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Case Report

Pathology Section

High Grade Dysplastic Villous Adenoma Arising from a Giant Hamartomatous Polyp- A Rare Case Presentation

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ABSTRACT

Adenomatous polyps can be found throughout the colon, most commonly in right colon. Microscopically, they are classified as tubular, villous or tubulovillous subtypes. Tubular adenomas are the most common subtype with villous component less than 25%. Tubulovillous adenomas have a villous component that accounts for 25-75%, while villous adenomas have a villous component, that accounts for more than 75% of the polyp. Peutz-Jeghers syndrome which is an autosomal dominant condition is characterised by gastrointestinal hamartomatous polyp with distinctive arborisation of smooth muscle within the lamina propria. Peutz-Jeghers type polyp is a hamartomatous polyp without associated mucocutaneous pigmentation or a family history of Peutz-Jeghers syndrome. In the present case study, a 82-year-old male presented with the chief complaint of constipation and abdominal distension since six months. A polypoidal rectal growth was identified on sigmoidoscopy. The clinical diagnosis of mid-rectal growth with acute colonic obstruction was made. Positron Emission Tomography and Computed Tomography (PET CT) was done which was suggestive of malignancy and therefore, Hartmann's procedure was performed and lesion was excised. On gross examination, a portion of large intestine including sigmoid colon and rectum was received and a pedunculated polypoidal lesion measuring 4.5×3.5×3 cm along with stalk measuring 2.5 cm was seen. On microscopy, the polyp with extensive arborisation of muscularis mucosa into the lamina propria was seen with one area showing features of villous adenoma with high-grade dysplasia. Hence, a final diagnosis was given as villous adenoma with high grade dysplasia arising from a hamartomatous polyp consistent with Peutz-Jeghers polyp. The identification of a villous adenoma with high-grade dysplasia in a Peutz-Jeghers type polyp is essential in such situations, since it is a precursor of invasive malignancy.

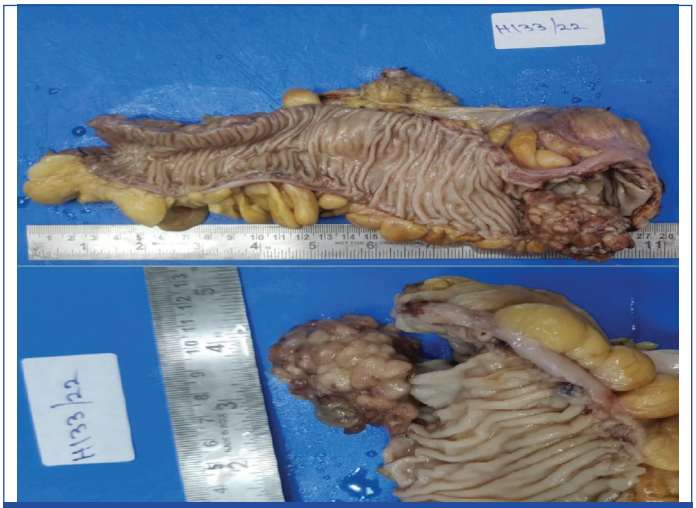
Keywords: Arborisation, Christmas tree pattern, Giant polyp, Hartmann's procedure, Peutz-Jeghers polyp

CASE REPORT

An 82-year-old male presented to Surgical Gastroenterology Department with the chief complaint of constipation and abdominal distension since six months. He was a known case of hypertension since 20 years and Parkinsonism since 12 years and was on treatment. On physical examination, abdomen was soft, not tender and bowel sounds were heard. Power in bilateral lower limbs was reduced. On sigmoidoscopy, a polypoidal rectal growth was identified and a provisional diagnosis of mid rectal growth with acute colonic obstruction was made. Positron Emission Tomography and Computed Tomography (PET CT) was done and an intensely hypermetabolic, eccentric mural thickening measuring 5.8×2.9 cm in the sigmoid colonwas seen, suggestive of primary malignancy of distal sigmoid colon. No other significant lab findings were seen. Hartmann's procedure was performed by the Surgical Gastroenterology Team.

