Polyps in Children

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ABSTRACT

Children with polyps usually present with bleeding or pain. Most pediatric intestinal polyps are sporadic and are not associated with malignancy. Polyposis syndromes are also well described in children. Peutz–Jeghers syndrome is the most common hamartomatous polyposis condition. Although the polyps are not thought to be premalignant in most patients, there is an increased risk of other cancers. Familial adenomatous polyposis is also seen in childhood and is associated with a very high risk of malignant transformation as well as extracolonic adenomas and malignancy. The diagnosis and management of sporadic juvenile polyps, Peutz–Jeghers syndrome, and familial adenomatous polyposis, as well as rarer conditions associated with intestinal polyps are reviewed in this article.

KEYWORDS: Juvenile polyps, Peutz–Jeghers, familial polyposis

Objectives: On completion of this article the reader should be able to recognize colonic and intestinal polyps in children as well as diagnose and manage patients with Peutz–Jeghers syndrome or familial adenomatous polyposis.

Polyps are less common in children than in adults. The two most frequent symptoms are lower intestinal bleeding and abdominal pain. Because these symptoms are common, polyps are often in the differential diagnosis of pediatric patients with abdominal problems.[1] Intestinal polyps are protrusions of epithelial or submucosal growths that protrude into the lumen of the bowel. They generally cause bleeding, which is the most common presenting symptom, but polyps in children often present with abdominal pain. If the polyp extrudes sufficiently into the lumen it may be propelled distally by peristalsis and traction on the polyp can lead to an intussusception. The overwhelming majority of intestinal polyps in children are sporadic, few in number, and nonfamilial; they are not associated with malignant transformation. As discussed in detail below, in addition to the common juvenile polyp, there are several well-described polyposis syndromes (Table 1), most of which are inherited. They are associated with the development of numerous polyps (as the designation polyposis suggests), malignant transformation of the polyps, and with extraintestinal neoplasms (benign and malignant).

Before a detailed discussion of the specific conditions outlined above, we will briefly review the presentation and diagnosis of polyps in childhood.

CLINICAL PRESENTATION

Lower intestinal bleeding is by far the most frequent presenting symptom of intestinal polyps or polyposis conditions. Because the sporadic juvenile polyp of the colon is the most common polyp in children, the blood is generally red, indicating its distal source. Blood from proximal small bowel polyps is usually darker. Melena is only seen in rare cases of the duodenal or gastric polyps in patients with one of the polyposis syndromes.

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Table 1 Classification of Polyps and Polyposis Syndromes

Juvenile polyps
Inherited hamartomatous polyposis syndromes
Peutz–Jeghers syndrome
Juvenile polyposis
Cowden's syndrome
Ruvalcaba–Myhre–Smith syndrome
Inherited adenomatous polyposis syndromes
Familial polyposis coli
Gardner's syndrome
Turcot's syndrome
Noninherited polyposis
Lymphoid polyposis
Cronkhite–Canada syndrome

Crampy abdominal pain is a frequent symptom and can often occur without obvious or occult bleeding. Most of these episodes are of short duration and often occur intermittently, sometimes over a prolonged period, before the diagnosis of a polyp or polyposis is suspected.

A protruding pedunculated polyp can be propelled distally by peristalsis and be the lead point for an intussusception. Unlike the more common, idiopathic intussusception of infancy and early childhood, these are usually small bowel-small bowel intussusceptions rather than ileo-cecal, though colo-colonic intussusceptions are well described.

DIAGNOSIS

The diagnosis of polyps is generally made with an endoscopy or intestinal contrast studies. A lower endoscopy, preferably a colonoscopy[2] rather than proctoscopy or flexible sigmoidoscopy, is increasingly the most common initial diagnostic study. It has the potential to be therapeutic as well as diagnostic because the majority of patients will have polyps limited to the colon. Biopsies also confirm the type of polyp. This can help determine if there is a need for additional studies (such as upper endoscopy) or special follow-up, if other family members should be screened, and if genetic testing or screening is warranted. Endoscopy is of more limited value in small bowel polyps. Capsule endoscopy may be of some limited benefit,[3] but small bowel polyps can often be visualized with contrast studies. Combing endoscopy with laparotomy may be helpful in selected cases.

