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Gastrointestinal Polyps: Clinicopathological Aspects

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Abstract: Gastrointestinal polyps are still clinically confusing and proper objective identification is necessary for appropriate clinical management. Our aim was to estimate the frequency of polyps in different parts of gastrointestinal tract and to find out the malignant potentiality of these lesions and compare the results with literatures and texts and underscore the differences. This descriptive and retrospective study was performed on 298 patients with gastrointestinal polyps presenting to Shiraz University affiliated hospitals, Shahid Faghihi and Nemazee since 1989-1999. Our overall observations in this retrospectively collected series illustrate the frequency, symptoms, age and sex distribution and associated neoplasia in gastrointestinal polyps. There was vary low incidence of adenomatous and hyperplastic polyps in all parts of GI tract in our region. Juvenile (hamartomatous) polyps were more frequent in our area especially in rectosigmoid as compared with other countries. Adenomatous changes were detected in 13.86% of juvenile polyps.

Key words: Gastrointestinal polyps, inflammatory, hyperplastic, pathological aspects, clinical management

INTRODUCTION

The polyposis syndromes, a heterogeneous group of diseases, have been a major focus of study for the last decade and provide critical insight into the molecular pathogenesis of cancer. Despite intense study, these important syndromes are still clinically confusing and proper objective identification is necessary for appropriate clinical management (Sweet *et al*., 2005).

The term "polyp" derives from the Greek for "multiple feet" or "little nipple". In current clinical practice a polyp is defined as any nodule or mass that projects above the level of the surrounding mucosa, as in the gut, to form a macroscopically visible structure (Najib *et al*., 2002; Vinay *et al*., 2007). Traction on the mass may create a stalked, or pedunculated, polyp. Alternatively, the polyp may be sessile, without a definable stalk. The polyps that formed as a result of abnormal mucosal maturation, inflammation, or architecture, are non-neoplastic and do not have malignant potential, but those that arise as the result of epithelial proliferation and dysplasia are termed adenomatous polyps or adenomas. They are true neoplastic lesions and are precursors of carcinoma. Some polypoid lesions may be caused by submucosal or mural tumors. However, as with the stomach, the term polyp, unless otherwise specified, refers to lesions arising from the epithelium of the mucosa (Vinay *et al*., 2007).

Table 1: Tumors of the small and large intestines

Non Neoplastic tumors
Hyperplastic polyps
Hamartomatous polyps
Juvenile polyps
Peutz-Jeghers polyps
Inflammatory polyps
Lymphoid polyps
Neoplastic epithelial lesions
Benign polyps
Adenomas
Malignant lesions
Adenocarcinoma
Squamous cell carcinoma of the anus
Other tumors
Gastrointestinal stromal tumors
Orcinoid tumor
Lymphoma

Gastrointestinal polyps are being identified more frequently today because of increased awareness, screening and improved diagnostic tools. The entire gastrointestinal tract is at risk for polyp development but the adult colon and rectum account for the majority of polyps. Painless, bright red, rectal bleeding with normal stool frequency and consistency is the hallmark presentation of colorectal polyps at any age (Vinay *et al*., 2007; Attard and Young, 2006).

Gastric polyps are uncommon and are most frequently hyperplastic polyps, fundic gland polyps and adenomatous polyps. Hyperplastic and fundic gland polyps are essentially innocuous. In contrast, there is a

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definite risk of an adenomatous polyp harboring adenocarcinoma, which increases with polyp size (Vinay *et al*., 2007).

The classification of intestinal tumors is the same for the small and large bowel (Table 1). Hyperplastic polyps are the most common polyps of the colon and rectum. When single, they do not have malignant potential. However a lesion known as sessile serrated adenoma, which has some similarities with hyperplastic polyps, may have malignant potential (Vinay *et al*., 2007; Jass, 2003; Bariol *et al*., 2003; Snover *et al*., 2005; Torlakovic *et al*., 2003).

The aim of this study was to estimate the frequency of polyps in different parts of gastrointestinal tract and to find out the malignant potentiality of these lesions and compare the results with literatures and texts and underscore the differences if there is any.

