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HISTOPATHOLOGICAL STUDY OF LESIONS OF ANAL CANAL

Pathology

Dr. Medha Kulkarni Associate Professor, Department of Pathology, Government Medical College and Hospital, Miraj

Dr. Akshata Parab MBBS, M.D., DNB Pathology

Dr. Shubhangi Gaikwad* Junior Resident, Department of Pathology, Government Medical College and Hospital, Miraj*Corresponding Author

Dr.(Mrs.) Y. A. Momin Professor & HOD, Department of Pathology, Government Medical College and Hospital, Miraj

ABSTRACT

Background. Diverse diseases including congenital anomalies like Hirschsprung disease, anorectal agenesis, infections like tuberculosis, parasitic infestations, inflammatory disorders like Crohn's disease ulcerative colitis, and neoplasms like adenomas, adenocarcinomas, squamous cell carcinoma etc, involve the anal canal. Despite its short length, the anal canal produces a variety of tumor types reflecting its complex anatomic and histologic features (WHO). Majority of these disorders present with common symptoms like constipation, per rectal bleeding, altered bowel habits and difficulty in defecation. **Aim:** The study was undertaken with the aim of analysing the histopathological lesions of anal canal with clinicopathological corelation. **Materials and methods:** Total 116 lesions affecting anal canal over a period of January 2013 to June 2017(4.5 years) were included in this study. Demographics of patients, presenting symptoms and pathologic features were recorded. **Results:** Out of 116 lesions, 106 were nonneoplastic, greatly outnumbering the eight neoplastic lesions. Anal fistula was the most common lesion accounting for 49 cases. Most common age group affected was 31-40 years. **Conclusion:** Histopathological examination of every anal lesion is important since clinical presentation of neoplastic and nonneoplastic disorder is same. Rare entities like anal gland carcinoma can be diagnosed only on histopathology.

KEYWORDS

Anal fistula, Anal gland carcinoma.

INTRODUCTION:

Unlike other organ systems, the gut is in continuity with the outside environment. Gastrointestinal diseases develop as a result of abnormalities within or outside the gut and range in severity from those that produce mild symptoms and no long-term morbidity to those with intractable symptoms or adverse outcomes. Diseases affecting anal canal may be localized or exhibit diffuse involvement at many sites.1They vary from inflammatory to malignant conditions and many times require colonoscopic biopsy for confirmatory diagnosis. In India with the adoption of westernized lifestyle and diet practices, the incidence of anal cancer is increasing. It is the third most common cancer in men and second most common cancer in women worldwide.[2]

Even with the availability of newer modalities for diagnosis, histopathology is mandatory in differentiating benign from malignant lesions which present with similar complaints.

MATERIAL AND METHODS:

116 lesions were included in the study. Clinical details of the patients like age, sex and presenting symptoms were noted. The specimens were fixed in 10% formalin. Careful gross examination of the specimens was done and representative sections were submitted for tissue processing. Sections were stained with hematoxylin and eosin. Microscopic examination was done. Gross, microscopy and clinical features were correlated to arrive at a final diagnosis.

RESULTS:

Out of total 116 patients, 76 were males and 40 females. Most common age group affected was from 31-40 years.

DISTRIBUTION OF LESIONS OF ANAL CANAL

Category	No of cases	Percentage
Non-neoplastic	106	91.30%
Neoplastic	8	6.80%
Inadequate for opinion	2	1.70%
Total	116	100%

DISTRIBUTION OF NON- NEOPLASTIC LESIONS OF ANAL CANAL

Lesions	No. of cases	Percentage
Fistula in ano	49	(46.22%)
Hemorrhoids	35	(33.01%)
Fibroepithelial polyp	21	(19.81%)
Chronic non specific inflammation	01	(0.94%)
Total	106	100

Out of 116, 106 (91.3%) were nonneoplastic lesions, which were significantly more than the neoplastic lesions which accounted for only 8 (6.8%). Commonest nonneoplastic lesion was anal fistula contributing 49 out of 106 cases i.e. 46.22% followed by hemorrhoids (35 cases, 33.01%.)

