and depth of invasion (Wanebo *et al.,* 1981).

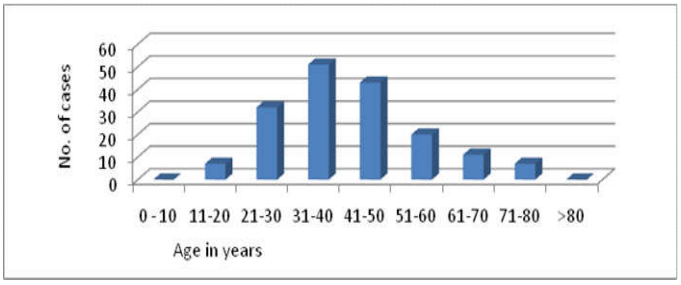
MATERIALS AND METHODS

A study of 171 patients presenting with C/O abdominal pain and bleeding per rectum at B.J. Medical college, Civil Hospital, Ahmedabad over a period of three years from 2014 to 2016was undertaken. Allspecimens of resected intestine (anal canal) as well as small biopsies were received and over-night fixation in 10% formalin was done. Gross examination findings were noted followed by routine paraffin embedding and tissue sectioning. Slides were stained using H&E stain, examined microscopically and staging was done followed by comparison with other studies.

RESULTS AND DISCUSSION

A retrospective study of 171 cases was undertaken and following observations and results were noted.

Table 1. Age wise distribution of lesions of anal canal



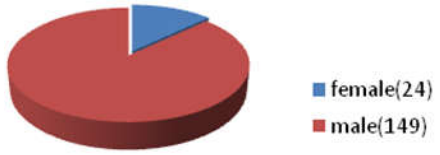
Highest number of cases of lesions of anal canal was distributed in the age group of 30-50 years of age. In the present study, age incidence of malignant anal canal lesions was maximum between 41-70 yers. This was also in concordance to a study by Dougherty BG *et al.,* in which they concluded that anal canal malignancies are most common in 5^{th} to 7^{th} decade.

Table 2. Comparison of malignant anal canal lesions according to age

Age group(years)	Present study		Dougherty BG et al.	
	No. of cases	Percentage	No. of cases	Percentage
0-9	0	0	0	0
10-19	0	0	0	0
20-29	0	0	1	1.2
30-39	1	25	3	3.7
40-49	1	25	13	16.45
50-59	1	25	24	30.37
60-69	1	25	29	36.7
>70	0	0	9	11.39
Total	4	100	79	100

Table 3. Sex wise distribution of lesions of anal canal

ex	No of cases	Percentage
Male	149	87.14
Female	22	12.86
Total	171	100



Lesions of anal canal showed a male predominance accounting for 87.14 % of total cases with male: female ratio of 7:1.

Table 4. Distribution of lesions of anal canal according to type

Small intestinal lesions		No. Of cases	Percentage
Non neoplastic		159	93
Neoplastic	Benign	8	4.67
	Malignant	4	2.33
Total		171	100

Majority of lesions of anal canal were of non-neoplastic nature(93%) followed by the benign neoplasms accounting for 4.67% of total lesions of anal canal. Malignant neoplasms were only 2.33% of total lesions of anal canal.

Table 5. Comparison of distribution of lesions of anal canal according to type

Anal canal lesions		Present study(%)	Riteshsulegaon et al. (%)
Non neoplastic		93	85.94
Neoplastic	Benign	4.62	0
	Malignant	2.33	14.06

In the present study majority of lesions of anal canal were of non-neoplastic nature (85.94%) and similar results were seen in study done by Riteshsulegaon et al.

Table 6. Categorization of lesions of anal canal

Category	No of cases	Percentage
Anal Fistula	107	62.5
Koch's inflammation	9	5.26
Hemorrhoids	43	25.14
Benign	8	4.67
Malignant	4	2.33
Total	171	100

The most common lesion of anal canal was anal fistula(62.5%) followed by hemorrhoids(25.14%). Neoplastic lesions (7%) comprised only a small portion of total lesions of anal canal.

Table 7. Categorization of non neoplastic lesions of anal canal

Category	Lesion	Present study		Riteshsulegaon et al.	
		No.of cases	Percentage	No.of cases	Percentage
Non-neoplastic	Anal Fistula	107	67.3	33	61.1
	Koch's inflammation	9	5.7	0	0
	Hemorrhoids	43	27	19	35.1
	Hypertrophied anal papillae	0	0	3	5.55
	Total	159	100	54	100

In the present study it was observed that the most common non neoplastic lesion of anal canal is anal fistula (62.5%) followed by hemorrhoids (25.14%). The results were comparable to study of Riteshsulegaon *et al.,* with anal fistula and hemorrhoids accounting for 61.1 % and 35.1 % cases respectively.