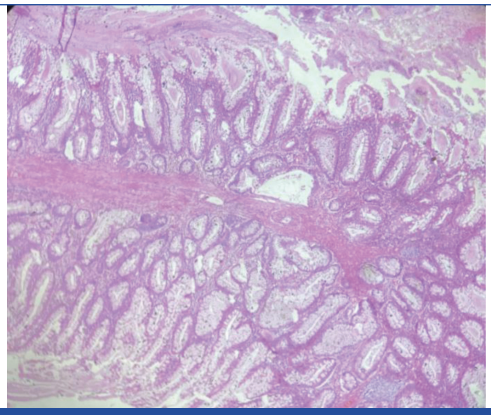
A segment of resected sigmoid colon and rectum was received in the pathology laboratory. On gross examination, a pedunculated, polypoidal lesion located in the mid-rectum was seen, involving almost the whole circumference, 21 cm from the proximal resected margin and 4 cm from distal resected margin. It measured 4.5×3.5×3 cm with stalk measuring 2.5 cm [Table/Fig-1].

No evidence of infiltrating firm or hard areas was seen and the rest of the mucosa appeared to be normal. Multiple sections were taken from the specimen and the histopathological examination showed a large pedunculated polyp showing extensive arborisation of muscularis mucosa into the lamina propria indicating a hamartomatous polyp showing a characteristic christmas tree appearance [Table/Fig-2]. Focal glands in the polyp showed serrations and mucosa lining the stalk of the polyp appeared normal. This hamartomatous polyp has a component of villous adenoma with high-grade dysplasia showing nuclear enlargement, pleomorphism, hyperchromasia, enlarged nucleoli, loss of polarity and loss of goblet cell mucin [Table/Fig-3,4]. However, there was no evidence of invasive malignancy in any of the sections examined. The resected margins and the rest of the colon were free from tumour. One lymph node was also identified, that showed only reactive changes and was negative for malignancy.

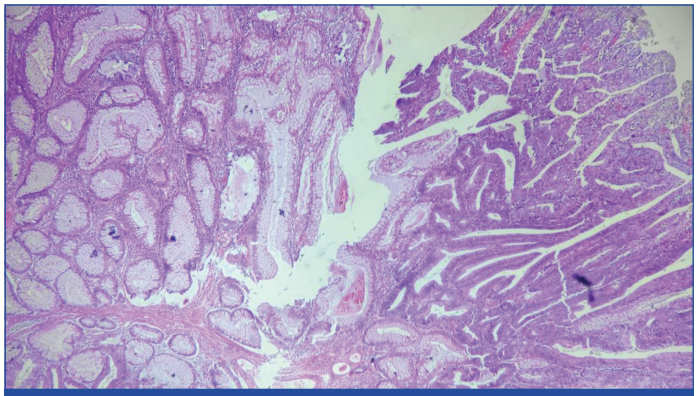


[Table/Fig-1]: Photomicrograph showing gross image of the resected specimen with a large polypoidal mass.

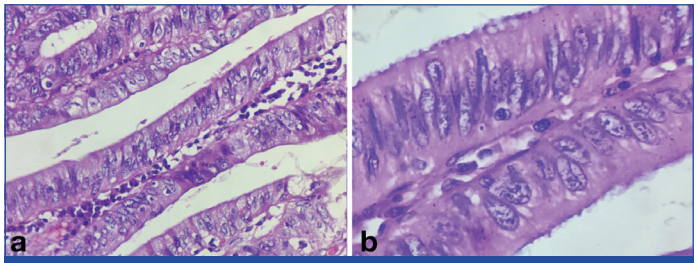
Based on the above findings, as per World Health Organisation (WHO) classification of tumours fifth edition-Digestive System Tumours [1], the final impression of villous adenoma with high-grade dysplasia arising from a hamartomatous polyp consistent with solitary Peutz-Jeghers type was made. The patient recovered fully after surgery but later developed acute myocardial infarction on the day of discharge and succumbed to death.



[Table/Fig-2]: Photomicrograph showing hamartomatous polyp with arborisation of muscularis mucosae into lamina propria showing characteristic christmas tree pattern (H&E, 10X).



[Table/Fig-3]: Photomicrograph showing low power view of villous adenoma with high-grade dysplasia with adjacent areas showing arborising muscularis mucosa in the lamina propria (H&E, 10X).



