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Pathology

CASE SERIES OF 5 CASES OF TUBULAR ADENOMA WITH DYSPLASIA AND REVIEW OF LITERATURE

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ABSTRACT Tubular adenomas are the most common types of adenomas and have the potential to turn malignant. Sometime they are seen as incidental finding and associated with dysplasia, carcinoma in situ or malignancy. Risk factor involves first-degree relative family history, smoking history, excessive alcohol intake, diabetes mellitus, and a higher body-mass index. Incidence of adenoma are increasing in developing countries. Due to the silent presence of the disorder, all people must be educated to undergo screening colonoscopy after 50 years of age. Individuals with a positive family history are the target population for earlier and more frequent screening processes. Hereby we present case series of 5 cases of tubular adenomas of low grade dysplasia, tubulovillous adenoma and tubular adenoma of high grade dysplasia.

KEYWORDS : Tubular adenoma, malignant potential, dysplasia, chromosomal instability, screening

INTRODUCTION

Colonic adenomas are elevated polyps made of glandular tissue that protrude from the colonic mucosa. Contrary to hyperplastic polyps, which have no malignant potential, these benign tumors are called adenomas, which are typically thought to be precancerous and capable of developing into malignant structures.[1] The prevalence of large intestinal adenomas varies in different parts of the world. Adenomas are common in westernized cultures and uncommon in developing countries. [2] Several studies have reported a higher risk of colon cancer in patients with a first-degree relative family history, smoking history, excessive alcohol intake, diabetes mellitus, and a higher body-mass index, which can be a reflection of a high-fat, low-fiber diet and limited physical activity. [3]

The incidence of adenomas parallels the incidence of colorectal cancer, and countries with high rates of colorectal cancer also have high rates of colorectal adenoma.[4] Adenomas occur more frequently as people age, with a 50% incidence in patients between the ages of 60 and 80. They are frequently detected in the rectum, sigmoid colon, transverse colon, and ascending colon.[5] There are three types of adenomas: conventional, flat, and serrated. The most frequent adenomas are conventional adenomas, depending on their main growth pattern.[5] Before the age of 40, adenomas are rare. Adenomas are comparatively uniformly distributed over the length of the large intestine, according to autopsy surveys. However, as people age, adenomas in the ascending colon become more common. [6] Grossly, adenomas assume one of the three major growth patterns. (a) Pedunculated (b) Sessile, or (c) flat or depressed.

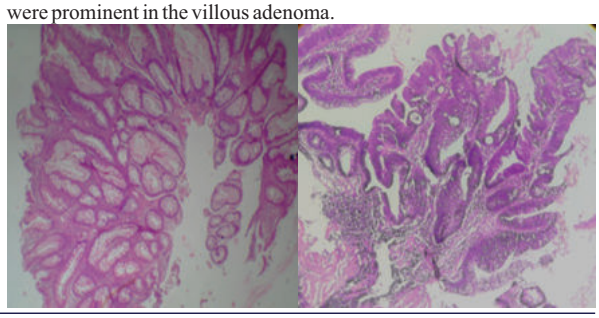
Depending on the pattern of growth, these tumors can be villous, tubular, or tubulovillous. Villous adenomas are polyps that contain more than 75% villous features, such as long projections that resemble fingers or leaves, while tubular adenomas are primarily made up of tubular glands and have fewer than 25% villous features. An adenoma with combined characteristics is referred to as tubulovillous. The most prevalent type of colonic adenomas, with a prevalence of more than 80%, are tubular adenomas.[7]

PATIENT AND CASE STUDY

We report a case series of five cases of colorectal adenomas diagnosed in tertiary center of South Tamil Nadu. All patient presented in department of surgery on OPD basis. One patient present in the department of surgery with the complain of abdominal pain. Two patient came for routine checkup. One was known cases cervical cancer and was referred from the gynaecology department. On examination she also had colon cancer. One of patient was previously presented colon cancer and now she had recurrence. A detailed interview, physical examination, and laboratory monitoring are performed for each of the patients. Age of the patient ranged from 40 years to 80 years with a mean age of 47 years. Three cases were male and two were female. Two of patient had iron defiency anaemia with hypertension and type 2 diabetes. All the patient had low hemoglobin ranging 5.7 to 11.2 g/L. Only one case had random blood sugar was 260 mg/dl. Rest have random blood sugar within normal range. Liver function test and kidney function test were within normal limit.

Colonoscopy was planned and colonoscopic biopsy was sent for histopathological confirmation in our pathology department. One gross examination grey white polypoidal tissue pieces received ranging from 0.1x0.2 to 2x2 cm. On histopathology ,following diagnosis was made. One case was diagnosed as adenocarcinoma at hepatic flexure and tubular adenoma with low grade dysplasia for colonic polyp .She was known case of cervical carcinoma IIb .Other case was diagnosed tubulovillous adenoma with high grade dysplasia. He was known case of colon cancer with recurrence. Other three cases were diagnosed as tubular adenoma with low grade dysplasia.