MATERIALS AND METHODS

This descriptive and retrospective study was performed on 298 patients with Gastrointestinal (GI) polyps. We reviewed retrospectively all cases of GI polyps in surgical files of Shiraz University affiliated hospitals, Shahid Faghihi and Nemazee from 1989-1999.

To be included in the study, patients had to have a minimum of 5 gastrointestinal polyps on consecutive endoscopic and/or colonoscopic procedures. Patients were classified into 5 groups based on the pathological diagnosis from standard clinical pathology review from their respective hospitals of referral. All cases of GI polyps were reclassified accordingly into Neoplastic, Hyperplastic, Hamartomatous, Lymphoid and Gastric. Inflammatory polyps (pseudopolyps) were excluded from the study. Two hundred and 98 cases were found.

Medical records were requested and hematoxylin and eosin (H and E)-stained slides obtained. History of colorectal or other cancer was noted. Size and site of polyps were recorded from the accompanying endoscopic and/or colonoscopic requisition sheet or from the gross description on the pathology report. The histopathology slides were centrally reviewed by a single gastrointestinal pathologist without knowledge of the molecular findings.

RESULTS

Table 2 shows the number of each type of GI polyp. The results of each subtype of GI polyp will be discussed separately.

Gastric polyps: Gastric polyps were reviewed separately because of some differences in subclassification of polyps in the stomach. Overall, we encountered with 21 gastric polyps in our surgical files, which is 7.04% of the total GI polyps. The patients presented with epigastric pain in 75%, repeated vomiting in 12.5% and dyspepsia with vomiting in 12.5% of cases. Nearly all cases had the history of chronic gastritis. The mean age of the patients was 38.2 years with age range between 20-60 years. All of the polyps were located in the prepyloric and antral portions. Our series showed slight female preponderance with Female-to-Male ratio of 1.25 (13 female vs. 8 male). On microscopic examination, 85.7% were type I (hyperplastic) and 14.3% type III (2 layer type). No cases of type II and type IV were found.

Adenomatous polyps: Out of 298 GI polyps, 21 (7.04%) were adenomatous type. All of these polyps were located in large bowel. Microscopic architecture of these polyps was tubular, villous or tubulovillous. Table 3 shows the

Table 2: Frequency of each type of gastrointestinal polyp

				Hamartomatous			
Polyp	Gastric	Neoplastic (Adenomatous)	Hyperplastic	Juvenile	Non-juvenile (Peutz-Jeghers)	Lymphoid	Total
Number	21 (7.04%)	21 (7.04%)	18 (6.04%)	236(79.19%)	2 (0.67%)	0 (0%)	298 (100%)

Table 3: Neoplastic (Adenomatous) polyps

Subtype	Number (%)	Sex	Mean age (years)	Age range (years)	Symptoms	Location	Associated conditions
Tubular	15 (71%)	10F 5M	34.7	17-62	Abdominal pain, Rectal bleeding, Asymptomatic	Rectosigmoid	-
Villous	3 (14.5%)	2F 1M	47.3	30-65	Rectal bleeding	Left colon	Adenocarcinoma of sigmoid
Tubulovillous	3 (14.5%)	1F2M	27.3	24-58	Rectal bleeding, Asymptomatic	Rectum, cecum	Peutz-Jegher syndrome

Table 4: Hyperplastic polyps

Number (%)	Sex	Mean age (years)	Age range (years)	Symptoms	Location
18 (6.04%)	70%F 30%M	28.4	1-65	Rectal bleeding, Pus discharge, Perianal pain, Diarrhea	Rectum, Sigmoid

Table 5: Hamartomatous polyps

Subtype	Number (%)	Sex	Age range	Symptoms	Location	Adenomatous
Juvenile	236 (79.19%)	43.1% F 56.9% M	7 month-75 years	Fresh rectal bleeding, protrusion of mass, Abdominal pain	Rectum, Sigmoid, Left colon	13.8%
Non-Juvenile	2 (0.67%)	2F	10-16 years	Rectal bleeding	Small bowel	50%

number and percentage of each subtype of adenomatous polyps. All cases of adenomatous in our series showed moderate degree of dysplasia (Table 3).

