

Puetz Jegher Syndrome in a Family in Ghana: A Case Series and Clinicopathologic Review

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Received April 10, 2015; Revised May 03, 2015; Accepted May 14, 2015

Abstract Background: Peutz Jegher syndrome (PJS) is a condition in which multiple hamartomatous polyps are present in the gastrointestinal tract in association with distinctive mucocutaneous pigmentations. Some patients are diagnosed as children, where others might not be diagnosed until they reach their teen or adult years. **Methodology:** We studied a family of 7 with 5 having symptoms and signs of Peutz-Jegher syndrome using the review of clinical notes, diagnostic and interventional endoscopy, surgical intervention and histopathological assessment over a period of 6 years. **Result:** Mother and 3 have polyps and muco-cutaneous pigmentation, one has polyps only, one has muco-cutaneous pigmentation only and one has neither muco-cutaneous pigmentation nor polyps. **Conclusion:** The report demonstrated that PJS is a hereditary disease with variable penetrance. A molecular and genetic assessment of this family is recommended.

Keywords: PJS, buccal pigmentation, hamartomatous polyps, endoscopy

Cite This Article: Mary Y Afihene, and Babatunde M Duduyemi, "Peutz Jegher Syndrome in a Family in Ghana: A Case Series and Clinicopathologic Review." *American Journal of Medical Sciences and Medicine*, vol. 3, no. 2 (2015): 14-19. doi: 10.12691/ajmsm-3-2-2.

Peutz Jegher syndrome a rare disease with very limited reports in our environment.

1. Introduction

Peutz-Jeghers syndrome (PJS) is a condition in which multiple hamartomatous polyps are present in the gastrointestinal tract in association with distinctive mucocutaneous pigmentations [1,2,3].

Individuals with PJS have hamartomas predominantly in the small intestine and varying number of polyps in the large intestine and stomach. Pigment spots are often found on the lips, face and body which disappear sometime in the teen years. The age at diagnosis depends on the severity of symptoms [4]. PJS manifests in varying ranges of severity and symptom development. Some patients are diagnosed as children, where others might not be diagnosed until they reach their teen or adult years. The onset of symptoms is the usual catalyst for finding a diagnosis of PJS [5]. Patients will typically develop tens to thousands of hamartomas in the stomach and intestines most of which are found in the small intestine. Gastrointestinal endoscopy and X-rays are used in detecting polyps but are defective in showing polyps in the small intestine [6].

Recent studies have shown that there is an increased risk of cancer over the general population and STK11 gene locus has been identified for the syndrome. Current genetic testing can identify a mutation in 30-80% of PJS patients [7]. A new method is in testing that promises to increase genetic identification [8]. We present report of a family with 5 out of 7 having symptoms suggestive of

2. Methodology

We studied a family of 7 with mother and 4 children having symptoms and signs of Peutz-Jegher syndrome using the review of clinical notes, diagnostic and interventional endoscopy, surgical intervention and histopathological assessment. The family was followed up for 6 years for this preliminary study and they are still been followed at the medical outpatient department of the Komfo Anokye Teaching Hospital, Kumasi, Ghana.

3. Case Reports

3.1. Control

KA is a 44 year old male and father of the family who has no pigmentation or polyp. He serves as control for the rest of the family.

3.2. Case 1

JOM is a 44 year old female and mother of the family who is the index case. She had been attending surgical outpatient clinic since May 2003 with abdominal pains which she had experienced for 8 years.

Two years before, she developed pyelonephritis and was referred to medical outpatient where she was admitted

for treatment. An intravenous urogram done during this period was normal.

A year later, the surgeon who operated on her son for intussusception of the small bowel due to polyposis detected that both mother and her son had hyperpigmented spots on lips, feet and hands. He therefore referred her to the medical unit for further investigation to find out if her recurrent abdominal pains could be due to polyposis.

Since her referral, she and her children have undergone general examination and a series of upper and lower GI endoscopies and polypectomies (Table 1).

The upper gastrointestinal endoscopy showed chronic pan-gastritis and multiple gastric antral polyps. The largest polyp measured 10mm x10mm and three smallest ones measured 5mm x 5mm each. Histological sections showed hyperplastic polyps with chronic active gastritis without dysplasia or malignancy.

Lower GI Endoscopy showed two pedunculated rectal polyps and histology section showed polypoid tissue with hyperplastic glandular epithelium displaying no atypia or malignancy consistent with a benign polyp (Figure 1).