Table 8. Distribution of neoplastic lesions of anal canal according to histopathological diagnosis

Histological diagnosis	No of cases	Percentage
Benign lesion		
Fibro-epithelial polyp	4	33.34
Adenomatous polyp	1	8.3
Squamous papilloma	1	8.3
Anal wart	1	8.3
Lipoma	1	8.3
Malignant lesions		
Squamous cell carcinoma	2	16.8
Adenocarcinoma	1	8.3
Basaloid carcinoma	1	8.3
TOTAL	12	100

Among all neoplastic lesions of anal canal, Fibro-epithelial polyps (33.34%) were the commonest benign lesions and squamous cell carcinoma (16.8%) was the commonest malignant lesion.

TNM staging has not been included in the present study.

Table 9. Comparison of categorisation of anal canal malignancies according to histological type

Category	Present study(%)	Riteshsulegaon et al.(%)	Dougherty BG et al. (%)	James Klas et al.(%)
Squamous Cell carcinoma	50	55.55	86	74
Adenocarcinoma	25	33.33	0	19
Basaloid carcinoma	25	0	14	0
Malignant Melanoma	0	11.12	0	4
Others	0	0	0	3

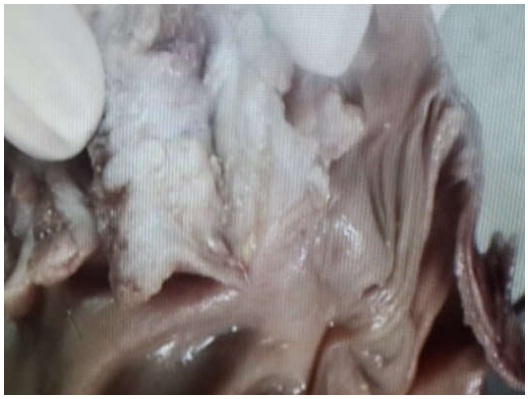


Figure 1. Gross photograph of carcinoma of anal canal showing tumor mass with grayish white cut surface

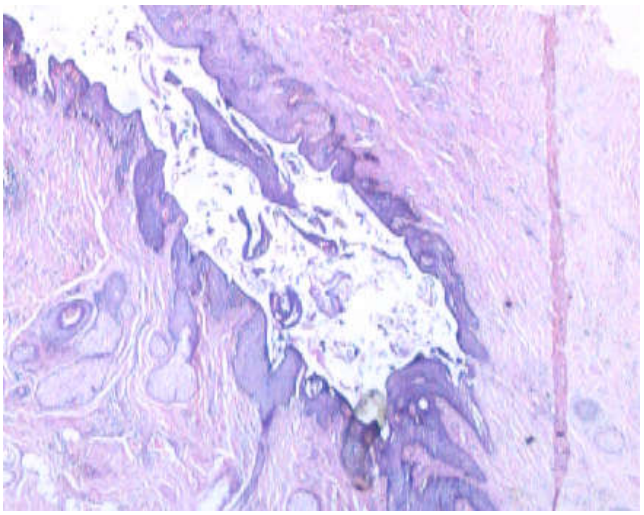


Figure 2. Microscopic photograph showing epithelized fistula tract in anal canal. (H&E, 2X)

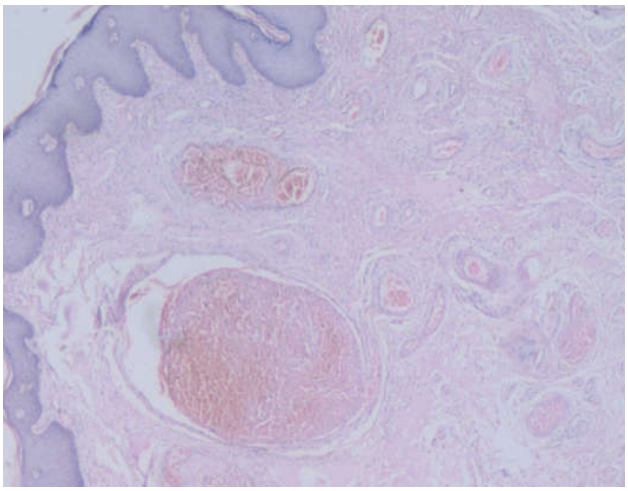


Figure 3. Microscopic photograph of haemorrhoids with thrombosed vessels. (H&E, 4X)

