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Case Report

Multiple genital tract tumors and mucinous adenocarcinoma of colon in a woman with Peutz-Jeghers syndrome: a case report and review of literatures

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Abstract: We report a very rare case of Peutz-Jeghers syndrome (PJS) composed of multiple genital tract tumors and mucinous adenocarcinoma. A 46-year-old woman presented to our hospital with lower abdominal pain resulting from PJS involves sex cord tumor with annular tubules (SCTAT), ovarian mucinous tumor, ovarian serous tumor, mucinous adenocarcinoma of colon. The CEA concentration is high before surgery, and decreases after the surgery and subsequent chemoradiotherapy. This case demonstrates a classic clinical presentation of a patient with PJS. PJS patients have increased risk of malignancy and early detection and regular surveillance of the high-risk patients with PJS is crucial. Surgery may be required for obstructive gastrointestinal lesions as well as those exhibiting malignant degeneration.

Keywords: PJS, SCTAT, ovarian mucinous cystadenoma, ovarian serous cystadenoma, mucinous adenocarcinoma of colon

Introduction

Peutz-Jeghers syndrome (PJS) is an inherited cancer syndrome characterized by mucocutaneous melanin pigmentation and hamartomatous. Gastrointestinal polyps can result in chronic bleeding and anemia and also cause recurrent obstruction and intussusception requiring repeated laparotomy and bowel resection. Mucocutaneous hyperpigmentation presents as dark blue to dark brown macules around the mouth, eyes, and nostrils, and on the fingers [1].

The incidence of PJS is estimated to be between 1 in 50,000 to 1 in 200,000 live births, and predisposition to benign and malignant tumors of the stomach, small intestine, pancreas, cervix, breast and ovaries. Polyps are the most common in the small intestine, but may occur anywhere in and outside the gastrointestinal tract [1-3]. We present the unusual case of a 46-year-old woman with PJS who had a sex cord tumor with annular tubules, ovarian mucinous tumor, ovarian serous tumor and mucinous adenocarcinoma of colon.

Case report

The patient was 46-year-old, she had complained of lower abdominal pain for 2 weeks, and visited our hospital for a close evaluation. Since early childhood, she was noted to have hyperpigmented lesions over the perioral region (**Figure 1A**) and fingers (**Figure 1B**), and a history of colon intussusception due to hamartomatous polyps that was treated by partial colectomy for twice when she was 15 and 29 years old. Since his partial colectomy surgery, the patient had been on a three-year colonoscopic surveillance schedule for his remaining colon. He was treated by hysterectomy for leiomyomata at 36 years old. The patient's father also has perioral pigmentation, and died for intestinal intussusception at years old. Lower endoscopy confirmed numerous 0.2-2.0 cm polyps, but

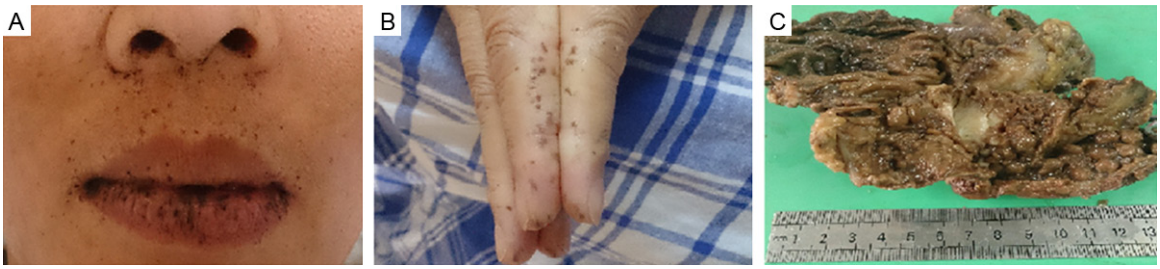

Figure 1. Pigmentation around her lips (A) and fingers (B). Surgical specimen from colon resection with the lumen opened displaying the numerous polyps and mass under the mucosa (C).