Tubular: In our series, tubular adenoma is the most frequent subtype. All of these are concentrated in rectosigmoid, except one which was located in cecum. As showed in Table 3, this subtype occurs in younger subjects than two others, with age range between 17-62 years. Abdominal pain, Rectal bleeding and pus discharge are the presenting symptoms. However, some of the patients were asymptomatic and diagnosed incidentally. Three of the patients are the cases of familial polyposis coli and Gardner's syndrome with numerous tubular adenomas in the large intestine.

Villous: There are only 3 cases of villous subtype in our series, all of them located in left colon and presented with fresh rectal bleeding. There is no patient with multiple villous adenomas in our series but in one case villous adenoma was associated with invasive adenocarcinoma of sigmoid, witch in addition to an isolated villous adenoma, remnants of another villous adenoma were identified in the carcinoma's border.

Tubulovillous: This subtype of polyps consists of 3 cases in our series. One of them is the 24 year old male who presented with perioral pigmentation. Colonoscopy showed an adenoma in the colon. The second case presented with fresh rectal bleeding and third one was found incidentally during hysterectomy. Rectum was the site in first two cases while cecum was the site of polyp in the third case.

Hyperplastic polyps: In our series only 18 out of 298 of surgically removed polyps are hyperplastic type (Table 4). Most of the patients (60%) presented with rectal bleeding; and pus discharge, Perianal pain, diarrhea and protrusion of mass are the compliant of reminder of patents. Ninety percent of polyps were located in the rectosigmoid and sites of the last 10% were not determined. In our series Male-to-Female ratio was reversed and there was female preponderance. One of the cases showed villous pattern of growth with typical cytomorphology of hyperplastic polyp. Adenomatous changes with moderate degree of dysplasia were seen in 12.5% of cases.

Hamartomatous polyps

Juvenile hamartomatous polyps: In this series, 236 out of 298 GI polyps were juvenile type (Table 5). Of these, the hospital charts of 166 patients are available for study of clinical signs and symptoms. Fresh rectal bleeding was the most common clinical symptom and protrusion of mass, abdominal pain and perianal pain were the next symptoms in the order of frequency. In one case constipation was the chief complain of patient.

There is a slight preponderance of male to female. Greatest numbers of polyps occurred in children younger than 10 years old (73.5%) with peak incidence between 4-5 years. In our study, 23.5% of polyps had occurred in patients older than 10 years. More than four- fifth (89.1%) of polyps were located in the rectum. The next most frequent site was sigmoid colon (6.8%). Only four of them are found in left colon.

In our study, microscopic examination of juvenile polyps showed hyperplastic changes in 55.46%, mixed adenomatous and hyperplastic changes in 13.86% and pure stromal form with hyperplastic changes in pedicle of polyp in 21.8%. Some morphologic findings in the stroma, worthy of mentioning here, are as below: lymphoid follicle with germinal center in 23.1%, stromal ossification in 1.26%, stromal calcification in 0.41% and foreign body granuloma in 1.26% of cases.

There was a case of juvenile polyposis syndrome in our series who was a young female with negative family history. Microscopic examination of multiple rectosigmoid polyps in this patient showed frank adenomatous changes in one of them. In another case, juvenile polyp was coexisting with adenocarcinoma of descending colon.

Non-juvenile hamartomatous polyps: Two cases of Peutz-Jegher Syndrome, who clinically presented with perioral pigmentation and obstruction in one of them, are found in our series. Microscopic examination of small bowel polyps in these patients showed typical non-juvenile hamartomatous polyp with a focus of dysplasia in one of them (Table 5).

DISCUSSION

Polypoid lesions of GI tract may have any one of various histological structures but this review is based on study of the mucosal epithelial polyps of the GI tract. It must be remembered that although this term is

commonly used for benign tumors, some malignant tumors may also appear as polyps. Occasionally, a lipoma or leiomyoma arising in the wall of the stomach may protrude from under the mucosa to produce an apparent polypoid lesion (Vinay *et al*., 2007).

