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Juvenile Polyposis Syndrome -Two Case Reports

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Abstract:

Juvenile polyposis syndrome is a rare condition characterized by the presence of numerous harmatomatous polyps in the gastrointestinal tract and associated with a risk for colorectal cancer. Juvenile polyposis syndrome has been scarcely reported in Africa and this will be the index cases reported in Ghana. We report two cases of juvenile polyposis syndrome diagnosed and managed in our facility. They both presented with gastrointestinal bleeding and the polyps were identified at endoscopy. Histopathological confirmation of the diagnosis in the first case was delayed leading to death of patient from severe anaemia but the second case underwent a pan-colectomy. The report highlights the occurrence of this precancerous condition, the variety in anatomic presentation of the disease, the diagnostic difficulties and the management challenges.

Key words: Polyps, Intestinal Polyposis, Adenoma, Gastrointestinal Hemorrhage, Colorectal Neoplasms, Humans.

Introduction

Juvenile polyposis syndrome (JPS) is characterized by polyps in the gastrointestinal (GI) tract. It is a rare condition of two forms; sporadic and an autosomal dominant hereditary forms. The multiple distinct juvenile polyps in the gastrointestinal tract are associated with an increased risk of colorectal cancer [1]. The diagnosis is mainly by genetic testing but clinical criteria for diagnosis include: the presence of six or more colorectal juvenile polyps, juvenile polyps throughout the gastrointestinal tract, or any number of polyps in a patient with a family history of juvenile polyposis [1].

The prevalence of colorectal cancer is low in Sub-Saharan Africa, estimated to be about 4.6/100,000 population [2], and equally so is that of polyps and adenomas from which these cancers develop. Syndromic polyps (Familial Adenomatous Polyposis, Peutz Jerghers Polyposis and Juvenile Polyposis syndromes) therefore are extremely rare entities in this environment, with very few scattered cases reported from the African continent. Two cases of juvenile polyposis syndrome are reported here highlighting its varied clinical presentation and the challenges in diagnosis and management of the condition.

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Case Reports

Case 1

In June 2008, a 16 year old girl being investigated for iron deficiency anaemia from occult gastro-intestinal bleeding was diagnosed with multiple gastric polyps at gastroscopy. She had no family history of gastrointestinal cancer and no other family member had been diagnosed of gastro-intestinal polyps. She had no other associated symptoms and examinations did not reveal any stigmata of genetic syndromes. She however had significant weight loss. The polyps were of varying sizes in the entire stomach [Fig.1]. Colonoscopy revealed four rectal polyps. Two polyps each from both the stomach and the rectum were snared for histopathological examination which suggested a diagnosis of lymphocyte infiltrated hyperplastic polyp for the gastric polyps and a benign adenoma for the rectal polyps.

These inconclusive histopathological findings on both specimens necessitated intra-departmental and inter-departmental consultations with other surgeons, haematologists and pathologists in order to achieve consensus on the possible diagnosis. In the interim the patient's clinical state deteriorated further with worsening gastro-intestinal bleeding presenting as haematemesis and melena. Patient could not be optimized for emergency surgery and subsequently died from severe anaemia. The stomach was harvested at autopsy and many more polyps investigated histopathologically from which a diagnosis of Juvenile polyposis syndrome was made.

Case 2

A 34 years old male was first seen in May 2013 with a single episode of bright red bleeding per rectum with clots without any associated symptoms and signs. He had a past medical history of being

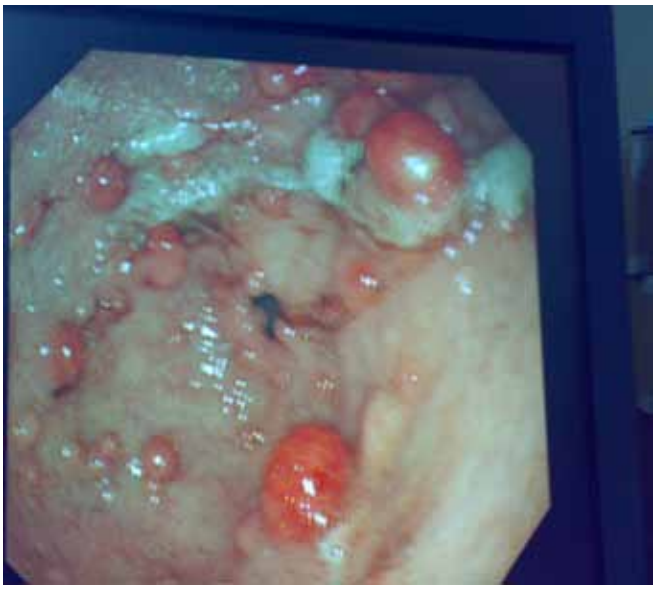

Fig.1: Endoscopic image for case 1.

managed for endoscopically diagnosed chronic gastritis ten years before and subsequently treated for presumptive bleeding peptic ulcer disease after a history of passage of melena following the ingestion of diclofenac after tooth extraction. He had no family history of note and his sister who was investigated colonoscopically for lower gastrointestinal bleeding with no evidence for any polyps.