DISCUSSION:

The study was carried out over a period of 4.5 years from January 2013 to June 2017 and included 116 lesions of anal canal affecting 70 males and 40 females indicating male predominance. There were 106 nonneoplstic and 8 neoplastic lesions. Most common clinical presentation was per rectal bleeding with pain and difficulty in defecation. Commonest age group affected was 31-40 years. In the nonneoplstic category, anal fistula accounted for largest number, 49 cases. The patients clinically presented with pus discharge, pain and difficulty in defecation. The age group affected was 31-60 years (48.97%). Histopathology in majority of cases showed fistulous tract lined by granulation tissue infilterated by plasma cells, lymphocytes and polymorphs. Foreign body giant cells were also seen. In two of our cases, well formed epithelioid granulomas with caseous necrosis indicating tuberculosis were seen underscoring the importance of histopathological examination.

Sulegaon R et al reported 64 anal canal lesions, out of which 55 were non neoplastic (85.94%) comprising of 33 cases of fistula in ano, 9 hemorrhoids and 3 hypertrophied anal papillae.[3]

Veerendra Kumar et al in their study of 50 cases during the period of 2 years found the most common age group as 31-60 years (62%) with male to female ratio of 11.5:1 and the common presenting complaint as pus discharge through anus(100%).[4]

Fistula is typically defined as a pathological communication between two epithelialized surfaces. Perianal fistula, or fistula-in-ano, is a common benign anorectal disorder often characterized by significant clinical manifestations, such as local pain, inflammation, purulent

drainage, incontinence, and decreased patient quality of life.[5]

The glandular crypts at the level of the dentate line are the typical origin of fistulas, which is induced by purulent and inflammatory processes.[5]The disease is characterised by a high recurrence rate. The highest incidence of anal fistula is observed between 30 and 50 years of age, and men are affected more often than women.[6]

In a study by Sahnan et al approximately one fifth of all patients with anorectal abscess developed a fistula.[7]

Parks postulated the concept that enteric microorganisms begin the process of acute inflammation by infiltrating perianal gland channels.[8] Thus perianal fistula is a pathological canal secondary to an inflamed perianal gland; however, the duct opening in the perianal skin makes it a fistula. Therefore, anorectal abscesses and perianal fistulas are continuous phases of a common pathogenic spectrum. Histopathology is very essential to rule out specific conditions like tuberculosis, Crohn's disease and rarely adenocarcinoma. Adenocarcinoma arising in anal fistula, though very rare, has been documented.[9] It accounts for 2-3% of the large bowel tumors.[10]

The word" Hemorrhoids" is derived from the Greek word "hemorrhoides phlebes" meaning bleeding veins. Because of their rich vascular supply, highly sensitive location, and tendency to engorge and prolapse, hemorrhoidal venous cushions are common causes of anal pathology.[11] Symptoms can range from mildly bothersome, such as pruritus, to quite concerning, such as rectal bleeding.

Hemorrhoids are classified by their anatomic origin within the anal canal and by their position relative to the dentate line; thus, they are categorized into internal and external hemorrhoid.

1. External hemorrhoids develop from ectoderm, are covered by squamous epithelium, innervated by cutaneous nerves and hence are painful

2. Internal hemorrhoids are derived from embryonic endoderm, lined by columnar epithelium, are not supplied by somatic sensory nerves and therefore painless.

Hemorrhoidal venous cushions arise from subepithelial connective tissue within the anal canal. Internal hemorrhoids have three main cushions, which are situated in the left lateral, right posterior (most common), and right anterior areas of the anal canal. Haemorrhoides are one of the sites of portal systemic anastomosis.