Gastric polyps are uncommon and are found in about 0.4% of adult autopsies, as compared with colonic polyps, which are seen in 25-50% of older persons (Vinay *et al*., 2007). Gastric polyps are small gastric lesions, asymptomatic in most cases and are generally discovered inadvertently during upper digestive endoscopy. The digestive endoscopy is the safest and efficient method for the diagnosis of the gastric polyps that in most of the patients does not show characteristic symptoms (Morais *et al*., 2007). Gastric polyps exist in a wide variety of types, most often benign. Endoscopic discovery of gastric polyps necessitates biopsies-not only of the lesion but also of the antral and fundic mucosa to determine the therapeutic strategy and subsequent surveillance. Fundic gland polyps are the most frequent type; they are asymptomatic with no malignant potential. They require neither treatment nor surveillance. Hyperplastic polyps, adenomas and tumors must be totally resected. Biopsies alone are insufficient to assess the extent of malignancy of adenomas and of hyperplastic polyps more than 5 mm in diameter. These polyps are associated with an elevated frequency of precancerous alterations of the gastric mucosa and consequently by an elevated risk of synchronous or metachronous cancer (Vallot, 2007). Fundic Gland Polyps (FGP) patients frequently complain of epigastric pain, burning, dyspepsia, probably related to the frequently associated esophageal pathology, namely reflux esophagitis-hiatus hernia (34%). Prevalence of FGPs and polyps number are linked to female sex (maximum rise for both values in perimenopausal age). Nonetheless, they are apparently more prone to colonic adenomas. So, every sporadic FGP patient should undergo colonic surveillance (Declich *et al*., 2005).

Our patients with gastric polyps presented with epigastric pain, repeated vomiting or dyspepsia with vomiting. The mean age of the patients was 38.2 years with age range between 20-60 years. Nearly all cases had the history of chronic gastritis. All of the polyps were located in the prepyloric and antral portions. Our series showed slight female preponderance with Female-to-Male ratio of 1.25.

Sotnikov *et al*. (2007) showed that of 298 patients with gastric polyposis, 135 cases were complicated and 163 cases were uncomplicated. Hyperplastic polyps were diagnosed in 281 patients. Along with hyperplastic polyps, solitary adenomas were diagnosed in 9 cases, Peutz-Jeghers polyps in 6 and juvenile polyps in 2 (Sotnikov *et al*., 2007). The most common type of gastric polyps is hyperplastic polyps, which account for nearly 85-90% of cases. They are usually seen in adults, over 60 years of age. These polyps are often pinkish, round-shaped, solitary and small (<2 cm) and classified as either sessile or pedunculated. While small polyps tend to be sessile, the larger ones may have a short stalk. Most of them are localized at the junction of fundic and pyloric mucosa. Multiple hyperplastic polyps are found in 20% of the patients. Rarely, they cause gastric outlet obstruction by prolapsing through the pyloric channel, when they arise in the prepyloric antrum. Gastric Outlet Obstruction (GOO) presents with nausea and vomiting and usually develops over weeks to months (Gancosmanoglu *et al*., 2003; Al (per *et al*., 2003). Gastric polyps are incidentally detected in 2-3% of upper gastrointestinal endoscopic examinations. Until recently it was believed that the hyperplastic polyps do not undergo malignant transformation, but carcinomas associated with hyperplastic polyps were reported in the literature over the past few years. Interestingly, an association between hyperplastic polyps and Helicobacter pylori gastritis has been proposed in some recent studies (Gencosmanoglu *et al*., 2003).