Colonoscopy on him showed multiple polyps of varying sizes that spanned the entire colon and rectum. He also had second degree haemorrhoids. The gastro-duodenoscopy done was normal. Polyps were biopsied in the ascending colon and the rectum for histopathological evaluation and the findings of ascending colon biopsy was suggestive of "non-specific colitis" while rectal biopsy was reported as "Juvenile Polyp" (consider multiple polyposis if several colo-rectal polyps, or Cronkhite-Canada syndrome if multiple colorectal polyps with ectodermal changes-alopecia, nail atrophy and hyperpigmentation).

In the clinical context, a clinical diagnosis of Juvenile

polyposis syndrome was made. Patient repeatedly had significant recurrent bleeding per rectum on which account he was counseled for and underwent a pan-colectomy with and ileo-anal anastomosis with an ileal continent J-Pouch. The gross findings on the specimen were multiple colorectal polyps of varying sizes as shown in figure 2.

His post-operative recovery was essentially uneventful. Patient moved his bowels averagely seven times daily initially but improved to an average of three times daily after two weeks semi-formed stools. He is currently being followed up with monitoring of stool frequency, nutritional assessment and also routine lower GI endoscopy to evaluate the distal small bowel as well as routine gastroscopy. He is also being evaluated for general and health-related quality of life.

Discussion

The two cases reported show two anatomic locations of juvenile polyposis syndrome and the variability in clinical presentation. In case 1, the histopathological diagnosis was at post-mortem whereas in the second, the diagnosis was possible with the rectal polyp and not the caecal polyp which was reported as an inflammatory lesion. The diagnosis therefore requires an index of suspicion, thorough clinical and pathological evaluation of patient data and confirmatory genetic studies which we are currently unable to do in our practice here. Due to the increased risk for gastro-intestinal cancers, this diagnosis must be established and the appropriate interventions implemented.

The incidence of juvenile polyposis syndrome, the most common hamartomatous polyposis syndrome is approximately 1/100,000 live births [3]. The clinical criteria for juvenile polyposis syndrome include any of the following; the presence of six or more juvenile polyps in the colon and rectum, juvenile polyps throughout the gastrointestinal tract

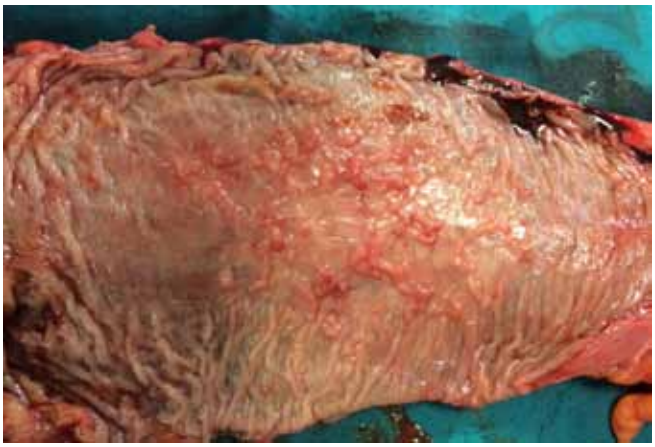

Fig.2: Gross specimen after colectomy.

or any number of juvenile polyps and a positive family history of juvenile polyposis syndrome [1,4]. The two patients were diagnosed based on the first criteria when the histopathology defined the polyps as juvenile polyps.

The genetic basis of juvenile polyposis syndrome is a germline mutation in SMAD4 or BMPR1A genes both involved in the bone morphogenetic protein/TGFβ signaling pathway [5-7]. These mutations are found in about 50-60% of patients. However in about 30-40% of patients with juvenile polyposis syndrome, no germline mutations in these two genes have been identified suggesting that alternate genetic processes are responsible [8]. These constitute the sporadic cases.

Genetic testing of index cases is indicated to identify the specific germline mutations in the BMP/TGFβ signaling pathways or other associated mutations. This could form the basis of testing other family members for the mutation. The absence of specific germline mutation excludes a hereditary form of the disease and as sporadic cases are not transferable to future generations the case is managed according to symptom severity only. Determination of germline mutation in our two cases could been informative but both the family of

the first case and the second case himself declined having this test done which will require shipping of their samples out of the country and at a cost.

These syndromic polyps mostly occur in the colo-rectum, vary in number from six to several hundred but can be found in the stomach, duodenum, jejunum and ileum. They are associated with an increased risk for colorectal cancer. The incidence of colorectal cancer in patients with this condition is estimated to be 17-22% by age 35 years and approaches 68% by age 60 years. The median age developing cancer is 42 years, a relative risk of 34.0 and a 38.7% cumulative lifetime risk [9]. The incidence of gastric cancer is 21% in those with gastric polyps.

The two cases presented with gastrointestinal bleeding which is the typical symptom of the disease. The polyps may also be diagnosed incidentally at endoscopy. Other gastrointestinal symptoms noted in this condition are abdominal pain, constipation, diarrhea, or malnutrition from protein losing enteropathy and intussusceptions. There are no characteristic extra-intestinal manifestations and patients are evaluated with complete upper and lower gastro-intestinal endoscopies and biopsies. Affected patients are then followed up with symptoms, blood counts, colonoscopy, and gastro-duodenoscopy.