We had 35 cases of hemorrhoids (33.01%) out of 106 nonneoplastic anal canal lesions. The commonest clinical presentation was per rectal bleeding. Histopathology of the hemorrhoids showed tissue lined by stratified squamous epithelium in external hemorrhoids while internal hemorrhoids were lined by columnar mucosa. The deeper tissue showed ectatic and thrombosed blood vessels. In one case there was papillary endothelial hyperplasia. Papillary endothelial hyperplasia in recanalizing thrombosed hemorrhoids may resemble vascular tumor but the former is confined to vascular spaces. In one case clinical diagnosis was hemorrhoid but histopathology revealed squamous cell carcinoma, highlighting importance of histopathological examination. Sulegaon et at al found 19 cases(34.55%) of hemorrhoids out of total 64 anal canal lesions in their study.[12]

We had 21 cases (19.8%) of anal tag, also called as fibroepithelial polyp (FEP), out of 106 nonneoplastic anal canal lesions. Clinically these polyps have the appearance of hemorrhoids. Anal tags are polypoidal masses of anal mucosa, usually squamous type, with underlying submucosal tissue.

The cut surface of anal tags may be edematous and soft or dense and fibrotic. The prominent dilated vessels of hemorrhoidal tissue are absent. Anal tags resemble cutaneous fibroepithelial polyps, with a squamous epithelial lining over loose fibrovascular submucosal tissue. They lack dilated veins and sinusoids, containing instead smaller branching thin walled vessels. The stroma contains fibroblastic tissue composed of spindle cells or enlarged stellate cells with bizarre or multiple nuclei if the lesion has been traumatised or irritated. Such stellate cells are evenly distributed within collagenous stroma and reflect an active or reparative atypia of no clinical significance. Groisman et al studied the immunohistochemical and ultrastructural features of a series of 40 FEPs (anal tags) and concluded that FEPs are characterized by presence of atypical, CD34+ stromal cells having fibroblastic and myofibroblastic differentiation.[13] It is necessary to differentiate these lesions from malignant tumors like leiomyosarcoma, anorectal carcinoma and malignant lymphoma which present as mass lesion at the anal verge.

Anal tumors are very rare constituting only 5% of the gastrointestinal tract tumors.[14,15]

According to WHO, a tumor of the anal canal is defined as a tumor that cannot be seen in its entirety or at all, when gentle traction is placed on the buttocks.[16]

Around 75% of tumors of anal canal are squamous cell carcinomas while over 20% are adenocarcinomas.[17]

Out of total 116 lesions, we encountered eight malignant lesions of anal canal (6.8%), 4 Squamous cell carcinomas (SCC), 2 adenocarcinomas and 2 malignant melanomas. SCC was the commonest with 4 cases (50%), finding consistent with the literature. Common age group affected was 50-70 years. Anal cancer rates are highest in homosexual men, particularly in those who are HIV-positive, in whom anal cancer is the most common cancer. SCC is also related to HPV, most common high-risk genotypes being 16, 18, 31, 33, 35. HPV oncogenes (*E5*, *E6*, *E7*) are involved in the pathogenesis. Incidence of anal SCC is increasing with increased use of immunosuppressive therapy.

Virtually all tumors below dentate line are SCC and present as painful mass or obstructive lesion. SCC may arise in condyloma acuminatum/AIN. The tumor may appear as ulcer, induration, fungating, or polypoid mass.

One case had well differentiated histology, rest three cases were moderately differentiated. Microscopically, well differentiated SCC revealed a tumor composed of round to polyhedral cells having pleomorphic hyperchromatic nuclei and moderate amount of eosinophilic cytoplasm arranged in sheets and clusters. Individual cell keratinization and few keratin pearls were noted. Sulegaon et al observed 5 cases of SCC (55.5 %) out of total 9 cases.[18]

Adenocarcinoma of anal canal (AA) arises in the epithelium of the anal canal including the mucosal surface, the anal glands, and the lining of fistulous tracts.[16] AA is of 2 types.

1. Perianal mucinous adenocarcinomas arising from anal canal are morphologically similar to rectum-based mucinous carcinomas but differ prognostically as the former have increased risk of metastasis to inguinal lymph nodes.