Although lower intestinal contrast studies, with water-soluble contrast or air, are used very often in the common, idiopathic ileo-cecal intussusception of infancy and early childhood, they are rarely helpful in patients with intussusception due to polyps. The intussusceptions due to polyps are almost always small bowel-small bowel and therefore not amenable to hydrostatic or air reduction. Furthermore, hydrostatic reduction of an intussusception due to polypoid disease is rarely successful and would not be definitive treatment. Surgical treatment with enterotomy and polypectomy, or segmental bowel resection to remove the lead point, is required.

JUVENILE POLYPS

Clinical Characteristics

Juvenile polyps are the most common intestinal polypoid lesions in children. They are hamartomatous polyps limited to the colon; they are also referred to as inflammatory polyps or retention polyps. They make up more than 90% of all colon polyps in children and also constitute the overwhelming majority of all intestinal polyps in children. They typically present with lower intestinal bleeding. The bleeding can be significant, but is typically self-limited. There is often a history of passing blood, which is followed by the passage of tissue in the stool. Between 25 and 35% of patients will present with microcytic, hypochromic anemia from chronic blood loss.[4] The typical age ranges from 3 to 10 years; sporadic juvenile polyps are uncommon before 2 years of age and are rare in the first year of life. Prolapse of a low-rectal polyp is well described and easily recognized. Colo-colonic intussusception is unusual and rarely leads to prolapse of the intussusceptum (inner, proximal portion of bowel).

Pathology

Juvenile polyps are variable in size, with clinical symptoms developing from polyps that range in size from < 0.5 cm up to ≥ 3 cm. The mucosa is usually erythematous and friable. Most are pedunculated and bleed easily during colonoscopic manipulation. They are mucosal lesions that contain dilated, mucous-filled glands with inflammation in the lamina propria; on cut surface, they often appear cystic. This combination of findings leads to the common reference to these as inflammatory or retention polyps.

These are hamartomas. In contrast to juvenile polyposis syndrome, these lesions are not neoplastic and are not associated with malignant transformation. There have been reports of adenomatous changes in juvenile polyps[5,6] and though rare, dysplasia may confer an increased risk of carcinoma.

Diagnosis and Treatment

These lesions occur much more often than clinically recognized. Many of these polyps simply outgrow their blood supply, become ischemic, and autoamputate. It was thought that these lesions were usually isolated and confined to the recto-sigmoid colon. However, through the increased use of colonoscopy we have learned that between 50 and 60% of patients have more than one

polyp,[2,4] though rarely more than a few. About 25% of patients have polyps in the cecum or ascending colon.[2,4]

Patients with an isolated episode of bleeding that is self-limited and who pass tissue in the stool should be observed. Patients with persistent or recurrent bleeding, or who are having pain or other symptoms should have an endoscopy. When the diagnosis is made with endoscopy, a polypectomy can safely be performed even in young children. The recent evidence that patients can have more than one polyp and that polyps may be found in the cecum and ascending colon makes a colonoscopy preferable to the traditional recommendation of proctoscopy or flexible sigmoidoscopy.[2] Lesions that present with prolapse through the anus may be ligated if feasible and an endoscopy performed for recurrent bleeding or other symptoms.

No further evaluation or follow-up is needed after removal of an isolated juvenile polyp. In the rare case in which adenomatous changes are found in a juvenile polyp, follow-up and screening endoscopy is recommended. Though the recommendations for the rare patient with adenomatous changes in a juvenile polyp are evolving, repeat endoscopy should be performed for recurrent bleeding, or every 2 years.

INHERITED HAMARTOMATOUS POLYPOSIS SYNDROMES

Peutz–Jeghers Syndrome

The association of intestinal polyposis with mucocutaneous pigmentation was first reported in three generations of a Dutch family by Peutz in 1921.[7] In 1949 Jeghers[8] reported 10 similar patients establishing the now well-described condition. In 1969 a review of 321 ethnically and geographically diverse patients[9] confirmed the autosomal dominant inheritance pattern suggested by Jeghers. There is greater than 95% concordance between the presence of polyposis and abnormal pigmentation,[10] but many patients are not diagnosed until adulthood. Despite this inheritance pattern, as many as 50% of patients will not have a family history at the time of diagnosis. The abnormal pigmentation appears as brown-black macules usually involving the lips and oral mucosa. They may also appear on the tongue, perineum, hands, feet, or digits. The pigmentation usually appears in infancy or early childhood. Although the skin pigmentation may fade, the oral lesions persist and are a more reliable clinical clue. Almost all patients will have multiple polyps, but the number and distribution vary. These hamartomas can appear throughout the gastrointestinal (GI) tract. They occur most often in the small intestines and are seen less frequently in the colon, stomach, or duodenum. They may be sessile or pedunculated and may vary widely in size as well as distribution. The polyps consist of glandular epithelium with extensive smooth muscle branching in the lamina propria.

