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Peutz-Jeghers Syndrome (PJS) with anemia, ileo-ileal intussusception and frequent recurrence of polyps: a case report and a literature review

Peutz-Jeghers syndrome (PJS) is genetically conditioned polyposis syndrome, an autosomal dominant disorder. Even 50% of cases are considered to be *de novo* mutations (11). For the first time it was described by Peutz in 1921 and then also by Jeghers in 1949. However, the first observations of patients with mucocutaneous pigmentation and anemia were made by J. R. T. Conner in 1895 (13).

Characteristic of this disease is germinal mutation of the gene serine-threonine kinase 11 STK11 (called LKB1) located on band 19 (19p13.3). It is observed in more than 50% of patients (5). The incidence of PJS is estimated at 1/8,300 to 1/29,000 live births and depends on the examined population (4). STK 11 is a protein which plays a role in the regulation of apoptosis pathway and its deficiency can result as a formation of hamartomas or neoplasms. Current findings sugest that there is also another mutation which has not been localized yet can be responsible for symptoms of the disease.

Penetration of this gene is variable, which causes a variety of phenotype symptoms. PJS is manifested by the presence of a changeable number of hamartomatous polyps in small and large intestines and stomach, mucocutaneous melanocytic macules in the oral and perianal area. Typical skin lesions appear in 93% of patients in childhood, in puberty period and later they often fade (13). Dimensions of the polyps can vary from a few milimeters to a few centimeters and they can be localized in the whole alimentary tract except for the oesophagus (17). The first symptoms of the illness usually appear in patients before 20 years of age (18). The most common complications are: obstruction, intussusception, adhesiones caused by frequent surgical intervention and the development of cancer.

CASE REPORT

A 17-year-old female patient M.M. was admitted to the 2nd Department of General Surgery Medical University of Lublin in July 2004. For the first time she was operated on multiple polyposis at the age of 3 (1990 – partial resection of the transverse colon and appendectomy), again at the age of 9 (1996 – partial resection of ileum) and 13 (2000 – second resection of ileum). She was admitted in order to be diagnosed.

Visible small brown spots and acne on the skin of the face were observed. There were no lesions on the skin of palms and feet. The patient has got two years older sister and 10 years younger brother, both of them similarly to their parents are free of symptoms and healthy.

The patient was anemic (RBC 3.85 M/ul, HGB 6.65g/dl, HCT 22.7%, MCV 58.9fl, MCH 17.3 pg MCHC 29.3 g/dl, RDW 21.2%). There was a gastrointestinal passage performed and a big amount of polyps in stomach, duodenum (Fig. 1, Fig. 2), and small bowel (Fig. 3) were found. Also colonoscopy was performed and it was ascertained that there were large pedunculated polyps in sigmoid and numerous polyps in rectum. All polyps were removed. During the second colonoscopy there was performed polypectomy of ileal polyp, two polyps of transverse colon and one of rectum. A big (3 cm) polyp in anus was found and also excised. In all cases histopathological diagnosis was *Adenoma tubulovillosum*. Because of the low level of blood cell count the patient was administered 2 units of erythrocyte mass.

Fig. 1. Polyps in stomach and duodenum

The patient was hospitalized for the next time in September 2005 for the evaluation of the condition of her alimentary tract. Parameters of her blood cell count were still below the mark (RBC 3.77M/ul, HGB 6.17g/dl, HCT 22.0%, MCV 58.4 fl, MCH 16.4 pg MCHC 28.0 g/dl, RDW 23.4%). She had thrombocytemia (PLT 425 K/ul) and also other parameters were deviated: GGTP 7 IU/l, BILI-T 1.17 mg/dl, BILI-D 0.49 mg/dl, protein 5.6 g/dl. The patient was given 2 units of erythrocyte mass and 2 units of fresh frozen plasma. During the colonoscopy 2 polyps of pepper grain dimension were removed from the transverse colon and 5 polyps of the same size from rectum. She was also subjected esophagogastroduodoscopy with polypectomy – in antrum (4 polyps, dimension about 6 mm), body (4 polyps, dimension 8 and 9 mm) and fundus of the stomach (numerous polyps). The outcome of the histopathological examination was *Polypus retentialis ventriculi, Inflamatio chronica, Stomatitis minoris gradus* and *Gastritis chronica exacerbata et polypus hyperplasticus.*