[Table/Fig-4]: (a): Photomicrograph showing villous adenoma with high grade dysplasia showing loss of polarity and marked enlarged nuclei with prominent nucleoli (H&E, 40X) (b) Photomicrograph showing features of high grade dysplasia-loss of nuclear polarity, enlarged nuclei, prominent nucleoli (H&E, 100X).

DISCUSSION

Adenomatous polyps can be found throughout the colon, most commonly in the right colon. They have an increasing incidence with age so that at the age of 60 years, they are found in about 20% of the population [2]. However, not all adenomas are polyps. Flat adenomas are defined as adenomas whose height is less than twice the thickness of the adjacent normal mucosa, and are increasingly recognised as an alternative precursor lesion of colorectal carcinomas [2].

There are two main histological types:tubular (75%) and villous (10%); the remaining 15% are intermediate in pattern and are designated tubulovillous [3]. Large size, villous content and distal location are all associated with severe dysplasia in colorectal adenomas [4]. Villous adenomas are more frequently sessile and larger. They are often over 20 mm in diameter and some extend over a wide area as a thick, carpet-like growth. Distal villous adenomas present with bleeding or mucus discharge. Giant adenomas are not amenable for endoscopic or transanal resection [5].

Microscopically, they consist of elongated villi in a papillary growth pattern. The villi are lined by columnar epithelium showing dysplasia. Tubulovillous adenomas have a villous architecture that comprises of 25% or more of the polyp, while villous adenomas have a villous component that accounts for 75% or more of the polyp [6].

Conventional adenomas are graded into two tiered classification as low-grade and high grade dysplasia. Features of high-grade dysplasia include marked complex glandular crowding, irregularity of glands, cribriform architecture and intraluminal necrosis along with loss of polarity, marked enlarged nuclei with prominent nucleoli, a dispersed chromatin pattern with frequent atypical mitosis.

Giant polyps are usually defined as more than 3 cm on endoscopy [7]. There is less than a 5% incidence of carcinoma in an adenomatous polyp less than 1 cm in size, whereas there is a 50% chance that a villous adenoma greater than 2 cm in size will contain cancer [8]. Bains L et al., reviewed a total of 25 giant villous tumours from 2001 to 2018, with size range 5-31 cm, which showed carcinoma (including invasive) in eight, high-grade dysplasia in six, low to moderate-grade dysplasia in six, whereas rest negative for malignancy. It puts the risk of dysplasia to about 50 % and malignancy in 33 % of cases of giant rectal villous adenomas [5].

Hamartomatous polyps are composed of the normal cellular elements of the gastrointestinal tract, but have a markedly distorted architecture. The autosomal dominant disorder Peutz-Jeghers Syndrome (PJS) is characterised by presence of hamartomatous polyps in the gastrointestinal tract. The Peutz-Jeghers syndrome is brought on by a germline mutation in the serine threonine kinase/liver kinase B1 gene (STK11, formerly known as LKB1) on human chromosome 19p13. More than 70% of the familial cases show STK11 mutation. In Peutz-Jeghers syndrome patients, loss of heterozygosity is found in 25-38 percent of colonic polyps and 64-100% of adenocarcinomas, respectively. Recent animal investigations, however, have revealed that biallelic deletion of STK11 is not required for polyp development [9].

Polyps are practically always seen as part of a Peutz-Jeghers syndrome and have microscopic features similar to their more common counterparts in the small bowel [6]. Histologically, Peutz-Jeghers polyps can be identified by their distinctive smooth muscle arborisation in the lamina propria. Peutz-Jeghers polyps of the colon can look like mucosal prolapse polyps or any other colonic polyp that prolapses. Lack of cellular atypia, disorganisation of glands, the occurrence of several cell types (including Paneth cells), and the presence of smooth muscle fibers from the muscularis mucosae (which give the lesion a “hamartomatous” appearance). This pattern of glandular disorganisation and epithelial misplacement, simulating invasion should not be confused with malignancy [10].

Most commonly the patients of Peutz-Jeghers syndrome present usually in the first three decades of life, but this patient was an elderly male. Clinically, they mostly present with the complaints of intestinal obstruction, abdominal pain, blood in the stool and anal extrusion of polyp. Rarely they are also diagnosed by prominent mucocutaneous melanin pigmentation [11]. Most commonly the lesions are found in the small bowel, however other sites of presentation are: colon, stomoach and rectum. In patient in the present case, it presented as a rectal lesion.

