Peutz Jeghers Syndrome

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ABSTRACT

Peutz-Jeghers Syndrome (PJS) is a rare condition that tends to run in families. Diagnosis of PJS is made if a person has polyps in the gastrointestinal (GI) tract and at least two of the following: polyps in the small bowel, melanin spots, and/or a family history of PJS. The typical clinical manifestation of the disease is associated with complications secondary to intestinal polyps often requiring surgical treatment.

A young woman, 29 years old with PJS had been hospitalized in Cipto Mangunkusumo hospital. She was suffering from GI complication secondary to her polyps such as abdominal pain, nausea, vomited every time she takes her meal and milk, anorexia, fatigue, weakness, chronic diarrhea with hematoschezia. Upper and lower endoscopy showed the multiple polyps along from esophagus, gaster, duodenum, and her colon. Histopathology examination confirmed the type of polyps is Peutz Jeghers with the unique morphology consisting of mucosa with interdigitating smooth muscle bundles that yield a characteristic branching tree appearance. We also found the family tree of this patient and it is a good evident how PJS can be inherited in a family.

Keywords: *Peutz-Jeghers syndrome, melanin spots, polyps*

INTRODUCTION

Peutz-Jeghers Syndrome (PJS) is a rare condition that tends to run in families.[1] This syndrome occurs in approximately 1 in 8,300 to 29,000 live births.[2] Other literature stated that 1 in 160,000 to 1 in 280,000 persons will develop PJS.[1] The original family was described by Dr. Jeghers in 1949.[3]

Scientists are studying which gene mutations may cause PJS. Some people with PJS carry a mutation in a gene called STK 11, also known as LKB1, which is located on chromosome 19.[1,4,5,6] In the early 1990's prior to identification of the genetic basis for PJS, about 50% of reported cases had a known family history, the remaining 50% were thought to be sporadic; updated statistics are anticipated as genetic testing becomes more widely used.[7,8,9]

Diagnosis of PJS is made if a person has polyps in the GI tract and at least two of the following: polyps in the small bowel, melanin spots, and/or a family history of PJS.[1,3,8,9] The typical clinical manifestation of the disease occurs in the first two decades of life and is associated with complications secondary to intestinal polyps often requiring surgical treatment.[10]

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Case

A young woman, 29 years old admitted to Cipto Mangunkusumo hospital due to difficulty to eat and drink since one week prior to admission. Actually, she got symptoms such as abdominal pain, nausea, vomited every time she takes her meal or drinks milk. She was anorexic, fatigue, weak, and had chronic diarrhea with hematochezia since one and half month prior to admission. Once she had the same symptoms when she was 8 years old.

Physical examination indicate her general performance was moderate, fully alert, her blood pressure 110/80 mmHg, pulse 108 times/minute, regular, her respiratory rate is 20 times/minute, regular and temperature is 36.9ºC. Her body mass index was 15.6. We found that many irregular melanin spot on her lip (figure 1). We also found tenderness on right upper and lower quadrant. There is no abnormality on her back, and the extremities.

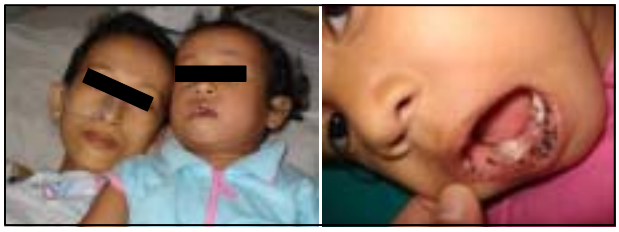

Figure 1. Melanin spot on the lips of a young woman and her daughter with Peutz Jeghers syndrome

Based on the laboratory examination, we found that her hemoglobin 11.6g/dL; hematocryt 37%; leukocytes 13,600/uL; trombocytes 542,000; MCV 63; MCH 20; MCHC 32.7; BUN 18 mg/dL; creatinine 0.3 mg/dL; AST 18 IU/L; ALT 12 IU/L; albumin 2.5 g/dL; bilirubin total 1.8 mg/dL; bilirubin direct 0.3 mg/dL; bilirubin indirect 1.5 mg/dL, random blood sugar 93 mg/dL; sodium 135 mEq/L; potassium 3.3 mEq/L; chloride 102 mEq/L. Urinalysis revealed normal.

