Research Article

Pancreatic Adenocarcinoma With Hyperplastic Polyps Seen in Duodenum and Rectum an Analysis To Rule Out Juvenile Polyposis Syndrome

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Abstract

Polyposis syndromes are of several types, they can be either inherited or acquired. Most of them are associated with increased colorectal cancer. Rare type of juvenile polyposis syndrome is associated with pancreatic cancer. JPS is characterized by multiple hamartomatous (hyperplastic) juvenile polyps in the stomach, small intestine and colon. Juvenile polyposis coli has polyposis restricted to colon. Whereas generalized juvenile polyposis has polyps throughout the gastro intestinal tract and may rarely be associated with pancreatic cancer. It has mutation in SMAD4 gene, located in chromosome 18q21 also called as DPC4. It is deleted in pancreatic carcinoma. Here we have a case of hyperplastic polyp in duodenum and rectum along with intestinal type of adenocarcinoma of pancreas in a 62 year old male.

Introduction

The common gastrointestinal polyposis syndrome includes juvenile polyposis, Peutz Jeghers, Cowden, Cronkhite-Canada, tuberous sclerosis. In FAP the polyps are of adenomatous type. Classic Familial Adenomatous Polyp, Attenuated Familial adenomatous polyposis, Gardners syndrome, Turcot syndrome, MUTYH polyposis are other adenomatous polyps.

Juvenile polyps are focal malformations of the epithelium and lamina propria. They maybe sporadic or syndromic. Can present in young age less than 5 years, and also present in old age. Here the polyps are located mostly in rectum usually hamartomatous type rarely as retention polyps. The hamartomatous polyps can vary from 3 to 100. Gastric polyps can undergo malignant transformation. Extra intestinal manifestations include pulmonary arteriovenous malformations. It has been proposed that mucosal hyperplasia is the initiating vent and that mutations in cellular growth regulator pathways. It can be a cause in autosomal dominant juvenile polyposis syndromes. Dysplasia can be seen in the polyps and rarely pancreatic adenocarcinomas can be an associated manifestations. In Peutz Jeghers syndrome characteristic histopathologic morphology is usually appreciated along with pigmented macules. They are also at risk of colon, breast, lung, pancreatic and thyroid tumors.

Peutz Jeghers has histological features of hamartomatous polyps. Lynch syndrome has specific mutation in MLH1, MSH2, PMS2 or PECAM and is associated with malignancies in several non-GI systems. They have few polyps and rapidly progress to cancer. They are usually of adenomatous type. In attenuated lynch syndrome, a subtype of lynch syndrome has increased risk of pancreatic cancer approximately 9 fold and the pancreatic cancer often exhibit MSI expression. Non adenomatous polyposis include hyperplastic polyps in GI. They require careful classification and screening. Under Non adenomatous polyposis we have juvenile polyposis syndrome, hyperplastic polyps, Cowden syndrome, Peutz Jeghers syndrome. Juvenile polyposis are rare inherited disorders. They have multiple benign hamartomatous (usually of hyperplastic polyps of GIT). Rarely associated with pancreatic carcinoma. It is associated with SMAD4 mutation. As per pathology outlines December 2023, juvenile polyps in small intestine and ampulla are discussed.

CASE REPORT:

A 62 years old male known diabetic came to our hospital with complaints of itching all over the body, pale colored stools for 10 days. UGIscopy was carried out which revealed lax lower esophageal sphincter, antral gastritis, duodenal polyp and bulky ampulla. Histopathological examination of duodenal biopsy showed hyperplastic polyp of

duodenum. Later, patient underwent colonoscopy and rectal polyp was found and biopsy was taken. Under histopathological examination, it was consistent with goblet cell rich hyperplastic polyp. With the CT imaging diagnosis of Peri ampullary Carcinoma was made and patient underwent Whipple's procedure with feeding jejunostomy, reconstruction done with pancreatico - jejunostomy - end of jejunum inserted into pancreatic stump and specimen submitted for histopathological examination. Common bile duct found dilated.