Ljubiciæ *et al* performed upper gastrointestinal endoscopy on 6.700 patients in a one-year period. Among them 42 benign gastric epithelial polyps were found in 31 patients: adenomatous gastric polyps in 7 patients, hyperplastic gastric polyp in 21 and fundic gland polyp in 3 patients. All patients with hyperplastic polyps had chronic active superficial gastritis, whereas most of the patients with adenomatous polyps had a chronic atrophic gastritis with high prevalence of intestinal metaplasia. Among 21 patients with hyperplastic gastric polyps, 16 (76%) patients were positive for H. pylori infection in contrast to only 2 patients (29%) with adenomatous gastric polyps and 1 patient (33%) with fundic gland polyp (Ljubicic *et al*., 2002). Fundic Gland Polyps (FGPs) are the most common gastric polyps (Abraham *et al*., 2001). FGPs occur in both sporadic and syndromic forms. Sporadic FGPs are identified in 0.8-1.9% of patients undergoing upper gastrointestinal endoscopy and are especially prevalent among middle-aged females. In patients with Familial Adenomatous Polyposis (FAP), FGPs are increased in prevalence, are more frequently multiple, occur at younger ages and show a more equal gender distribution than sporadic FGPs (Abraham *et al*., 2001).

In our series, out of 298 GI polyps, 21 (7.04%) were adenomatous type. All of these polyps were located in large bowel. Microscopic architecture of these polyps was

tubular, villous or tubulovillous. All adenomatous lesions arise as the result of epithelial proliferation and dysplasia, which may range from mild to so severe as to represent transformation to carcinoma. Furthermore, there is strong evidence that most sporadic invasive colorectal adenocarcinomas arise in preexisting adenomatous lesions. Adenomatous polyps are segregated into four subtypes on the basis of the epithelial architecture: Tubular adenomas, Villous adenomas, Tubulovillous adenomas and Sessile serrated adenomas. Tubular adenomas are by far the most common; 5-10% of adenomas are tubulovillous and only 1% are villous (Vinay *et al*., 2007). In our series, tubular adenoma was the most frequent subtype constituting the 71% of all adenomatous polyps; 14.5% of adenomas were tubulovillous and 14.5% were villous type.

It is widely believed that hyperplastic polyps have no malignant potential. Commonly seen on colonoscopic examination (10% of patients younger than 50 years, 50% of those younger than 70 years), they seldom exceed 0.5 cm and are often localized to the distal colon and rectum (17). However, there is evolving evidence linking the sessile serrated adenoma (SSA), a lesion related to hyperplastic polyp, with neoplasia ((Wynter *et al*., 2004; Hawkins *et al*., 2002; Jass *et al*., 2002)). Hyperplastic polyposis syndrome is not a single entity, as histological and molecular analysis has shown a mixed picture. This condition is characterized by multiple or large hyperplastic polyps. Recent studies suggest that the SSA may be a component of HPS and, as such, may be associated with the increased risk for neoplasia (Wynter *et al*., 2004; Hawkins *et al*., 2002; Jass *et al*., 2002). Patients with multiple (hyperplastic polyposis) or large hyperplastic polyps predominantly in the right-sided colon, have been reported to have an increased risk of Colorectal Cancer (CRC) (Yano *et al*., 2005).

In our series only 18 out of 298 of surgically removed polyps (6.04%) were hyperplastic type. the patients presented with rectal bleeding, pus discharge, Perianal pain, diarrhea and protrusion of mass. Nearly all of these polyps were located in the rectosigmoid. Age distribution showed the mean age of 28.4 years with the age range between 1-65 years. There was female preponderance. Adenomatous changes with moderate degree of dysplasia were seen in 12.5% of cases.

There is increasing evidence for several important categories of polyposis and GI carcinoma that may develop from alternative routes including the hamartomatous polyposis syndromes and the serrated neoplasia pathway, whose morphologic spectrum includes the hyperplastic polyp and sessile serrated adenoma. Given the attendant cancer risks and medical management issues inherent in these forms of polyposis, it is imperative that physicians recognize that variability in histopathology and molecular etiology can hinder appropriate diagnosis (Sweet *et al*., 2005).

The known forms of inherited hamartomatous polyposis include Peutz-Jeghers Syndrome (PJS), Juvenile Polyposis Syndrome (JPS) and Cowden syndrome. Although collectively accounting for less than 1% of colorectal cancer in North America (Nagy *et al*., 2004), hamartomatous polyps was constitutes the 79.86% of all GI polyps in our series. Proper identification of these clinically confusing syndromes remains of critical importance, because each syndrome carries significant risks for extraintestinal malignancy and other component features that must be managed (Nagy *et al*., 2004).