Fig. 2. Polyps in duodenal bulb and descending part of duodenum

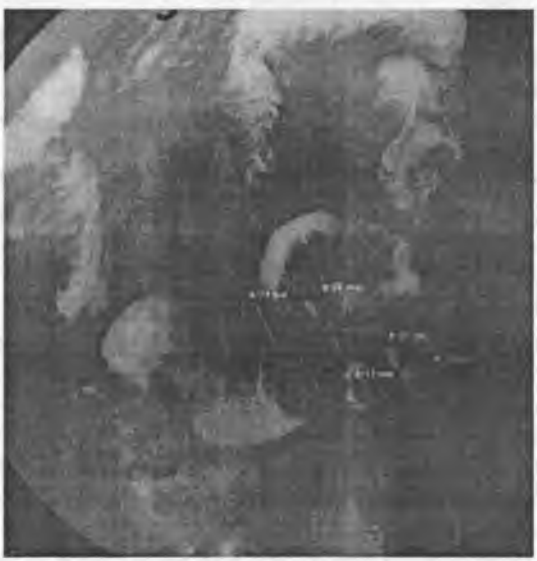

Fig. 3. Numerous polyps in ileum

6 days after the patient had left the hospital she re-entered with subileus symptoms lasting for 4 days (retention of gases, coprostasis, vomits) and body mass loss in anamnesis – about 3 kg (BMI 18,49). In the time of admission she had positive peritoneal signs. There were found the following deviations in laboratory tests: HGB 8.37 g/dl, HCT 27.8%, MCV 65.9 fl, MCH 19.8 pg MCHC 30.1 g/dl, RDW 36.7%, PLT 567 K/ul, uric acid 2.09 mg/dl, iron 12 ug/dl, creatinine 0.36 mg/dl, protein 5.26 g/dl, albumin 3.57 g/dl. Considering that in spite of the medical therapy the symptoms

were maintaining the patient was qualified to emergency surgical treatment. There was found total ileus caused by intussusception of 70 cm of the intestine. The front of the intussusception were large polyps, which closed the intestinal lumen. Partial resection of the ischaemic intestine and the side-to-side anasthomosis were made. The end of the intussusception was situated 20 cm from the Treitz ligament. During the operation also the previously exteriorized cecostomy was closed. The material (about 70 cm of the small bowel with multiple polyposus lesions of pepper grain dimension up to 2.5 cm) was sent to the histopathological laboratory, which claimed: *Polypus intestini tenuis in statu imbibitionis haemorrhagica, Adenoma tubulovillosum, Polypositas intestini tenuis.* During the postoperative period the patient was still anemic (RBC 3.99 M/ul, HGB 9.0 g/dl, HCT 18.20%, MCV 71 fl, MCH 22.6 pg MCHC 32 g/dl, RDW 27.8%). She had slight leucocytosis (WBC 10.6 K/ul) and thrombocytemia (PLT 469 K/ul). The deviated parameters in laboratory tests were: uric acid 1.11 mg/dl, creatinin 0.51 mg/dl, protein 4.23 g/dl. She was administered 2 units of plasma and albumins were added to the treatment. The blood cell count gave in better but still it was below normal. During 3 day 3 after the operation the patient claimed about muscular contractions most significant in the neck muscles. There were no pathologies in the electrolyte equilibrium (Ca 2.1 mmol/l, Na 136 mmol/l, K 3.54 mmol/l). She was given $MgSO_4$, KCl, $CaCl_2$ and Midanium, after this the symptoms withdrew. The patient was discharged from the hospital in good general condition.

Since September 2005 the patient has been staying in good health, she has not been hospitalized and she has no ailments. She is still followed-up in our clinic.

DISCUSSION

In Peutz-Jeghers syndrome polyps are usually localized in small bowel (96%), transverse colon (27%), rectum (24%) and stomach (24%) (2). The size of the lesions can vary giving complications like ulcerations, bleedings, obstructions and intussusceptions of the intestines. Bleeding from the alimentary tract often causes iron deficiency anemia (16) like in our patient. Anemia is caused by occluded or overt blood loss to the lumen of the alimentary tract, which is often noticed as one of the initial symptoms (17). Also Seenath in one of two observed patients found reduction of the hemoglobin and hematocrite (14). During every hospitalization our patient was anemic, and many times she was treated with haemotherapy.

Polyps in Peutz-Jeghers syndrome usually are not neoplastic but their huge size can cause intussusception and ileus of the alimentary tract, which is often the first symptom of the disease. In Taguchi's analysis all cases of PJS manifestated intussusception and all the patients underwent the surgical treatment (17).

According to Hinds' study, 30% of patients require laparotomy in the first decade of their life (10). According to the literature there were cases when 12 patients underwent 32 operations altogether and more than 70 endoscopic polypectomies (3). Also Taguchi et al. have made the observations in which 100% of the patients underwent more than one surgical intervention (17). Homan's study shows that the majority of the patients suffer from recurrent episodes of intussusception induced by polyps which require laparotomy. Half of the patients undergo two or more operations (11). A case reported by Akimaru also required second surgical intervention and the symptoms of ileus were accompanied by anemia and hyponatraemia (1).

The patient M. M. was operated on 4 times between the 3rd and 18th year of life and she underwent a large amount of endoscopic polypectomies.

According to Sokmen, every patient with ileus and anemia should be investigated in case of polyps and mucocutaneous lesions characteristic of PJS. The patients suffering from multiple

polyposis of the alimentary tract should be carefully controlled in order to decrease the number of surgical interventions, because they can cause adhesions and symptoms of the short bowel (16).