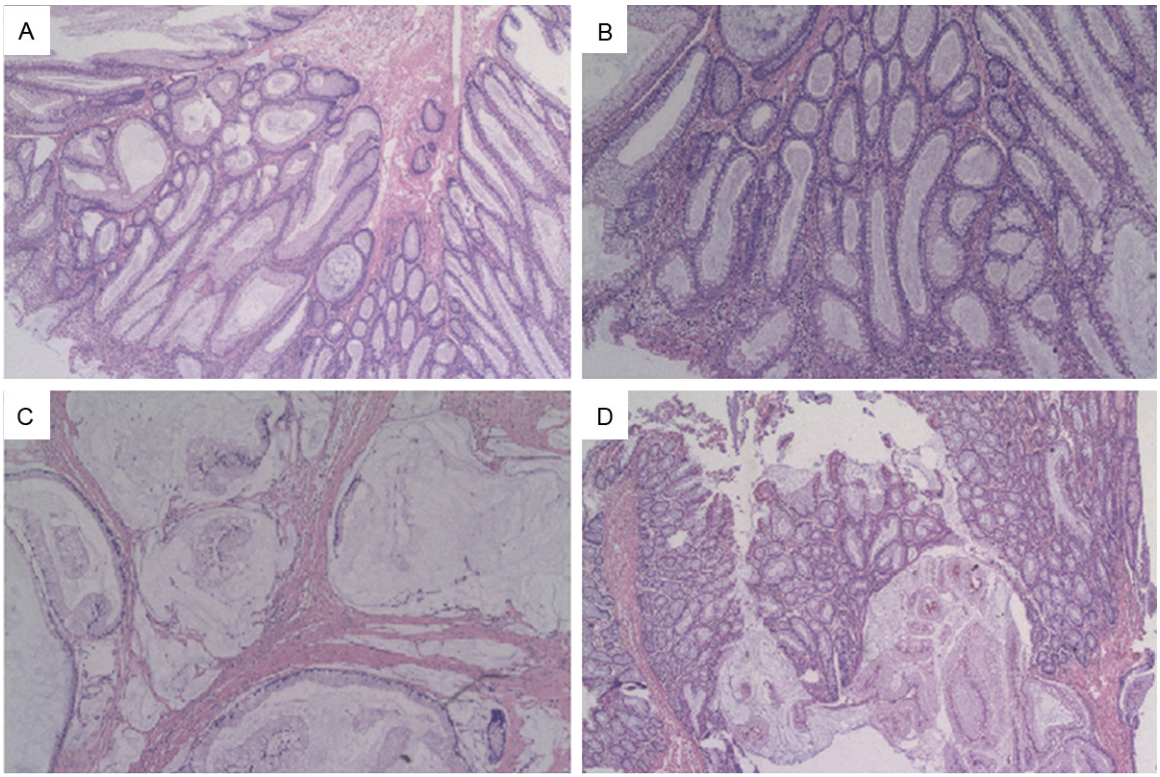

Figure 2. The cyst's walls are lined with a one-layered mucin producing cubic to cylindrical epithelium, which is similar to an endocervical epithelium (A, 50×). Prominence of the ciliated cell, producing small fan-like projections (B, 50×). Scattered small and calcified nests of sex cord tumors with annular tubules, and the sex cord element composed of multiple hyaline materials surrounded by clear cells in the cortex of the left (C, 100×) and right (D, 100×) cyst.

found no mass in the lumen of colon. The Pap smear showed normal cells. Pelvic ultrasound showed a cyst 15.1 × 13.8 × 12.6 cm at the left adnexal region, a cyst 4.7 × 4.4 × 4.1 cm at the right adnexal region and a mass 5.9 × 5.0 × 6.2 at the pelvic. The CEA levels were 53.8 ng/ml. A subsequent bilateral salpingo-oophorectomy was performed and a 25-cm large intestine with the mass and numerous 0.2-2.0 cm polyps removed surgically Macroscopically, the left and right ovary were cystic, 9.0 × 9.0 × 8.0 cm and 4.0 × 3.0 × 3.0 cm, respectively. Both oviducts were unremarkable on gross examination. There was numerous 0.2-1.5 cm polyps in the lumen and a pale yellow-tan and slimy mass under the polyps measuring 6 × 5 × 4 cm in the wall of the colon (**Figure 1C**).