In most cases, the cause appears to be a germline mutation of the *STK11/LKB1* located on the 19p chromosome.[11] The incidence of Peutz–Jeghers syndrome is estimated to be about one tenth that of familial adenomatous polyposis; estimates range from 1:75,000 to 1:300,000.

PRESENTATION

Between 25 to 50% of patients will be diagnosed in childhood or adolescence. The most common presenting complaint is abdominal pain. Many patients are diagnosed only after a prolonged period of unexplained, intermittent, crampy abdominal pain despite the presence of the characteristic abnormal pigmentation. These episodes are likely due to intermittent, recurrent intussusception. Most of these episodes reduce spontaneously and therefore do not progress to obstruction. Some patients present with a complete intestinal obstruction—laparotomy to treat the obstruction then leads to the diagnosis. However, the diagnosis should be suspected preoperatively when a previously healthy patient presents with a complete obstruction and has the characteristic oral lesions. Patients may present with microcytic, hypochromic anemia due to chronic blood loss. Significant intestinal bleeding is infrequently the dominant presenting symptom.

MANAGEMENT

Most episodes of abdominal pain in patients with Peutz–Jeghers syndrome are self-limited and resolve without surgical intervention. Temporary withholding of oral feedings, nasogastric decompression, and bed rest will usually be adequate for patients with intussusception due to Peutz–Jeghers syndrome.[9,10] The main indication for operative treatment is presence of obstruction. If an operation is not delayed too long, the intussusception(s) can be reduced by a straightforward enterotomy and polypectomy without segmental small bowel resection. The entire GI tract should be palpated and any other polyps removed in similar fashion. If the patient presents late and the intussusception cannot be reduced, resection with primary anastomosis should be performed.

These hamartomatous polyps are not considered premalignant. Nevertheless, like the isolated juvenile polyp, there are reports of polyps containing areas of adenoma, dysplasia, and carcinoma in patients with Peutz–Jeghers syndrome.[12] GI cancers (small bowel, colon, pancreatico-biliary) have been reported in patients with Peutz–Jeghers syndrome. The risk seems to be increased compared with the general population[13,14]; patients with stomach and/or duodenal involvement are probably at higher risk. Furthermore, the risk of extraintestinal malignancy is increased in patients with

Peutz–Jeghers syndrome. It is estimated that the risk of cancer is increased 18-fold over the general population. In addition to the GI tumors, cancers of the breast, ovary, and cervix as well as germ cell tumors are more common than in the general population.[15–17] None of these cancers occurs at a frequency that justifies prophylactic removal of the organs, but awareness of the risk should guide surveillance. Physicians who follow these patients need to stay up-to-date on the most recent recommendations, as these will likely evolve.

Juvenile Polyposis Syndrome

Juvenile polyposis is also an autosomal dominant disorder with widely varied presentation. About 75% of patients will have a parent with the syndrome, but 25% do not have a family history suggesting a new mutation. Mutations in the *BMPR1A* or *SMAD4* gene have been identified,[18,19] but together these account for only 40% of patients.

Some patients will present in infancy. These patients present with rectal prolapse and anemia; occasionally they will present with significant GI bleeding. Hypoproteinemia, malnutrition, and electrolyte imbalances are usually present as well. Multiple polyps throughout the GI tract usually develop within the first few months of life. Although most develop in the colon and small bowel, they can occur in the stomach as well. These polyps are hamartomas and the term "juvenile" refers to the type of polyps seen in these patients, not the age of onset.

Many patients with juvenile polyposis syndrome will be diagnosed late in the first decade of life; almost all are diagnosed before 20 years of age. These patients must be distinguished from the more common patient with sporadic juvenile polyps. The most widely accepted diagnostic criteria are more than five polyps in the colon, multiple juvenile polyps throughout the GI tract, or any number of juvenile polyps with a family history of juvenile polyps. The location and number of polyps varies widely, so the endoscopic and surgical treatment must be individualized. If sufficient symptomatic relief can be obtained with endoscopic removal of the numerous colon polyps, the patient can be followed with yearly endoscopy along with surveillance biopsies. Laparotomy to perform enterotomies and polypectomies may be needed. If there are clusters of polyps in isolated areas, limited segmental resection may be appropriate. Patients with numerous polyps in the colon may benefit from proctocolectomy with ileo-anal anastomosis, which is required if adenomatous polyps with epithelial dysplasia are found.