Had a repeat sigmoid colonoscopy one year after which revealed a sessile and multilobulated polyp measuring 15mm x15mm and a pedunculated polyp measuring 10x 10mm. Patient had polypectomy done and part of the samples was sent to Mayo Clinic for histology and possible genetic studies.

Patient has been having yearly upper and lower GI endoscopies which have been essentially normal with no polyps.

She developed bilateral breast masses associated with bloody nipple discharge 5 years ago which were resected and histology showed bilateral duct papilloma (Figure 2).

Table 1. Endoscopic, surgical and histologic features of polyps in Case 1

Date	Procedure	Findings	Largest size of polyp	Histology
May 2005	Upper GI endoscopy	Chronic pangastritis with multiple antral polyps	10mm	Moderate chronic active gastritis with inflammatory polyp.
October 2005	Upper GI endoscopy	Multiple gastric antral polyps	10mm	Hyperplastic polyp
May 2005	Lower GI endoscopy	2 polyps in the sigmoid colon	40mm	Hyperplastic polyp
2007	Upper and lower GI endoscopy	Normal, no polyps		
2008	Upper and lower GI endoscopy	Normal, no polyps		
2009	Upper and lower GI endoscopy	Normal, no polyps		
2009	Lumpectomy	Left and right soft to cystic breast masses	38mm	Bilateral duct papilloma

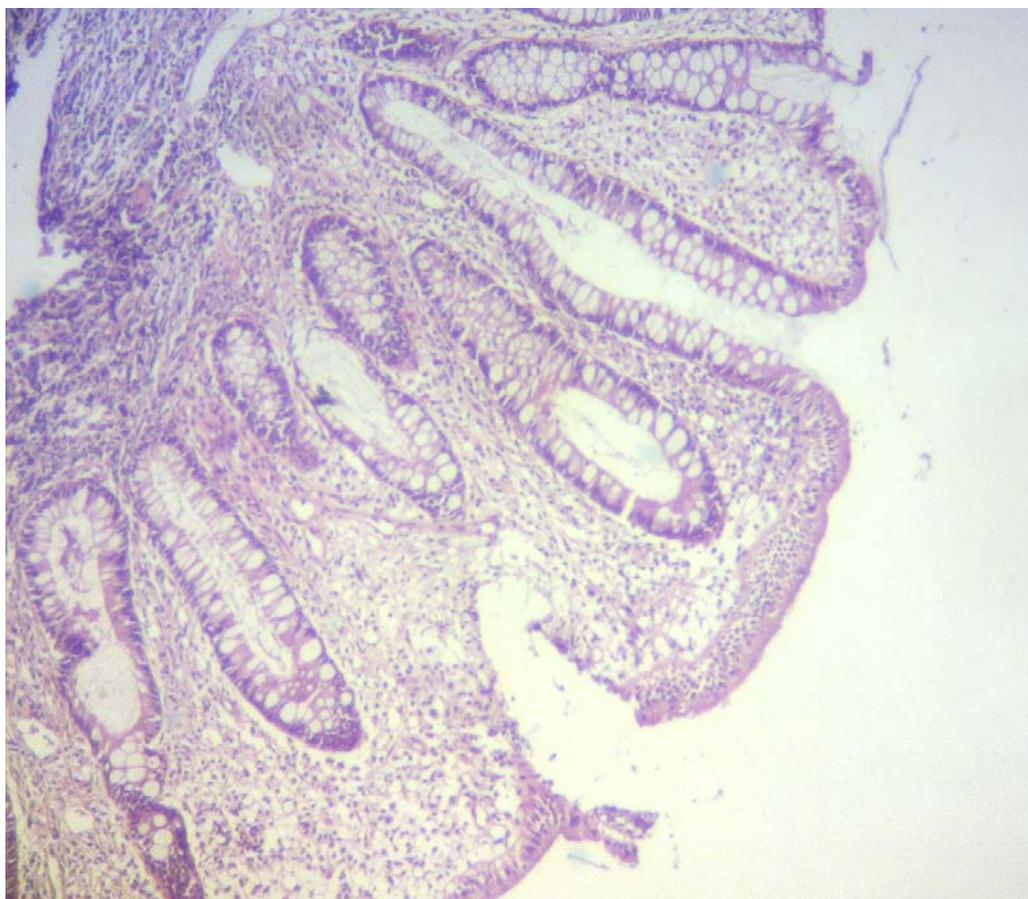


Figure 1. Section of colonic polyp showing hamomatous/hyperplastic glands and moderate inflammation of the surrounding stroma and submucosa