Histologically, the left and right ovary showed benign mucinous cystadenoma (**Figure 2A**) and benign serouscystadenoma (**Figure 2B**), respectively. Additionally, there were scattered

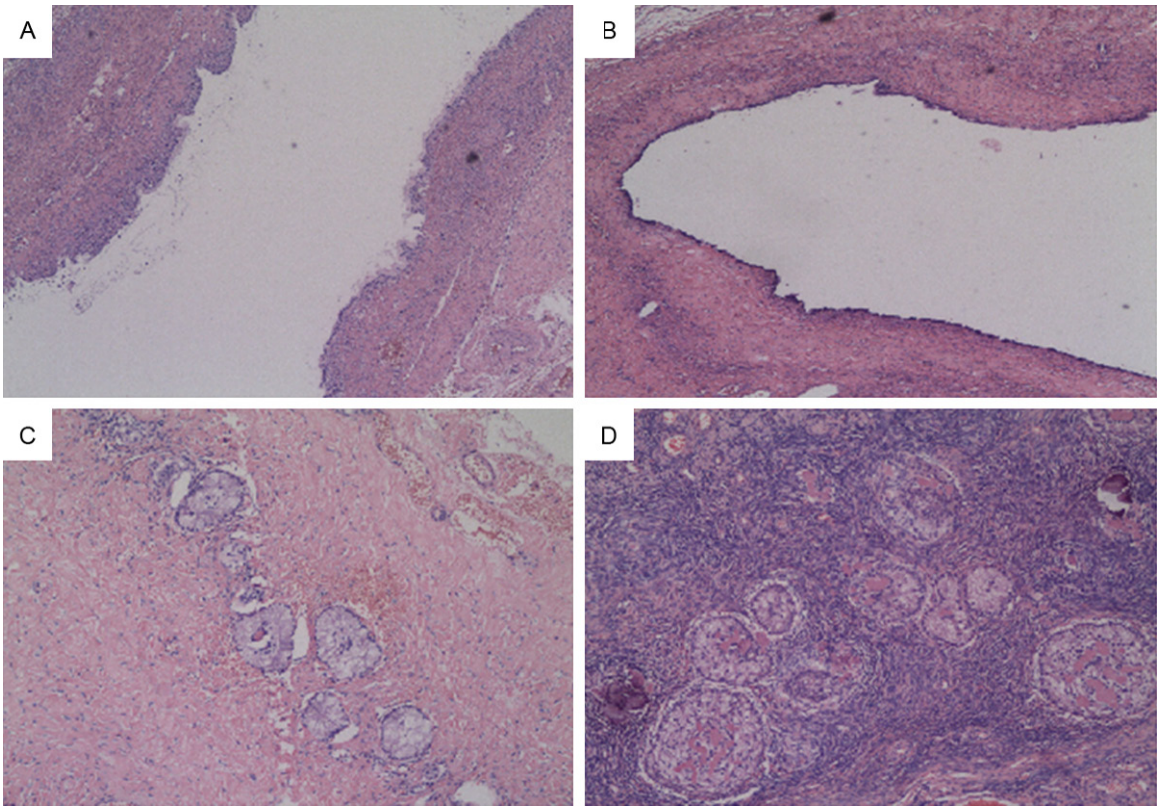

Figure 3. Histologically, hamartomatous polyps showing arborizing musculature and hyperplastic glands without dysplasia (A, 25×). Tubular adenomas shows a slightly modified mucosal architccture,glands are lined by enlarged columunar cells with mild dysplasia (B, 50×). The architecture of the mass varies with the amounts of mucin produced, cellular differentiation and prominence of stroma. Epithelium formed by tall columnar cells with basally located nuclei and clear cytoplasm (C, 50×, D, 25×).

small nests of sex cord tumors with annular tubules, some of which were calcified, in the cortex and septa of the cysts from the both the ovaries (**Figure 2C**, **2D**). Polyps from the colon revealed mild acute inflammation superimposed on architectural disorganization without dysplasia, suggestive of P-J polyps (**Figure 3A**), there are some adenomas with mild dysplasia in the colon (**Figure 3B**). The mass of the colon showed a deeply infiltrative, but well differentiated mucinous adenocarcinoma, which have penetrated through to the outer wall of the colon. The epithelial cells that lined the mucinous glands were 2 to 3 times taller than conventional mucinous cells and the cytoplasm appeared pale and homogenous without distinct goblet cell vacuolation (**Figure 3C**, **3D**).