There are many theories behind the pathophysiology of the hamartoma adenoma carcinoma cascade in PJS. Several studies have explained, how second hit mechanism of LKB1 causes loss of heterozygosity (LOH) in adenomatous lesions and carcinomas in PJS polyps. A hamartomatous polyp without associated mucocutaneous pigmentation or a family history of Peutz-Jeghers syndrome is diagnosed as a solitary Peutz-Jeghers type hamartomatous polyp [12]. The incidence of solitary Peutz-Jeghers type polyps is extremely low [13]. The solitary Peutz-Jeghers type polyp can be found in the gastrointestinal tract; more cases occur in the small intestine, followed by colorectal region. The solitary gastric Peutz-Jeghers type polyps are the rarest.

Burkart AL et al., reviewed all reported cases of solitary Peutz-Jeghers type polyps in the hospital in 22 years and concluded that solitary Peutz-Jeghers-type polyps are extremely rare, they are also associated with the risk of cancer similar to PJS, and they may be incomplete PJS. Eight cases with malignant components were found in the Peutz-Jeghers type polyp [14]. The adenomatous transformation seen in hamartomatous polyps also had B-catenin and K-Ras mutations and LOH of p53. This suggests that mutations in these genes can also lead to carcinogenesis in PJS polyps [15]. In patient in the present case, there is villous adenomatous transformation with high grade dysplasia which is very rare.

It has been suggested that, mucosal prolapse plays a role in the pathophysiology of the distinctive hamartomatous polyps in PJS. There is no such thing as a hamartoma adenoma carcinoma sequence, according to this theory, and PJS polyps are a precancerous state. STK11/LKB1 is a tumour suppressor gene that regulates cellular polarity and intracellular signalling. The importance of LKB1 in cellular polarity and the loss of polarity function in PJS may impact asymmetric stem cell division and result in the enlargement of the stem cell pool. It could cause polyp growth as well as raise the risk of cancer. Mesenchymal cells which were STK11-deficient produced less TGF and had faulty TGF signalling to epithelial cells, according to a recent study, which correlated with epithelial proliferation. This explains, why tumour suppression mechanisms derived from the stroma are also important in PJS [16].

Laparotomy and bowel resection have been the primary treatment for PJS for many years to remove symptomatic gastrointestinal polyps. Several different syndromes have been described with the propensity to develop hamartomatous polyps in the upper and lower gastrointestinal tracts. These include juvenile polyposis, Peutz-Jeghers syndrome, hereditary mixed polyposis syndrome, and the PTEN hamartoma tumour syndromes (Cowden and Bannayan-Riley-Ruvalcaba syndromes), which are autosomal-dominantly inherited, and Cronkhite-Canada syndrome, which is acquired [17]. Solitary Peutz-Jeghers type polyp is itself a rare entity. Adenomatous transformation in a Peutz-Jeghers type polyp is even rarer. In the PubMed database, the terms “Solitary Peutz-Jeghers type polyp” yielded 81 cases around the world. The terms Peutz-Jeghers and giant polyp gave seven case studies. Adenomatous transformation of the Peutz-Jeghers type polyp was seen in only seven cases [12,18,19]. Limaiem F et al., described a 27-year-old patient with solitary 15 cm sized hamartomatous Peutz-Jeghers type polyp in the lower rectum with features of adenoma [18]. Sekino Y et al., 84-year-old Japanese man had hamartomatous polyp-branching bundles of smooth muscle fibers covered by hyperplastic duodenal mucosa with a focus of well-differentiated adenocarcinoma [12]. Matsui T et al., presented a case of adult intussusception in the transverse colon with an advanced ileal Peutz-Jeghers type polyp associated with cancer [19].

CONCLUSION(S)

The present exceedingly singular rare case of a villous adenoma with high grade dysplasia arising from a giant hamartomatous Peutz-Jeghers type polyp highlights the importance of vigilant histopathological examination. The need for careful and diligent assessment for detection of malignant pathology in a hamartomatous polyp is crucial, as it changes the treatment and prognosis of the patient.

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