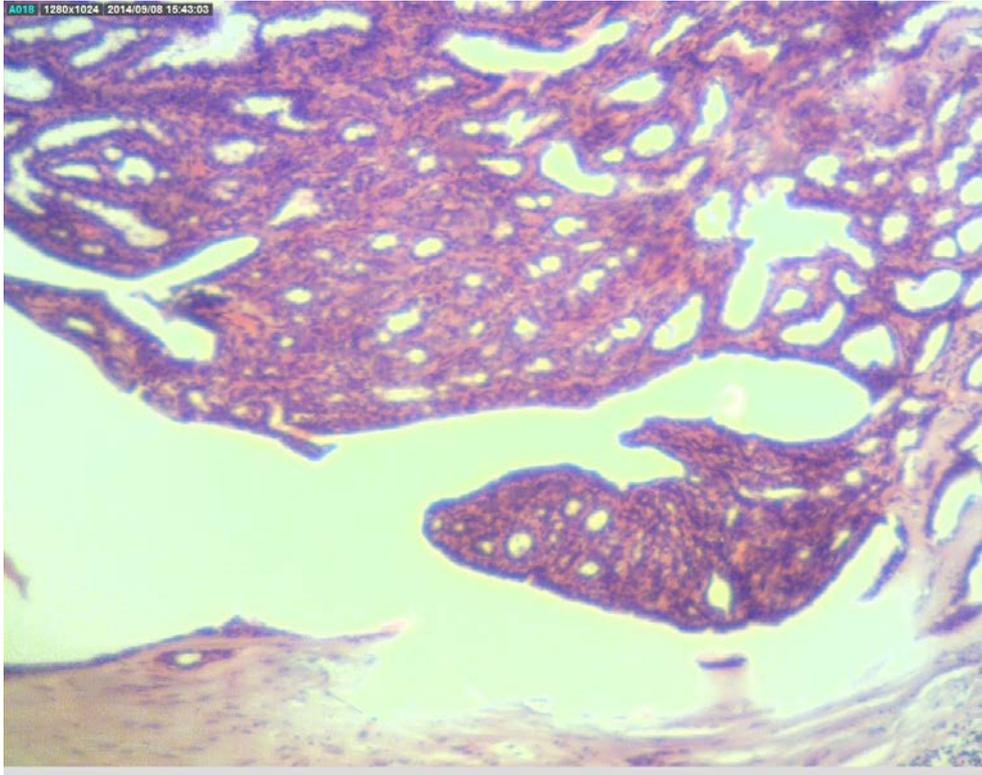


Figure 2. Section of the breast mass showing duct papilloma with epitheliosis in case 1

3.3. Case 2

OPB is 19 year old male child of the family who had surgical operation in 2004 for intussusception having presented with features of acute intestinal obstruction. At surgery, multiple polyps were found in the ileum.

Gross section revealed multiple polyps on the mucosal surface of ileum, the largest measures 3.0 x 2.5 x 1.8 cm with indurated surface. The tissue has soft consistency and cut sections reveal grey-brown appearance.

Microscopic sections showed a polypoid tissue with hyperplastic and adenomatous change. There is marked

infiltration by chronic inflammatory cells but no evidence of malignancy. These features are consistent with hyperplastic and adenomatous polyps.

Two years later, a lower GI Endoscopy was done and three polyps were found in the rectum each measuring 13mm x 13mm, 10mm x 10mm and 4mm x 4mm; and one polyp was found at the sigmoid colon measuring 7mm in widest diameter.

He had polypectomies done and histology showed hyperplastic and adenomatous polyps. Part of these samples was sent to Mayo Clinic, Rochester, USA for molecular and genetic studies.