Patients with juvenile polyposis syndrome are at high risk of developing cancer.[20] It has been suggested that juvenile polyposis syndrome patients be treated similarly to familial adenomatous polyposis syndromes with the exception that regular colonoscopic surveillance may avoid the need for total proctocolectomy.[21]

Cowden's Syndrome

Cowden's syndrome is a relatively rare disorder in which patients manifest hamartomas of all three tissue types: ectoderm, mesoderm, and endoderm. This too is an autosomal dominant disorder; 85% of patients have a mutation in the tumor suppressor gene PTEN on chromosome 10q.[22] It usually presents in adolescence or early adulthood. Hyperkeratotic papillomas of the lips, tongue, and nares are the most common extraintestinal findings. Most of the GI polyps are in the colon; the stomach is the next most frequent site. Gastrointestinal cancer is not increased in these patients. Lesions of the breast are common in females with this condition. Fibrocystic lesions as well as fibroadenomas are quite common. Intraductal carcinoma has been reported but it is not clear if the risk is increased compared with the general population. Nodular hyperplasia and follicular adenoma of the thyroid develop in many patients.

Ruvalcaba–Myhre–Smith Syndrome

Described in 1980, this autosomal dominant inherited disorder involves the association of juvenile polyps, macrocephaly, and pigmented macules of the genitals. Macrocephaly may not be present at birth, but is noted early in infancy. Additional features of this syndrome are mental retardation, abnormal lipid storage, delayed motor skills, and ocular abnormalities. Possibly a variant of Cowden's syndrome, it is associated with mutations in the PTEN gene encoding a protein tyrosine phosphatase (cell growth inhibitor). There has been no evidence of increased risk of colorectal cancer in patients with this disorder.[23]

INHERITED ADENOMATOUS POLYPOSIS SYNDROMES

Familial Polyposis Coli

Familial polyposis coli (FAP) is an inherited disease involving truncating mutations of the tumor suppressor adenomatous polyposis coli gene (*APC*). The gene is located on chromosome 5 and suppresses canonical Wnt signaling. Mutation of the *APC* gene leads to activation of Wnt signaling. This activation then leads to tumor genesis and alterations in cell adhesion and migration, intracellular signaling, and gene transcription. There are over 800 known mutations of the *APC* gene that are associated with FAP. The location of the mutation along the *APC* gene appears to correlate with the clinical presentation of FAP. Clinically, the result in the colon

is hundreds to thousands of adenomatous polyps that begin to appear as early as puberty. Early symptoms of patients with FAP include rectal bleeding and diarrhea. Ultimately, by age 40, polyp transformation to adenocarcinoma occurs in all patients with FAP.

Diagnosis of FAP is based upon the finding of >100 adenomas in the colon. Patients with FAP and their first-degree relatives are recommended to undergo genetic counseling and genetic testing for detection of the truncated protein product of the mutated *APC* gene. The genetic testing is only beneficial for screening if the affected relative tests positive for the mutation. At-risk relatives who have not undergone genetic testing, or in whom the test did not identify a mutation in the affected relative, should undergo yearly screening with flexible sigmoidoscopy beginning at age 10 to 12. If the individual with FAP has a detected mutation on genetic testing, first-degree relatives that test negative for the mutation are advised to undergo screening endoscopy once per decade starting at age 10 to 12.

Current therapies with nonsteroidal antiinflammatory drugs have been shown to cause regression of adenomatous polyps; however, progression to adenocarcinoma in patients with FAP is inevitable without definitive surgery involving removal of the colon and rectum. Optimal operative therapy is a proctocolectomy with restorative ileo-anal reconstruction–ileal pouch anal anastomosis (IPAA). An endorectal pull through of an ileal J-pouch is one of the preferred methods for the pediatric patient. Most advocate surgical intervention when the patient is ~15 years old and is able to understand and participate in treatment decisions. Recent literature has reported short-term outcomes after laparoscopic IPAA to be equivalent to that after open IPAA.[24] IPAA, however, does not eliminate the development of adenomatous polyps. Endoscopic surveillance is recommended as polyp formation and progression to malignant transformation after IPAA is well described.