2. The extramucosal adenocarcinoma is a rare entity characterized by primarily extramucosal or intramural growth without a luminal component. The tumor invades the submucosa widely, and since the overlying mucosa is uninvolved, it can be mistaken for metastatic gastrointestinal carcinoma.[5]

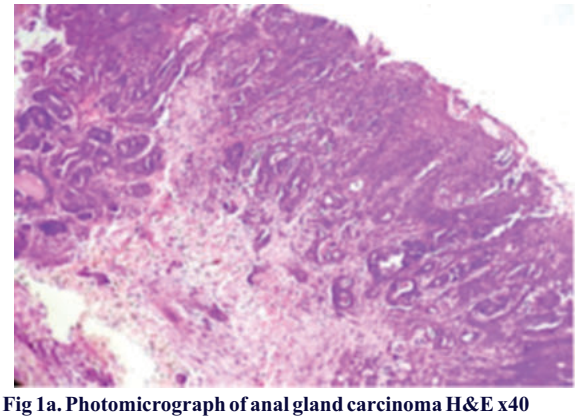

Fig 1a. Photomicrograph of anal gland carcinoma H&E x40

We had two cases of adenocarcinoma of anal canal. One was a 57 year old male presenting with bleeding per rectum on and off and pain during defecation for 6 months. He also complained of groin swelling

since 1 month. On per rectal examination, concentric growth was felt in the anal canal measuring 5 cm in length. There was no fistula. Rectum did not have any growth. Bilateral internal iliac and inguinal lymph nodes were enlarged and showed punctate calcification. Fine needle aspiration cytology (FNAC) of the inguinal lymph nodes was positive for malignant cells and revealed metastatic mucin secreting adenocarcinoma. We received a tiny biopsy. On microscopy, the tumor was composed of small acini and tubules with scant mucin production. Continuity was clearly evident between the tumor and the anal gland epithelium. Also, the overlying squamous mucosa was nonneoplastic. (Figure 1a).

A diagnosis of mucinous adenocarcinoma of anal canal was offered. On immunohistochemistry (IHC), cytokeratin 7 (CK7) was negative, whereas CK20 and CDX2 were positive, confirming the colorectal phenotype [Figure 1b-c].