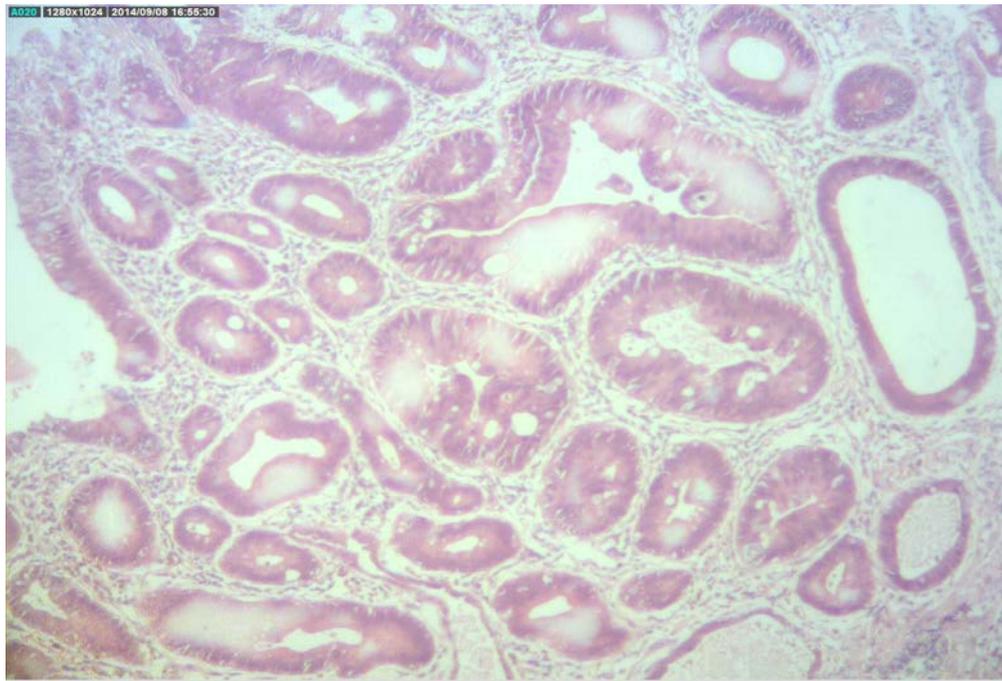


Figure 3. Section of rectal polyp showing adenomatous glands with high grade dysplasia and mild chronic inflammation

Table 2. Endoscopic, surgical and histologic features of polyps in Case report 2

Date	Procedure	Findings	Largest size of polyp	Histology
2004	Laparotomy	Multiple polyps in the ileum	30mm	Adenomatous and hyperplastic polyps
2006	Lower GI endoscopy	Multiple polyps in the sigmoid colon and rectum	13mm	Adenomatous and hyperplastic polyps
2007	Lower GI endoscopy	Multiple polyps in the sigmoid colon	20mm	Adenomatous and hyperplastic polyp
2008	Colonoscopy	Normal, no polyps	-	-
2009	Lower GI endoscopy	Multiple polyps in sigmoid colon and rectum	60mm	Hyperplastic polyp
2010	Lower GI endoscopy	Single polyp in the rectum	45mm	Tubulovillous adenoma with low grade dysplasia

The summary of procedures, endoscopy and the findings on histology are shown in the [Table 2](#) and [Figure 3](#).

3.4. Case 3

GK is a 15 year old male child of the family who first seen in 2008 with pigmentation in the buccal mucosa and had lower GI endoscopy done which revealed a sessile polyp measuring 10 x 10mm. He also had serial endoscopies every year as summarized in the [Table 3](#) below.

Table 3. Endoscopic and histologic features of polyps in Case report 3

Date	Procedure	Findings	Size of largest polyp	Histology
2008	Lower GI endoscopy	Sessile polyp in rectum	10mm	Hyperplastic polyps
2009	Colonoscopy	Normal, no polyps	-	-
2010	Lower GI endoscopy	Lobulated sessile polyp in sigmoid colon	15mm	Hyperplastic polyp

3.5. Case 4

MA is a 26 year old male child of the family who was first seen in 2006 having presented with pigmentation of the buccal mucosa and no other symptoms. He had upper and lower GI endoscopy which revealed solitary sessile polyp in the distal rectum measuring 4mm in widest diameter. Histology revealed a hyperplastic polyp with no dysplasia.

Patient has been lost to follow up since then due to relocation out of the city. He was advised to continue routine endoscopy and other necessary investigations in his new abode.

3.6. Case 5

AA is 24 year old female child of the family who was first seen in 2006 having presented with pigmentation of the buccal mucosa and no other symptoms. She had upper and lower GI endoscopies yearly till 2008 and all were normal with no polyps.

3.7. Case 6

CA is 13 year old male child of the family who was first seen in 2010 having presented with pigmentation of the buccal mucosa and no other symptoms. He has not had endoscopy done.