Screening for extracolonic lesions such as duodenal polyps and hepatoblastoma is advocated. Mortality from duodenal cancer ranks second to colon cancer in patients with FAP. Early surgery for hepatoblastoma is potentially curable, thus offspring that have FAP by genetic testing can undergo screening with serum α-fetoprotein levels and abdominal ultrasound.

Gardner's Syndrome

Eldon J. Gardner, a teacher of genetics, described this variant of FAP. It is an autosomal dominant disorder characterized by intestinal polyps, multiple osteomas, and mesenchymal tumors of the skin and soft tissues. Congenital hypertrophy of the retinal pigment epithelium has been described in patients with this syndrome. Other associated neoplasms include carcinoma of the ampulla of Vater, adrenal and thyroid.

Symptoms may present anywhere from 2 months of age to 20 years of age. Usually, the extracolonic manifestation of skin tumors and osteomas present before the adenomatous polyps. Osteomas of the skull and long bones present in ~50% of patients with this syndrome. Skin manifestations throughout the body include sebaceous cysts (66%), lipomas, fibromas, and pigmented lesions. Mesenchymal tumors, desmoids, have been reported to occur in 3.5 to 12.4% of patients.[25] Intraabdominal desmoid tumors compress and invade intraabdominal organs requiring surgical intervention.

Turcot's Syndrome

This syndrome, named after a Canadian surgeon, Jacques Turcot, originally was characterized by adenomatous polyps and tumors of the central nervous system. However, it also describes hereditary nonpolyposis colon cancer due to a mutation of DNA mismatch repair genes associated with a primary brain tumor (usually cerebellar glioblastoma). When the colorectal polyps are due to a mutation of the *APC* gene, the primary brain tumor is usually cerebellar medulloblastoma. The incidence of brain tumors in patients with this variant of FAP is most significant in patients before the age of 20.[26] Specific codon mutations of the APC gene may identify FAP patients at higher risk of developing medulloblastoma and thus can be used to screen at-risk individuals.

NONINHERITED POLYPOSIS

Lymphoid Polyposis

Lymphoid polyps are focal hyperplasia of lymphoid follicles in the colon. Though recognized in children, these are rare polyps that are considered benign and have an overlying normal colonic mucosa. Treatment for these polyps is local excision and histopathological analysis to differentiate this benign polyposis from malignant lymphoma of the colon.

Cronkhite–Canada Syndrome

This is a noninherited syndrome of juvenile polyps in association with ectodermal abnormalities. Patients can present with alopecia, nail dystrophy, and hyperpigmentation of the face and eyelids. Often, the gastric mucosa of these patients is hypertrophic leading to malabsorption and protein loss resulting in anemia, diarrhea, weight loss, edema, hypokalemia, and tetany. The pathogenesis of this rare syndrome is unknown and management is supportive. In a review of the literature, 34 of 280 cases of Cronkhite–Canada syndrome had an association with colorectal cancer.[27]

CONCLUSION

Polyps of the intestinal tract in children, as in adults, are mucosal or submucosal growths that bulge into the lumen of the intestine. Polyps in the pediatric population occur less frequently than in adults, with the most common lesions being the juvenile "inflammatory" polyp and the hamartomatous Peutz–Jeghers polyp. Polyps with malignant potential include adenomatous polyps that are associated with polyposis syndromes such as FAP, Gardener's syndrome, and Turcot's syndrome. The etiology, diagnosis, clinical presentation, and management of these intestinal polyps depend on the type of polyp or polyposis syndrome. A change in bowel habits, abdominal pain, rectal bleeding, rectal prolapse, and even intussusception may be the initial presentation in children. In addition to a careful history, including a detailed family history, a physical examination, contrast studies, and endoscopic examination are vital diagnostic tools. Endoscopy allows an excisional biopsy to obtain tissue for diagnosis. Management of benign polyps ranges from simple observation of benign polyps to more aggressive intervention, medical and surgical, for neoplastic polyps. Management of children with malignant polyposis involves the affected child and his or her family as well. Genetic counseling, genetic testing, and recommendations for screening are available to first-degree relatives at risk for the syndrome. A few children present with more life-threatening symptoms from polyps such as bowel obstruction or perforation. These patients require appropriate resuscitation and prompt operative management.

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