PJS is considered to be a cancer predisposing syndrome. The risk of dying from a gastrointestinal cancer in patients with PJS is 13 timer greater (11). Some authors consider that there is a characteristic evolution: hamartoma–adenoma–carcinoma of the polyps in stomach, small and large intestine (9). The patients with PJS are more subjected to suffer from neoplasms localized beside the alimentary tract (breast, uterine cervix, ovary, testis, gallbladder, pancreas, biliary tree, thyroid, skin). The risk of incidence of malignancy in patients with PJS is even 20 times greater than in general population (19).

Seung-Hun reports a case of a 41-year-old female patient who was diagnosed not only a PJS but also a breast cancer, uterine cervix adenocarcinoma, mucinous tumor of ovary that had borderline malignancy and numerous metastases in the lymph nodes of pelvis (15).

Controversial is the topic of formation of neoplasms on the basis of polyps. Bartholomew claims that even 20% of the patients would fall ill from the cancer of the alimentary tract (2), instead of the Dozois observation where only in 11 out of 321 patients the cancer was diagnosed: 4 cases of stomach cancer, 3 – duodenum, 1 – ileum, 3 – large bowel. The investigators also noticed that there is no connection between localization of the malignant tumor and polyps (8). Also Linos did not ascertain tendency to cancer growth on the basis of polyps – anyone of his 21 observed patients with PJS was diagnosed for intestine cancer (12). However, there are publications that in the group of patients older that 30 years death was attributed to malignancy in 60% of cases (7).

Patients with PJS should be in medical care and perform periodic follow-up examinations such as blood cell count determination, gastrointestinal passage, colonoscopy, esophagogastroduodenoscopy in order to avoid complications of the disease.

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SUMMARY

Peutz-Jeghers syndrome (PJS) is a genetically conditioned polyposis syndrome, an autosomal dominant disorder. The incidence of PJS is estimated at 1/8,300 to 1/29,000 live births and depends on the examined population. PJS is manifested by the presence of changeable number of hamartomatous polyps in small and large intestines and stomach, mucocutaneous melanocytic macules in the oral and perianal area. The most common complications are: obstruction, intussusception, adhesiones caused by frequent surgical intervention and development of cancer. A 17-year-old female patient was admitted to the 2nd Department of General Surgery, Medical University of Lublin in July 2004. Visible small brown spots and acne on the skin of the face were observed. The patient was anemic, she had gastrointestinal passage and twice colonoscopy performed and there were found numerous polyps in stomach, small and large bowel. All polyps were removed. The patient was hospitalized for the next time in September 2005. During the colonoscopy a big amount of polyps was removed. 6 days after the patient had left the hospital she re-entered with subileus symptoms lasting for 4 days. The patient was qualified to emergency surgical treatment. There was found total ileus caused by intussusception. During the postoperative period the patient was still anemic. Since September 2005 the patient has been staying in good health, she has not been hospitalized and she has no ailments. She is still followed-up in our clinic.

Zespół Peutz-Jeghersa (PJS) z ciężką anemią, wgłobieniem krętniczo-krętniczym oraz częstymi nawrotami polipów: opis przypadku i przegląd literatury

Zespół Peutz-Jeghersa (PJS) jest genetycznie uwarunkowanym zespołem polipowatości, dziedziczącym się w sposób autosomalny dominujący. Częstość występowania PJS szacowana jest na 1/8300 do 1/29000 żywych urodzeń w zależności od badanej populacji. Zespół ten manifestuje

się obecnością zmiennej liczby polipów hamartomatycznych w jelicie cienkim i grubym oraz w żołądku, przebarwieniami błon śluzowych i skóry okolicy jamy ustnej i odbytu. Wśród najczęściej występujących powikłań wymieniane są: niedrożność jelit, wgłobienie, zrosty, powstające na skutek częstych interwencji chirurgicznych, a także rozwój raka. 17-letnia pacjentka została przyjęta do II Katedry i Kliniki Chirurgii Ogólnej AM im. Prof. Feliksa Skubiszewskiego w Lublinie w lipcu 2004. Na skórze twarzy widoczne były niewielkie brązowe plamki oraz trądzik. U pacjentki rozpoznano niedokrwistość, wykonano pasaż przewodu pokarmowego oraz dwukrotną kolonoskopię, w trakcie których stwierdzono liczne polipy w żołądku, jelicie cienkim i grubym. Wszystkie polipy usunięto. Kolejny raz pacjentkę hospitalizowano we wrześniu 2005 roku. Podczas kolonoskopii usunięto liczne polipy. W sześć dni po opuszczeniu szpitala pacjentka zgłosiła się ponownie z utrzymującymi się od czterech dni objawami subileusowymi. Chorą zakwalifikowano do zabiegu operacyjnego w trybie doraźnym. Stwierdzono niedrożność jelita cienkiego spowodowaną wgłobieniem. W okresie pooperacyjnym morfologia krwi nadal utrzymywała się na niskim poziomie. Od września 2005 roku pacjentka czuje się dobrze, nie była hospitalizowana, nie odczuwa żadnych dolegliwości. Nadal pozostaje pod kontrolą naszej kliniki.