Peutz-Jeghers Syndrome (PJS) is a rare disorder characterized by typical pigmented perioral macules, pigmented spots in the buccal mucosa which are present in 90% of patients and multiple, although rarely more than 20 hamartomatous polyps predominantly in the Gastrointestinal (GI) tract. Polyps may occasionally be absent. Polyp sizes vary from a few mm to 6 or 7 cm. Most patients have a characteristic clinical course of recurrent episodes of polyp induced bowel obstruction and bleeding. The disease affects males and females equally (Homan *et al*., 2005). Peutz-Jeghers syndrome causes gastrointestinal polyposis, especially of the upper jejunum (78%) and mucocutaneous pigmentation (Sweet *et al*., 2005). Moreover, Burkart *et al* suggest that individuals with a single PJP may have a cumulative lifetime risk of cancer similar to those with the syndrome (Burkart *et al*., 2007).

Two cases of Peutz-Jegher Syndrome, who clinically presented with perioral pigmentation and obstruction in one of them, are found in our series. Microscopic examination of small bowel polyps in these patients showed typical non-juvenile hamartomatous polyp with a focus of dysplasia in one of them.

Juvenile Polyposis (JP) is an autosomal-dominant syndrome characterised by the development of hamartomatous gastrointestinal polyps and is associated with colorectal cancer. However, the relative and absolute risk of colorectal malignancy in these patients is not known (Brosens *et al*., 2007). Most of the children with colorectal polyp had juvenile polyp that is commonly found in the rectosigmoid colon. However, a significant number of patients had carrying polyps proximal to the rectosigmoid region, which would be easily missed by sigmoidoscopy. With the concern of malignancy change particularly in children with polyposis coli, routine colonoscopy should be considered as an initial investigation in children with colorectal polyp

(Waitayakul *et al*., 2004; Pyatt *et al*., 2006). Brosens *et al*. concluded that Patients with JP have a markedly increased relative risk and absolute risk for colorectal cancer and require vigilant colorectal surveillance starting at young age. A low threshold for recommending surgery with consideration for removal of the entire colorectum seems warranted (Brosens *et al*., 2007).

In this series, 79.19% of GI polyps were juvenile type. Fresh rectal bleeding was the most common clinical symptom and protrusion of mass, abdominal pain and perianal pain were the next symptoms in the order of frequency. There is a slight preponderance of male to female. Greatest numbers of polyps occurred in children younger than 10 years old (73.5%) with peak incidence between 4-5 years. In our study, 23.5% of polyps had occurred in patients older than 10 years. More than four-fifth (89.1%) of polyps were located in the rectum, 6.8% were in sigmoid colon and four of them are found in left colon. Microscopic examination showed hyperplastic changes in 55.46%, mixed adenomatous and hyperplastic changes in 13.86% and pure stromal form with hyperplastic changes in pedicle of polyp in 21.8%.

Pratap *et al* reported 2 cases of an 8-year-old girl and a 5-year-old girl who suffered massive lower GI hemorrhage. Neither patient had a family history of polyposis. After the patients were stabilized, radiological evaluation, laparotomy and intraoperative colonoscopy revealed multiple polyps in the colon. Both patients underwent total colectomy, mucosal proctectomy and ileoanal anastomosis. The diagnosis of nonfamilial juvenile polyposis was based on the histological findings and the absence of a family history. They concluded that although juvenile polyposis is a rare condition in children, it should be considered in the differential diagnosis of life-threatening GI hemorrhage (Pratap *et al*., 2007).

Boukthir *et al*. (2006) studied retrospectively A total of 34 patients (20 boys and 14 girls, mean age: 5.4 years) in this 14-years. Most of the polyps corresponded histologically to juvenile polyps (96.2%). They suggested that rectal bleeding is the most frequent finding of polyps of the colon and rectum in childhood (Boukthir *et al*., 2006). Juvenile colorectal polyps are the most common cause of pediatric hematochezia and contribute to significant morbidity if not treated early. Juvenile colorectal polyps contribute to a substantial morbidity in children and do carry a minimal risk of developing dysplastic changes and therefore should be removed early (Mandham, 2004).

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