The polyps are frequently diagnosed in children however they could be found in adults [10,11]. In our cases one was 16 years and the other 34 years. The second patient could have harbored his polyps since he was an adolescent but diagnosed at this age because they have become symptomatic.

Juvenile polyps may be reported as inflammatory or hyperplastic histopathologically, sometimes delaying the diagnosis of juvenile polyposis syndrome [12] as happened in the first case. However, true juvenile polyps are distinguished by inflammatory stromal tissue with mucus-filled cystic glands [13] and the absence of smooth-muscle proliferation [14]. Again, the clinical information of the patient including the number and distribution of the polyps in the gastrointestinal tract and the family history of polyposis syndrome will assist in diagnosis.

Routine colonoscopy with endoscopic polypectomy is the most effective treatment of solitary polyps however, sub-total or total gastrectomy or pan-colectomy may be necessary to alleviate symptoms and/or reduce cancer risk when a large number of polyps are present and causing life-threatening conditions. The first case needed a total gastrectomy. An initial diagnosis that did not warrant this invasive treatment delayed the intervention till the patient died of severe anaemia when the diagnosis was established. In the second case a pan-colectomy was done because of the repeated severe bleeding and also because the diagnosis of juvenile polyposis syndrome was made timely.

Conclusion

Gastrointestinal polyposis syndromes are extremely rare in Africa where the incidence of colorectal cancer is lowest. Two cases of juvenile polyposis syndrome, one mainly in the stomach and the other in the large bowel which presented differently, managed differently with different results highlights the importance of this disease in our sub-region calling for a high index of suspicion and inter-departmental consultations when confronted with such cases.

References

1. Jass JR, Williams CB, Bussey HJ, Morson BC. Juvenile polyposis-a precancerous condition. Histopathology 1988;13(6):619-630.
2. Ferlay J, Soerjomataram I, Ervik M, Dikshit R, Eser S, Mathers C, *et al*. (2013). GLOBOCAN 2012 v1.0, Cancer Incidence and Mortality

Worldwide: IARC Cancer Base No. 11 [Internet]. Lyon, France: International Agency for Research on Cancer. Available from http://globocan.iarc.fr. Accessed on 15 August 2014.
3. Burt RW, Bishop DT, Lynch HT, Rozen P, Winawer SJ. Risk and surveillance of individuals with heritable factors for colorectal cancer. Bull WHO. 1993;68:655-664.
4. Giardiello FM, Hamilton SR, Kern SE, Offerhaus GJ, Green PA, Celano P, *et al*. Colorectal neoplasia in juvenile polyposis or juvenile polyps. Arch Dis Child. 1991;66(8):971-975.
5. van Hattem WA, Brosens LA, de Leng WW, Morsink FH, Lens S, Carvalho R *et al*. Large ge¬nomic deletions of SMAD4, BMPR1A and PTEN in juvenile polyposis. Gut. 2008;57:623-627.
6. Calva-Cerqueira D, Chinnathambi S, Pechman B, Bair J, Larsen-Haidle J, Howe JR. The rate of germline mutations and large deletions of SMAD4 and BMPR1A in juvenile polyposis. Clin Genet. 2009;75:79-85.
7. Aretz S, Stienen D, Uhlhaas S, Stolte M, Entius MM, Loff S, *et al*. High proportion of large genomic deletions and a genotype phenotype update in 80 unrelated families with juvenile polyposis syndrome. J Med Genet. 2007;44:702-709.
8. Howe JR, Sayed MG, Ahmed AF, Ringold J, Larsen-Haidle J, Merg A, *et al*. The prevalence of MADH4 and BMPR1A mutations in juvenile polyposis and absence of BMPR2, BMPR1B, and ACVR1 mutations. J Med Genet. 2004;41:484-491.
9. Brosens LA, van Hattem A, Hylind LM, Iacobuzio-Donahue C, Romans KE, Axilbund J *et al*. Risk of colorectal cancer in juvenile polyposis. Gut. 2007;56:965-967.
10. Muthuphei MN. Multiple juvenile polyposis: A report of 2 cases. S Afri J Surg. 1994;32(2):97-98.
11. Ibirogba SB, Algar U, Golberg PA, Duffield M, Vorster A, Ramesar R. Clinical and pathological features of hereditary mixed polyposis syndrome: report on a South African Family. S Afri J Surg. 2008;46(3):90-92.
12. Aretz S, Stienen D, Uhlhaas S, Kaufmann A, Vogt S, Propping P, *et al*. High proportion of large genomic deletions and a genotype phenotype update in 80 unrelated families with juvenile polyposis. J Med Genet. 2007;44(11):702-709.
13. Menko FH, Kneepkens CM, de Leeuw N, Peeters EA, Van Maldergem L, Kamsteeg EJ, *et al*. Variable phenotypes associated with 10q23 microdeletions involving the PTEN and BMPR1A genes. Clin Genet. 2008;74(2):145-154.
14. Zbuk KM, Eng C. Hamartomatous polyposis syndromes. Nature clinical practice. 2007;4(9):492-502.