We did not find any abnormality on her ECG and the chest X-ray examination. The USG abdomen examination previously indicated there were heterogenic lesion (isoechoic and hypoechoic) oval on the colon ascenden and flexura hepatica projection. The size of lesion was 72 mm x 53 mm x 50 mm. The colonoscopy examination show many of polyps along her colon, and bulging mass in the colon transversum, fragile, macroscopic appearance as a malignancy closed to flexure hepatica and it almost obstruct the lumen.

From the preliminary data include her history of illness, physical finding, and laboratory and imaging examination, the problems of this patient was include familial type multiple polyposus, low intake, hypoalbuminemia, anemia micrositic hypochromic, hypokalemia, leukocytosis, and underweight

Problems familial type colonic multiple polyposus type is made based on her GIT symptoms such as diarrhea, hematokezia, abdominal pain, nausea, vomited. Based on physical finding, there is tenderness in RUQ and epigastrium region and macula hyper-pigmentation on her lips. We found many polyps and bulk mass along her colon. We also found that her daughter had colonic polyps too.

The others problems such as low intake is made based on not adequate intake, loss of appetite, and vomited. Hypoalbuminemia (2.5 g/dL) occurred due to intake problem and her GI condition. These conditions will make her body weight decrease and become underweight. We found also that patient has problem of anemia. It strongly suggested due to chronic hematoschezia as a consequences of her polyps. Electrolyte imbalance in this patient due to her nutrient absorption was not optimal and her intake also had not been adequate. Beside that she suffers from vomit every time she takes her milk. Leukocytosis also can be happen due to her infection since there is many polyps can obstruct the intestinal lumen, and micro-organism colonized there. We gave the treatment to this patient include partial parenteral nutrition by nasogastric tube and infusion, buscopan injection, ranitidine injection 1 amp twice daily, cefotaxim injection 1 gram three times daily, and KSR 1 tablet three times daily.

In term of definite diagnostic, we evaluate the patient with some examination including imaging examinations (abdominal X-ray 3 position, upper endoscopy, OMD follow through, USG), serial laboratory and histology examination. Result of abdominal X-ray 3 positions was normal. There was no sign of intestinal obstruction. Upper and lower endoscopy showed the multiple polyps along from esophagus, gaster, duodenum, and her colon (figure 2a, 2b). Histopathology examination confirmed the type of polyps is Peutz Jeghers with the unique morphology consisting of mucosa with interdigitating smooth muscle bundles that yield a characteristic branching tree appearance (*figure 3*). Meanwhile, the CEA level was 10.3 and 2 weeks later increase to become 14.4.

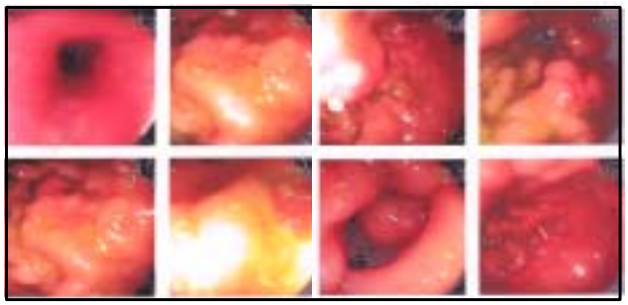

Figure 2a. Upper endoscopy show multiple polyps from the esophagus, gaster, and duodenum

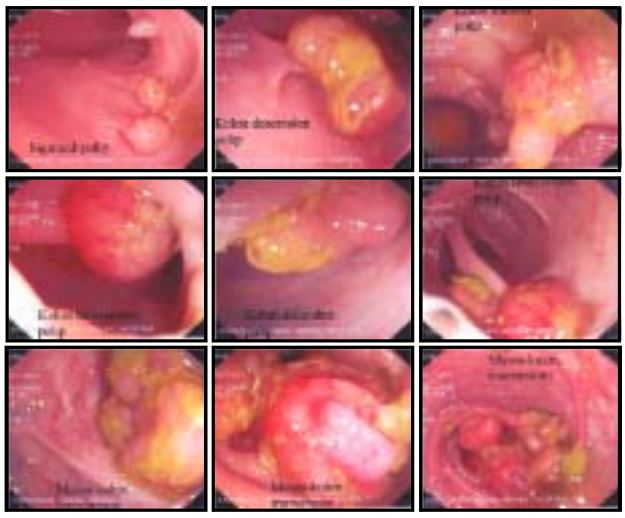

Figure 2b. Colonoscopy show the multiple polyps from rectum to colon transversum with varies in size