By immunohistochemical methods, the tumor cells of mucinous tumor were strongly positive for cytokeratin 7 (CK7); negative for CK20 and CDX2 (**Figure 4A-C**). While the tumor cells of the colon were strongly positive for CK20 and CDX2; negative for CK7 (**Figure 4D-F**). The CK7+/CK20- and CK7-/CK20+ pattern is typical of epithelial ovarian tumors and intestinal tumors, respectively. CDX2, a critical nuclear transcription factor for intestinal development, is expressed in intestinal epithelium and adenocarcinomas. The pattern of this case indicated that both the mucinous tumor of left ovary and mucinous adenocarcinoma of the colon are primary tumors. The CEA concentration is high (53.8 ng/ml) before surgery, and decreases after the surgery and subsequent chemoradiotherapy.

Discussion

PJS is an autosomal dominant disorder characterized by the development of hamartomatous polyposis in the gastrointestinal tract from the stomach to the large intestine and melanin-pigmented macules on the skin mucosa, includ-

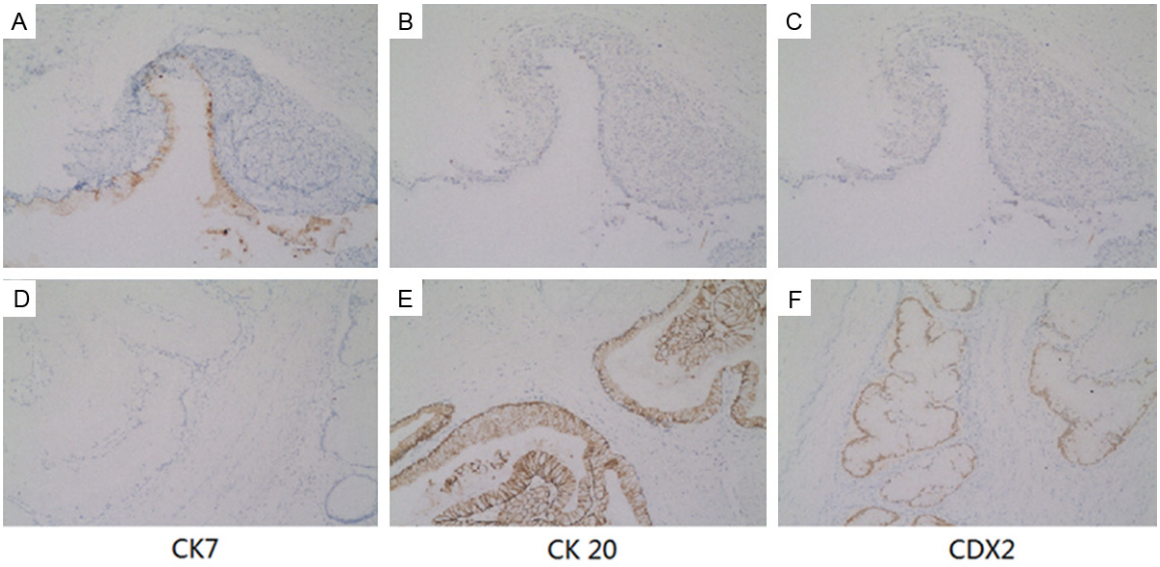

Figure 4. Immunostain for CK7, CK20 and CDX2 of ovarian mucinous cystadenoma (A, 100×, B, 100×, C, 100×) and mass of colon (D, 100×, E, 100×, F, 100×).

ing the oral mucosa, lips, nasal wings and interdigits. The diagnostic criteria for PJS include the presence of small bowel hamartomatous polyps, characteristic mucocutaneous pigmentation, and family history. Two of these criteria must be met in order to make a clinical diagnosis of PJS [1].

The responsible gene is a tumor suppressor, STK11/LKB1, on chromosome 19p13.3. PJS complicates with benign and malignant tumors in various organs.