Histologically tubular adenomas showed tubular architecture with back to back gland arrangement having stratification of lining epithelium with mild hyperchromatic nuclei, mitosis and mucin depletion. The nuclei are crowded, elongated and stratified. All the three tubular adenomas showed low grade. Dysplasia. The tubulovillous adenoma showed tubular areas along with elongated finger like non branching fronds and dysplastic epithelium showing stratification of the lining epithelium with hyperchromatic nuclei and mitoses. Considerable architectural abnormality present in the form of crowding and back to back gland arrangement was present. Nucleoli were prominent in the villous adenoma.



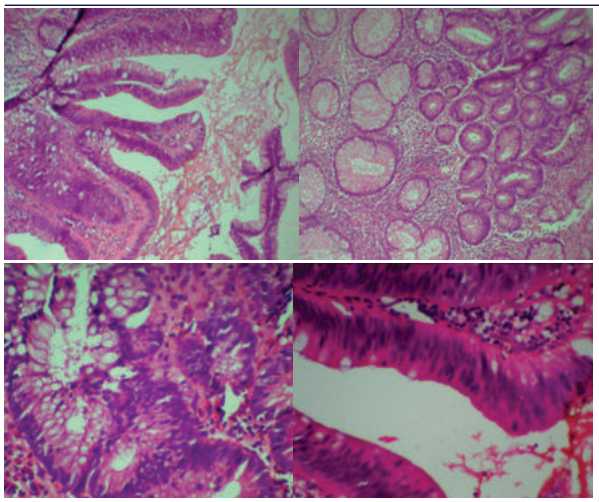


Figure 1: Polypoidal colonic fragment of superficial colonic mucosa , disposed in tubular configuration[HE 40X]; Figure 2: Polypoidal colonic fragment disposed in tubulovillous configuration [HE 40X]; Figure 3: HE 100X];Figure 4,5:Mucosa is composed of crowded crypts lined by columnar cells exhibiting enlarged elongated hyperchromatic and pencillate nuclei and esoinophilic to vacuolated cytoplasm. [HE 400X] Figure 6: Nuclear stratification is mostly more than one half of epithelial cells thickness with ocassional mitotic figure[HE 1000X]

Cases reported as tubular adenoma with low grade dysplasia and tubulovillous adenoma were kept under close follow up and subsequent screening being done. Case reported as adenocarcinoma at hepatic flexure and tubular adenoma with low grade dysplasia for colonic polyp underwent total colectomy and ileorectal anastomosis. Subsequantly chemotherapy was given after colectomy.

DISCUSSION

Tubular adenomas are more frequently pedunculated lesions. They represent the majority of adenomatous polyps, accounting for nearly two-thirds of lesions identified. Polyp with more than 75% villous features, is called a villous adenoma, while tubular adenomas are mainly comprised of tubular glands and have less than 25% villous features. A tubulovillous adenoma is referred to as an adenoma with both features. Tubular adenomas are the most common type of colonic adenomas, comprising a prevalence of more than 80%.

The molecular alterations that result in the development of carcinoma from adenomas are explained by the adeno-carcinoma sequence. Colonic polyps are the cause of more than 95% of colon adenocarcinomas, and 1.5% to 9.4% of adenomas develop into malignant lesions during an 8–10 year window. The adenoma-adenocarcinoma interval's duration is influenced by the adenoma's size, morphological characteristics, and pathological subtype. Our analysis revealed a predominance of men. Our study showed a male preponderance. Four cases are male and one case is female. In study by Fenoglio-preiser CM, adenoma occurred more frequently in men than women, with 61.6% cases in men and 38.4% cases in women.[8]

Four cases in our study involved people above the age of 50, and one was under the age of 40. 45% of the cases, according to William et al., were reported to be between 51 and 65 years old[12]. Adenomas less than 1 cm have a 0.2% risk of being malignant, those between 1 and 2 cm have a 4.2% chance, and those greater than 2 cm have a 27% likelihood. [9] Size, growth pattern, and dysplasia grade are morphological characteristics that identify an adenoma's risk for malignancy. Majority of colorectal adenomas are tiny, with 95% measuring less than 2 cm at their largest. However, there is a correlation between the degree of villous component and polyp size at diagnosis. Adenomas under 5 mm almost never host cancer, but as they get larger and more villous, their invasive capacity increases in a positive linear fashion.[10]

According to the classification of adenomas into those with a predominantly tubular pattern, those with a predominantly villous pattern, and those with a mixture of tubular and villous areas (tubulovillous adenoma), the villous pattern adenoma generally has a higher malignant potential than the tubular pattern adenoma. Multiple adenomas, a big adenoma, severe dysplasia, a tubulovillous or villous adenoma, and an adenoma in the proximal colon are among the recognized risk factors for recurrence. [11] In conclusion, adenomas typically have no symptoms. Larger adenomas may bleed, and occult blood testing may be used to detect this. The most frequent dysplasia in adenomas is mild, while the least frequent is severe. The diagnosis of invasive cancer requires demonstration across the muscularis mucosae. It is important to distinguish between innocent displacement (pseudoinvasion) through the muscularis mucosa and into the submucosa. It is recommended that all polypoidal lesions be removed for a thorough histological analysis. Adenomas must meet criteria by having more than 75% tubular characteristics.[10]