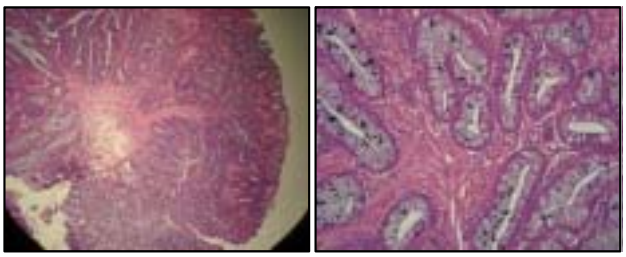

Figure 3. Histopathology show tree-like structure of musculature cover with normal mucosa

During her hospitalization, she got many GI complications, such as chronic diarrhea and prolonged melena, nausea, vomit, abdominal pain and low intake. Due to these complications, her condition was getting worse day by day. It is also reflected from the laboratory parameter such as albumin, electrolytes. The albumin and electrolytes especially sodium and potassium were getting lower.

As a symptomatic treatment we did many things such as we gave her attalpulgite tablet to control diarrhea. We gave antibiotic, anti fungal, and also probiotic. Unfortunately, the diarrhea was not stopped. We also gave PRC transfusion to replace the blood loss, albumin infusion, and electrolytes correction.

In term of definitive therapy, finally, we decided to remove the entire polyp by total colectomy (together with Digestive Surgery). During preoperative preparation, we tried to improve conditions such as giving the blood transfusion, albumin infusion, change the antibiotic to meet the sensitivity test, replaced the electrolytes imbalance. Unfortunately we face the difficulties, especially financial support from her family. They asked to stop medication and refuse the surgical intervention.

DISCUSSION

In the literature, it is states that diagnosis of PJS is made if a person has polyps in the GI tract and at least two of the following: polyps in the small bowel, melanin spots, and/or a family history of PJS. Even though the polyp can be found along the GI tract, based on the literature the most common site is jejunum and stomach. The size is varies, from less than 1/10 of an inch to 1 to 2 inches. In this case, it proved that she has multiple polyps along her GI tract system from esophagus to colon with a few giant polyps on her colon transversum.

In term of melanin spot, based on the literature it is state that it manifests itself as freckle-like macules about the hands, perioral skin, and intraorally to include the ginggiva, bucal, and labial mucosa. Pigmented spots are 1 to 10 mm in diameter. Pigmented spots are particularly found on the lower lip and buccal mucosa but rarely on the upper lip, tongue, palate, and ginggiva. In this case, we found the melanin spots on her lip and it has been there since she was a baby.

In the literature stated, those patients with PJS have a 50% chance of passing on the mutation to each of their children, as described below. In this case, we found the evidence that her daughter has the same disease. We found also her daughter has melanin spot on her lips and buccal mucosa. Beside that according to the patient, her mother died due to the same symptoms. Unfortunately, we do not have medical record or data about her mother.

A definite diagnosis of Peutz-Jeghers syndrome requires the histo-pathologically confirmed hamartomatous polyps. The polyps that occur in individuals with Peutz-Jeghers syndrome can have a unique morphology consisting of mucosa with interdigitating smooth muscle bundles that yield a characteristic branching tree appearance. Polyps in PJS can displace the underlying epithelium and appear as a pseudocarcinomatous invasion of the muscularis mucosa. In this case, Even though histology examination indicates there is no sign of malignancy, we found a slightly increased in blood CEA level. We should do serial evaluation of this patient to find the malignancy in the early stage.

All the above data can conclude that we face the patient with Peutz Jegher Syndrome. Based on the anamnesis, physical finding, endoscopy and colonoscopy examination, and histopathology examination, all the requirement of definite diagnosis of PJS has been found in this patient.

In term of management of PJS, in the literature stated that if polyps are found during an upper endoscope or a colonoscopy, they should be removed. Alternatively, the doctor may recommend a laparotomy, a surgical procedure in which an incision is made in the belly or pelvic region and polyps are removed.[11] If cancer is found during a test, the patient and doctor will discuss the best course of action, which may include more extensive surgery and, perhaps, additional treatment such as chemotherapy.