We received container A labelled as Whipple's procedure specimen and dissection was done as per recommendations (Susan and Lester 3rd edition, chap 19.) with stomach - 9cm along the greater curvature. Duodenum with portion of jejunum-34cm long, CBD-5.5cm long, thickened and dilated. C/S - Through the ampulla shows a grey white, firm mass-1.5x1cm, adjacent to the pancreatic duct. Pancreatic duct dilated and shows squamous metaplasia, no dysplasia noted. No polyps noted in rest of duodenum, jejunum and stomach.

The peri ampullary growth under histopathological examination revealed pT3a -periampullary intestinal type adenocarcinoma. No nodes were identified. No perineural or vascular invasion. All pancreatic margins were free of tumor. The expressions of PMS2 and MSH2 were negative on the pancreatic growth.

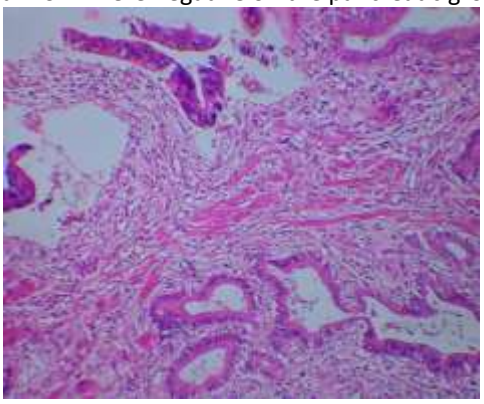

Image 1 : Adenocarcinoma pancreas, with malignant glands invading the muscular layer.

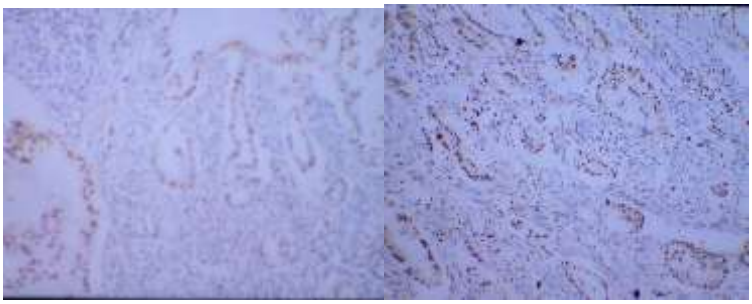

Image 2&3 :IHC markers PMS2 and MSH2 stains showing nuclear staining retention respectively ruling out microsatellite instability which further rules out Lynch syndrome.

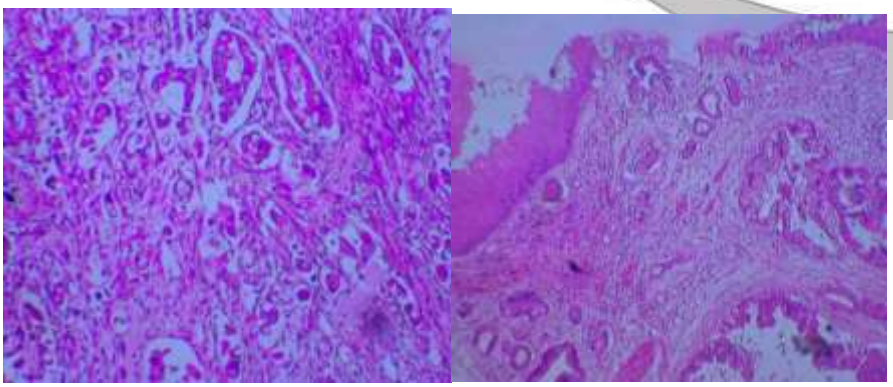

Image 4 : Poorly formed glandular structures. Image 5 : Adenocarcinoma with adjacent duct showing squamous metaplasia.