Table 4. Summary of the clinical features for the entire family

Cases	Age at first contact	Sex	Pigmentation	Polyp	Additional information
1(Control)	44	Male	-	-	-
2	44	Female	+	+	Duct Ectasia of breast
3	19	Male	+	+	Intussuception
4	15	Male	+	+	-
5	26	Male	+	+	-
6	24	Female	-	+	-
7	13	Male	+	-	-

4. Discussion

PJS is a rare disease. The incidence is 1 in 30000 to 120000 live births (13). It is an inherited GI hamartomatous polyposis syndrome that is associated with muco-cutaneous pigmentation. Pigment spots are often found on the lips, face and body which disappear sometime in the teen years [1,9]. Pigmentations can also be present in other parts of the body, such as fingers, toes, hands, feet and the mucosa of the nose, conjunctiva and rectum [10].

The diagnosis of PJS requires histopathological confirmation of hamartomatous gastrointestinal polyps and two of the following features: small bowel polyposis, positive family history and pigmented skin or mucosa [1,2,3,4].

In our study of this family, polyps and muco-cutaneous pigmentation were found in cases 2, 3, 4, 5 and 6. This conforms to most reported cases [1,2,3,4,11].

The histopathological findings include hyperplastic and adenomatous polyps in all the cases with polyps. The hyperplastic polyps are benign and are the most common histological types seen in PJS [12]. The adenomatous polyps are premalignant lesions which are less commonly seen in PJS. The presence of adenomatous polyps in PJS lends credence to the ability of the otherwise benign lesion to transform to malignancy [13]. Therefore it is recommended that patients should be followed up with periodical endoscopy. There are few reported cases of malignant transformation of PJS polyps [14]. None of our cases has malignant transformation of the polyps during the study period. Through observation of the microscopic changes in some malignant bowel lesions, malignancy could arise in a polyp with the typical Peutz-Jeghers

morphology and this could be due to the progression of hyperplasia, stratification, and atypia to frank carcinoma [15]. The estimated lifetime risk of cancer development (especially gastric and colorectal cancers) is 15% by age 50 years and 57% by age 70 years [16,17].

Case 1 of our study developed bilateral duct papilloma a benign breast lesion as additional feature. Benign and malignant lesions of the breast and endometrium have been reported in association with PJS in patients on follow up for a long period [18].

Case 2 of our study presented ab initio with acute abdomen secondary to intussusception which necessitated a surgery and the precipitating factor was a polyp. Although benign, polyps can lead to complications including bowel obstruction, rectal prolapse, and severe GI bleeding with secondary anaemia, and intussusceptions [19].

Cases 3 and 4 have pigmentations and polyps with no additional features. This form of presentation is the most common although a few cases may present with either pigmentations or polyps as seen in cases 5 and 6 of our study [1,2].

The diagnosis of PJS is based on the clinical findings and can be made in a patient presenting one of the following signs: two or more histologically confirmed PJ polyps; any number of PJ polyps and a family history of PJS; characteristic mucocutaneous pigmentation and a family history, or any number of PJ polyps associated with characteristic mucocutaneous pigmentation [20].

Molecular genetic testing of the STK11 gene confirms the diagnosis although this mutation is not present in small percentage of cases. It therefore follows that genetic counselling is important in the management of these patients [7,8]. We were unable to do molecular testing in our centre but we have the paraffin embedded tissue block for future analysis.

Management of patients with PJS depends on the presenting symptom. Polypectomy should be done by endoscopy or laparoscopic surgery. The overall management recommendation for PJS patients should be gastrointestinal multiple polyp resolution and regular lifelong cancer screening with colonoscopy, upper endoscopy, computed tomography, magnetic resonance imaging or ultrasound of the pancreas, chest X-ray, mammography and pelvic examination with ultrasound in women, and testicular examination in men [7,21,22].

Our patients are still on periodical follow up with the overall aim of prompt detection and treatment of any associated lesion.

5. Conclusion

This clinicopathological study of PJS is presented to inform clinicians in this environment of the need to critically evaluate polyps with all the seriousness it entails and should not be dismissed as ordinary benign polyps but attempt to rule out PJS and other polyposis syndromes should be made. The mother (case 1) is the primary carrier in our case with variable transmission to the children. This study further elucidates the importance of family surveillance in a suspected case of PJS. Genetic counselling plays a major role in the management of this

syndrome and therefore molecular analysis of the polyps is recommended.

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