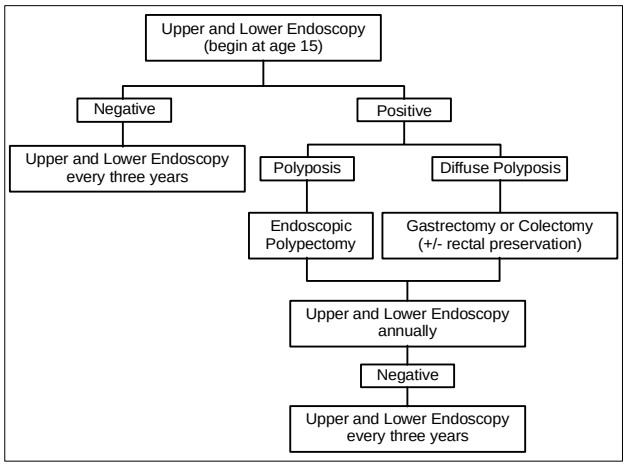

Figure 2. Proposed algorithm for endoscopic surveillance and treatment of first degree relative.[11]

In this case, since there are many polyps along her GI tract system from esophagus to colon descendent, it affects the management more difficult. It is not realistic to do polypectomy by endoscopic to all the polyps. Based on coordination with Department of Digestive Surgery, it was decided to conduct total colectomy. In other literature also stated to conduct colectomy to cure the diffuse polyposis.

Previous studies has reported that PJS is often accompanied with a higher incidence of other malignancies, such as breast cancer, adenoma maligna of the uterine cervix and ovarian tumors, and the incidence of cancer among the patient suffering with PJS has been estimated to be 15-fold higher than the incidence of cancer in the general population. In other literature stated that individuals with Peutz-Jeghers syndrome are at increased risk for intestinal and extra-intestinal malignancies. In a large collected series, Giardiello et al,[10] observed a 93% cumulative lifetime risk of cancer (see table 1). In this case, result of histology examination indicates the growth of polyp and smooth muscle with tree structure from the muscular mucosa. The conclusion of histology finding is Peutz Jeghers polyp. There is no sign of malignancy.

Table 1. Relative risk for cancer in 210 individuals with Peutz-Jeghers syndrome.[10]

Type of cancer	Relative risk
All	15
Esophagus	57
Stomach	213
Small intestine	520
Large bowel	84
Pancreas	132
Lung	17
Breast	15
Ovary	27
Endometrial	16

As consequences of polyp, the patient had a lot of problems such as difficulty to eat, hypoalbuminemia, anemia, electrolytes imbalance, leukocytosis, and underweight. Basically the above matters as a consequences happen due to the polyp itself.

GI complications are the most common symptoms of this disease. Bleeding that may or may not be seen in the stool, diarrhea, constipation, crampy pain and/or bloating in the belly, weight loss, and lack of energy, anemia (low red blood cell count), nausea, and precocious (early) puberty can occur with PJS. Sometimes, children and adults may develop sudden, severe abdominal pain caused by polyps blocking the intestine called intussusceptions. In this case, the patient seeks medication due to gastrointestinal problem such as difficulty to eat, abdominal pain, nausea and vomiting. These symptoms happen as a consequence of the underlying disease that is polyp along her GI tract system from esophagus to colon descendent.

During her hospitalization, her condition and performance was getting worse. It is described in her laboratory parameter. Her hemoglobin was decreased. Electrolytes imbalance was frequently occurred. Albumin level was decreased significantly, and her body mass index was decreased from 15.6 to 13.67 at the end of her medication.

We tried to give supportive therapy to reduce and minimize the complication. We gave her the nutrition via oral and supported by partial parenteral nutrition (triofusin E 1,000 twice a day and combine with amino acid, lipid and the vitamin). We also replaced the electrolytes imbalance with potassium infusion and or tablets, infusion of NaCl 3% and or NaCl 9%. To reduce the symptoms we also gave anti emetic, anti spasmodic, and analgesic if necessary.

After 1 month hospitalization, the patient and family face the financial problem. It caused the treatment was ineffective, thus, the patient's condition was getting worse.

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