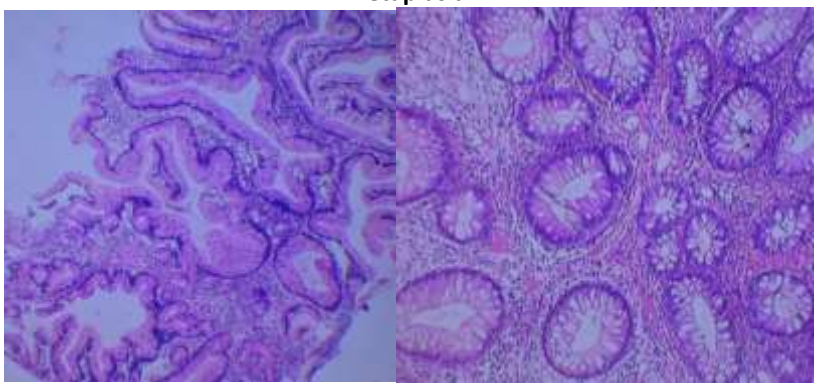

Image 6&7 duodenal and rectal biopsy showing hyperplastic polyps.

DISCUSSION:

Juvenile polyposis syndrome is a genetic precancerous condition which causes gastrointestinal cancers. It is an autosomal dominant disorder affecting one in 100,000[1]. The diagnostic criteria according to Mills and Sternberg textbook include at least 5 colorectal polyps, any number of extra colonic polyps and GI polyps in family members[1]. The polyps of JPS can be of two types. One is stroma-predominant juvenile polyps associated with BMPR1A which are often red brown with a smooth, granular surface and adherent inflammatory exudate and other is epithelium-predominant associated with SMAD4 mutation which has pedunculated mulberry like polyps. Stroma-predominant polyps contain mucin filled cystic spaces with eosinophil rich edematous lamina propria. Epithelium-predominant juvenile polyps has crowded, irregularly shaped crypts showing dysplasia. The risk of colorectal carcinomas is 70% by 60 years of age[1] with associated risk of pancreatic cancer[1]. People with variants in the SMAD4 gene can sometimes have both JPS and HHT (hereditary hemorrhagic telangiectasia), which is called as juvenile polyposis/hereditary hemorrhagic telangiectasia syndrome. JPS is inherited in an autosomal dominant pattern. Dominant genetic pattern occur only when a single gene copy of disease causing gene variant is expressed. The gene variant can be inherited from either parent, or it can be the result of a new (de novo) change in the affected individual that is not inherited. The risk of passing the gene variant from an affected parent to a child is 50% for each pregnancy. The risk is same for both males and females. Approximately 75% of cases causes by a variant in the BMPR1A or SMAD4 gene defects are inherited from one of the parents. 25% arise from a new (de novo) variant that appears for the first time in the affected person and is not inherited. In people with variant-negative JPS, less than 10% have a family history of JPS. Some people have the features of JPS but lack identifiable disease causing variants in the BMPR1A and SMAD4 genes. This is called variant- negative JPS. It is not known yet why people with variant-negative JPS develop polyps, but it is thought that in these people, JPS is caused by variants in other genes which are not yet identified.

JPS may be suspected when someone has the following clinical features: 1. Anemia or rectal bleeding. 2. More than one juvenile polyp. 3. One or more juvenile polyp and a family history of JPS.

In our case patient had biopsy proven hyperplastic polyps. One in upper GI and one in rectum. Well differentiated

grade 1 pancreatic adenocarcinoma in the periampullary region directly invading pancreas up to 0.5 cm. Squamous metaplasia noted in the duct adjacent to the tumor[2]. Final impression given was pT3a pancreatic intestinal type adenocarcinoma. There was no lymphovascular invasion and perineural invasion. SMAD4 mutation shows negative staining. MSH2 and PMS2 were negative in our case favouring a non adenomatous polyposis syndrome. Variant negative JPS lack identifiable disease causing BMPR1A and SMAD4 genes.

Rarely JPS is associated with pancreatic adenocarcinoma. The polyps can occur at any age even though termed as juvenile polyposis syndrome. These polyps are usually benign but have increased chance of malignant transformation.

CONCLUSION:

Hamartomatous polyps in duodenum and rectum along with well differentiated adenocarcinoma of intestinal type in ampulla with its extensive squamous metaplasia are unique to this case.

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