A significantly increased risk of both gastrointestinal and nongastrointestinal malignancies has been demonstrated for patients with PJS. A report of 133 Dutch PJS patients from 54 families [2], a meta-analysis has been performed by Giardiello et al. [3], assessing 210 patients from six studies and Hearle et al. [4] examined the incidence of cancer in 419 individuals with PJS, 297 of which had documented STK11 mutations. These three articles offer the most comprehensive data for cancer risk, demonstrate that PJS patients carry a markedly elevated cancer risk in PJS patients, and higher in females than in males, but independent of family history and STK11 mutation status [2-4].

The incidence of malignant gastrointestinal tumors is highest in the large intestine, followed by the stomach, small intestine, duodenum and pancreas, and the incidence of malignant tumors in other organs is highest in the uterine cervix, followed by the ovary and lung [2-4]. In this case, the mucinous adenocarcinoma is well differentiated, and the glands lined by tall columnar cells in comparison with conventional mucinous glands with goblet cells. So, we can not exclude the possibility of metastasis, such as cervical malignancy minimal deviation adenocarcinoma (MDA) and pancreatic cancer. But the CK7-/CK20+ pattern and expression of the CDX2 are highly specific of colorectal origin.

The exact mechanism of carcinogenesis in PJS remains to be established. Two possible modes of cancer development have been proposed in PJS: de novo carcinogenesis and a hamartoma-adenoma-carcinoma sequence [2]. In this case, P-J polyps had hyperplastic glands and the epithelial misplacement was florid and extended into the serosa. Chains or irregular cell clusters floating freely in mucinous lakes. Thus, the carcinomas may occur in contiguity with p-j polyps. There are some tubular adenomas with dysplasia in the colon, so the colon cancer might have developed through hamartoma-adenoma-carcinoma sequence.

In gynecology, there has been a particular focus on complications of PJS with SCTAT, epithelial ovarian tumors and minimal deviation adenocarcinoma (MDA), which are rare diseases. Approximately 36% of patients with SCTAT

are complicated with PJS. Scully [5] et al. proposed the hypothesis that SCTAT occurred in ovarian granulosa cells and grew in a pattern specific to sertoli cells. An alternative hypothesis suggests that SCTAT consists of sex cord-derived immature cells with the potential for differentiating to granulosa and sertoli cells.

The clinical manifestations of SCTAT differ between patients with and without PJS. Young [6] et al. conducted a comparative study in 21 SCTAT patients with PJS and 47 SCTAT patients without PJS, and found that SCTAT complicated with PJS is commonly multifocal, bilateral, small (detected microscopically), and calcified in >50% of cases, and has a good prognosis. In contrast, SCTAT without PJS is unilateral, large (palpable), calcified in 12% of cases, and has a poor prognosis in 20%. Song [7] et al. described the case of a 41-year-old woman with PJS who had multiple genital tract tumors and breast cancer. In our case, the woman had SCTAT, epithelial ovarian tumors and colon cancer with PJS.

Mucinous and serous epithelial ovarian tumors are also seen with increased frequency in patients with PJS and benign lesions that develop into tumors with mucinous to serous ratios of 8:1 [8]. Serous cystadenoma of one ovarian and mucinous cystadenoma of the other one with PJS in a patient is very rare and interesting. Three cases of serous tumor of the ovary associated with PJS have been published [7, 9, 10]. Mucinous ovarian tumors with PJS can be benign, borderline, malignant [11-15], one of them was diagnosed as ovarian mixed serous and mucinous borderline tumor, three ovarian mucinous adenocarcinoma were metastatic from the cervix, and in three cases the ovaries contained both primary and metastatic tumors. In our case, the mucinous tumor of right ovary is primary tumor for the CK7+/CK20- pattern.

Conclusion

The case with the multiple genital tract tumors and mucinous adenocarcinoma of colon in a person with PJS has not been reported to date. This case demonstrates a classic clinical presentation of a patient with PJS. PJS patients have increased risk of malignancy and early detection and regular surveillance of the high-risk patients with PJS is crucial. Surgery may be required for obstructive gastrointestinal lesions as well as those exhibiting malignant degeneration.

Disclosure of conflict of interest

None.

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