Only 5% to 10% of all adenomas are villous adenomas, the least frequent kind of adenomatous polyp. Compared to other polyps, they are more frequently sessile and frequently have a "cauliflower-like" look that is multilobated and friable. Epithelial fronds, which may be solitary or branching, are distinctive histologically. Villous lesions have a more significant link with cancer than other adenomatous polyps. Importantly, sampling error with endoscopic biopsy may occur, especially with bigger lesions, and due to the high risk of associated malignancy, all villous adenomas should be thoroughly excised.[10] It can be difficult to distinguish between villous structures and elongated separated tubules. The length of the glands exceeding twice the thickness of the normal colorectal mucosa is what arbitrarily defines villus architecture.[11] Advanced adenocarcinomas are more likely to develop later in life in people who had reported advanced adenomas, i.e., higher dysplasia grade and larger villosity in the first colonoscopy. As a result, they require more active and regular colonoscopic supervision. In general, the histological type and degree of dysplasia of an adenoma are correlated with its size. In contrast to villous adenomas, which typically have higher polyp sizes, tubular adenomas primarily consist of smaller adenomas (less than 1 cm). High-grade dysplasia is less common in the tiny tubular adenomas.[13]

Adenomas that have tubular and villous components are known as tubulovillous adenomas. These lesions don't happen as often as tubular adenomas.[10] Microscopically, compared to the normal mucosa, there are more glands and cells per unit area. The cells are packed tightly together, have enlarged hyperchromatic nuclei, and undergo a greater number of mitoses, some of which may be abnormal. Adenomatous polyps commonly contain focal regions with a villous configuration.[14] The number of polyps per patient, size of the polyps, and presence of villous alterations are all connected to advancing age, as well as the degree of atypia exhibited in adenomatous polyps. There are three levels of severity: mild, moderate, and severe; the latter level is equal to cancer in situ. [14] Sometimes, clusters of atypical glands in an adenomatous or villoglandular polyp are seen beneath the muscularis mucosae and may lead to a mistaken diagnosis of malignant transformation.[15]

Two main molecular pathways lead to adenocarcinoma of the colon. The chromosomal instability (CIN) pathway is the most attributed pathway and accounts for almost 80% of colorectal adenocarcinomas in the U.S. In this pathway, cancer develops within adenomas through a series of progressive mutations in several genes, including adenomatous polyposis coli (APC), K-RAS , SMAD4, and p53, as follows: The first step in the adenoma-carcinoma sequence is sporadic or germline inactivation of the tumor suppressor gene, APC, that increases the likelihood of developing a polyp due to β-catenin accumulation, which can then translocate to the nucleus and drive cell proliferation. K-RAS mutation occurs afterward and leads to the formation of the polyp. Inactivation of the other tumor suppressor gene, p53, and increased expression of COX allow for progression to carcinoma. Aspirin may play a role in this process by impeding the progression from adenoma to carcinoma, which leads to improved survival outcomes in colorectal cancer. Carcinomas that develop in this pathway exhibit CIN are microsatellite stable (MSS) and mismatch repair proficient (MMR-P). In the second pathway, called the serrated pathway, cancer develops through the malignant transformation of sessile serrated adenoma/polyp (SSA/P) precursor lesions. This pathway is not the focus of the present report.[16]

The screening should start at age 50 for everyone and continue until age 75, according to the recommendation. The choice should be made specifically for each adult between the ages of 76 and 85, taking into account their overall health and screening history. Testing for fecal occult blood and the gold-standard colonoscopy are typically used for

polyp screening. Screening is advised in less than three years if the examiner finds more than ten adenomas or even if an adenoma displays villous characteristics, whereas repeat screening should be done in three years for those who have three to ten adenomas. If there are only one or two small tubular adenomas, the interval may last five to ten years.[17] Recent studies have revealed that despite these surveillance guidelines, adherence to follow-up evaluations is low, and more must be done to increase this value.[18]

CONCLUSION

Tubular adenomas are the most common types of adenomas and have the potential to turn malignant. Sometime they are seen as incidental finding and associated with dysplasia, carcinoma in situ or malignancy. Recommendations include educating the general population on the nature of polyps and their outcomes. All people should be aware that colon cancer is generally asymptomatic, and if symptomatic, presents with hematochezia. Due to the silent presence of the disorder, all people must undergo screening colonoscopy after 50 years of age. Individuals with a positive family history are the target population for earlier and more frequent screening processes. Thus any polyp seen in the colon should be reported and evaluated properly.

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