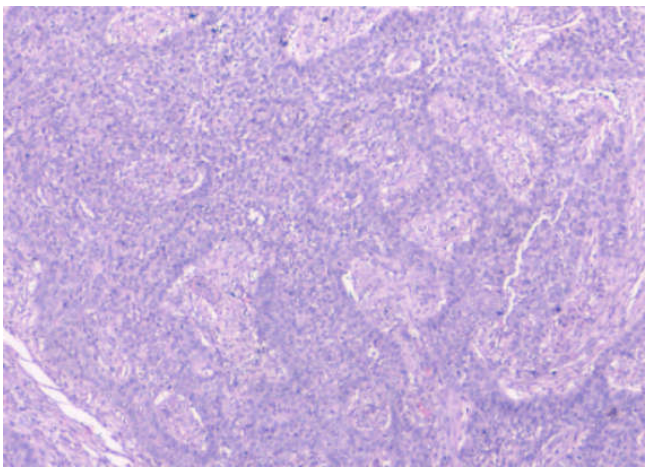


Figure 4. Microscopic photograph of basaloid carcinoma showing solid tumor nests with peripheral palisading. (H&E, 4X)

Squamous Cell carcinoma followed by adenocarcinoma was the most common malignancy of the anal canal as reflected in the present study (50 %) as well as in studies by Riteshsulegaon *et al.,* (55.55 %), Dougherty *et al.,* (86 %) and James V. Klass *et al* (74 %).

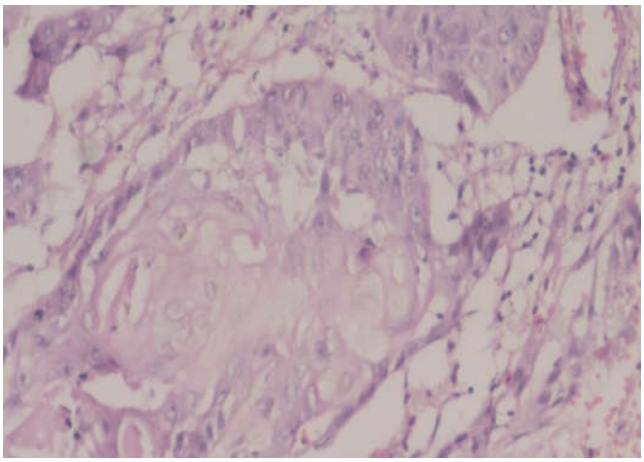


Figure 5. Microscopic photograph of well differentiated squamous cell carcinoma of anal canal. (H&E, 20X)

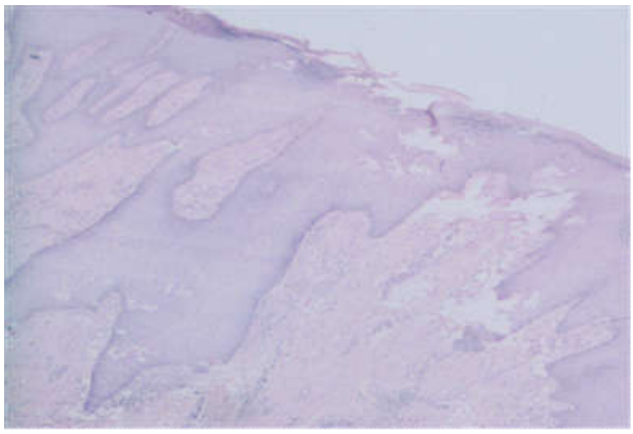


Figure 6. Microscopic photograph of squamous papilloma showing papillomatous squamous epithelium (H&E, 4X)

Conclusion

Following conclusions have been drowned from the present study. The histo-pathological examination is a useful tool in the diagnostic work up of lesions of anal canal. Majority of the lesions are affecting males of middle age group presenting with complain of bleeding per rectum. More than 90% lesions are of non- neoplastic in nature and highly curable. Even though neoplastic lesions are rare, their diagnosis and staging are very important. Thus, categorization of lesions of anal canal on histological grounds are helpful in therapeutic decisions providing better outcome.

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