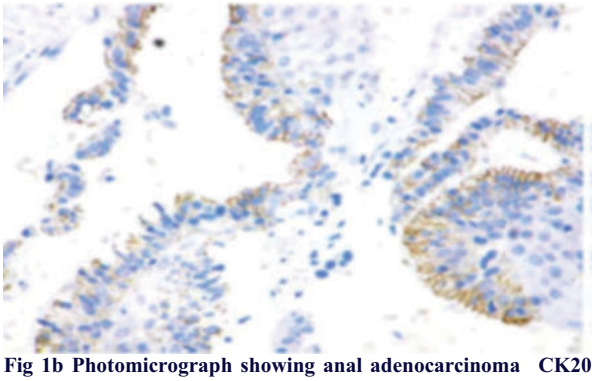

Fig 1b Photomicrograph showing anal adenocarcinoma CK20 positivity,

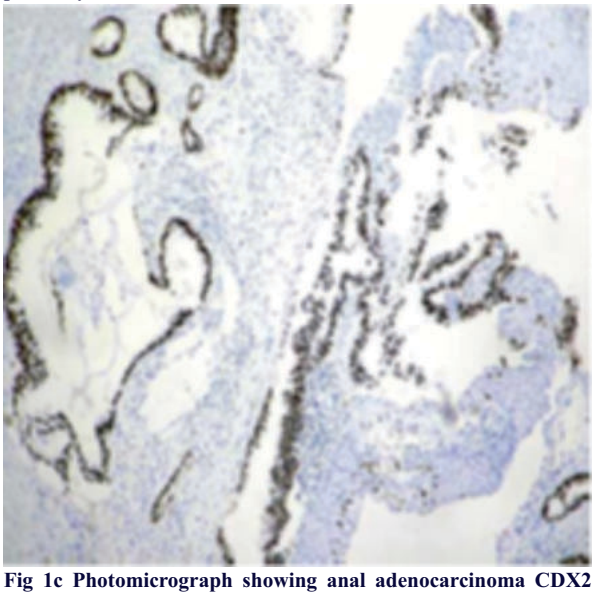

Fig 1c Photomicrograph showing anal adenocarcinoma CDX2 positive

Our second case was a 75 year old female who presented with progressively increasing difficulty in defecation and bleeding per rectum of 4 months duration. Per rectal examination revealed circumferential wall thickening 6 cm in length. There was no fistula. CT scan confirmed a heterogeneously enhancing concentric wall thickening of the anal canal measuring 5.5 cm × 7 cm × 4.8 cm. The rectum did not show any tumor. The growth also involved the adjacent ischiorectal and ischioanal fossae. She was nonreactive for HIV
Microscopy showed a tumor composed of cuboidal to columnar cells with pleomorphic vesicular nuclei and moderate amount of eosinophilic cytoplasm arranged in a tubular and acinar pattern. Scant intraluminal mucin was noted. The tumor was seen originating from the adjacent anal glands. The overlying mucosa was unremarkable. Diagnosis of anal gland adenocarcinoma was offered. IHC could not be done in this case as the biopsy was tiny Most adenocarcinomas in the anal canal are rectal carcinomas that have grown distally or arise from the rectal mucosa above the dentate line. The most significant clinical implication of distinguishing the anal canal origin of these tumors relates to its pattern of local spread which reflects its dual lymphatic drainage. These tumors carry a high risk of metastasis to the inguinal and femoral nodes than rectum-based adenocarcinomas.[18]

Hobbs *et al* have described anal gland carcinoma as a tumor composed of haphazardly dispersed small glands with scant mucin production invading the wall of anorectal area without an intraluminal component. According to the authors, 136 neither IHC nor continuity with anal glands is required for diagnosis of anal gland carcinoma.[19]

The first description of Anorectal melanoma (ARM) in the literature dates to 1857, by Moore and so far 500 cases have been reported in the literature.[20] The most common sites of melanomas are the skin (91.2%), followed by eyes (5.2%) and the anorectal region (less than 1%).[21] ARMs occur more often between the sixth and eighth decades of life and are more frequent in women. In the present study we encountered two cases of malignant melanoma of anal canal. One was 49 year male and another a 50 year female, both presented with per rectal bleeding and difficulty in defecation since 3 months. On per rectal examination a growth was seen 2cm away from anal verge. Ultrasonography (USG) of the abdomen in both the cases revealed multiple echogenic lesions in liver with necrotic areas suggestive of metastasis.

Microscopic examination in both revealed a tumor composed of round to oval to spindle cells having pleomorphic hyperchromatic nuclei with focally prominent eosinophilic nucleoli and eosinophilic cytoplasm arranged in dyscohesive sheets, clusters and focal alveolar pattern. Some of the cells showed intracytoplasmic black melanin pigment. Multinucleate tumor giant cells and mitotic figures were noted. ARM is very aggressive disease. It presents with per rectal bleeding like non neoplastic lesions. About 1/3rd of the patient may have pigmented lesions making the diagnosis difficult and biopsy necessary. In 29% of the patients distant metastasis is identified at the time of diagnosis. Perirectal, perianal and mesenteric lymph nodes are the most common sites of metastases followed by inguinal lymph nodes, liver and lung.

CONCLUSION

Clinical presentation of lesions of anal canal both neoplastic and non-neoplastic was PR bleeding. Meticulous evaluation and work up comprising of proper history, clinical examination and histopathology is important for correct diagnosis.

Histopathological examination is pivotal in differentiating malignant from benign lesions, recognizing precursor lesions and also in predicting the prognosis. More than 90% of lesions are of nonneoplastic in nature and highly curable. Even though neoplastic lesions are rare, their diagnosis and staging are very important. Thus, categorisation of lesions of anal canal on histological grounds are helpful in therapeutic decisions providing better outcome.

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