

CLINICAL CASE

Peutz-Jeghers syndrome combined with breast cancer, cervical carcinoma and ovarian gonadoblastoma: a case report

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Summary

Peutz-Jeghers syndrome (PJS) is a rare autosomal dominant condition characterized by gastrointestinal polyps, mucocutaneous pigmentation and an increased risk for cancer. In this report, a 34-year-old woman with

PJS associated with a rare ovarian tumor (gonadoblastoma) and synchronous breast and cervical carcinoma is discussed and the relevant literature is reviewed.

Key words: breast cancer, cervical carcinoma, gonadoblastoma, Peutz-Jeghers syndrome

Introduction

PJS is a rare hereditary disease characterized by melanocytic macules of the lips, gastrointestinal hamartomatous polyps and an increased risk for many types of cancer. Gastrointestinal polyps manifest themselves during puberty and adolescence and, generally, they are present in the small intestine [1]. Scully et al. first described in the 1970s that the most frequent malignancy which accompanies PJS is bilateral benign ovarian sex cord tumors with annular tubules (SCTAT) [2]. However, ovarian cystadenomas, granulosa cell tumors, germ cell tumors, serous and mucinous borderline tumors of the ovaries are rarely reported in the literature [3,4].

The overall incidence of carcinoma in these patients varies from 20-50%, and is generally seen with

breast, pancreas, colon and gynecological cancers [1,5,6]. The loss of function of SKT11/LKB1 tumor suppressor gene is responsible in the etiology of this syndrome [7]. PJS is now recognized as a cancer predisposition syndrome.

In this report, we describe a 34-year-old female patient with PJS, ovarian gonadoblastoma and synchronous multiple cancers.

Case presentation

A 34-year-old virgo, mentally retarded woman with PJS was admitted to the Gynecological Clinic complaining of menometrorrhagia. In the past she was operated twice for ileus due to intestinal polyps when she was 8 and 18 years old, and once for ovarian gonadoblastoma when she was 27 years old (Figure 1). Because she was virgo, a rectal digital examination was performed. An abdominal ultrasonography (USG) revealed a heterogeneous hypoechogenic mass measuring 5.5 cm in diameter, suspected to be myomatous, situated in the fundus of the uterus. Because she was previously diagnosed to have PJS, breast examination was performed and a solid, semi-mobile mass was found in the lower-outer quadrant on her left breast. On magnetic resonance imaging (MRI), an apparently malignant lesion 2 cm in diameter was detected. Quadrantectomy with axillary lymph node dissection was performed and histo-

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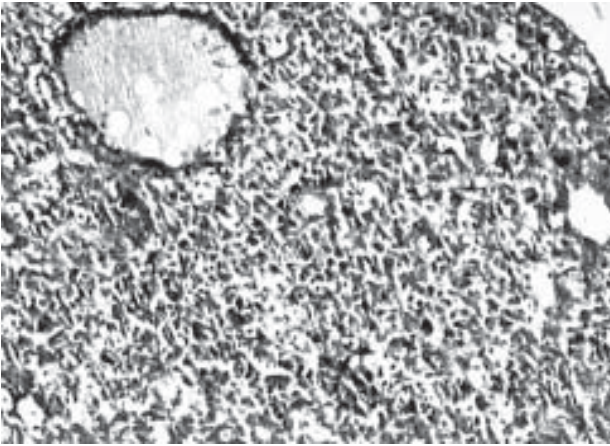


Figure 1. Gonadoblastoma. The sex cord derivatives form a coronal pattern along the periphery of the nests and also surround small round spaces containing hyaline material. A mixture of cells is present in the centre of the nests (H&E $\times 200$).

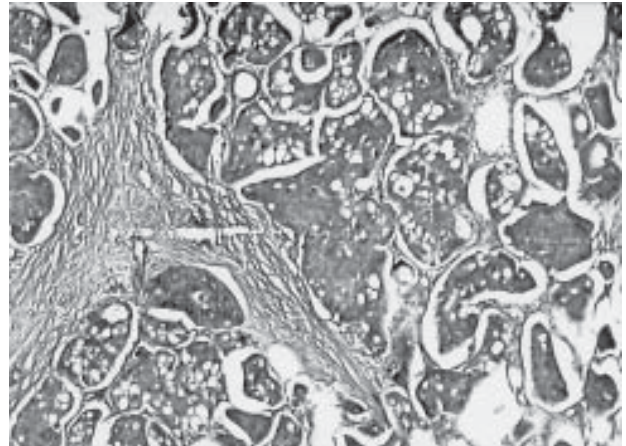


Figure 2. Invasive papillary carcinoma of the breast. Papillary structure lined by epithelial columnar cells (H&E $\times 100$).

pathological examination showed moderately differentiated invasive papillary adenocarcinoma (Figure 2), metastasis with capsular invasion in 1 of 13 dissected axillary lymph nodes, and positive hormone receptors. Mastectomy was performed further due to positive surgical margins. The pathological stage was IIB and her BRCA-1 was negative. Meanwhile, because of continuous vaginal bleeding, an abdominal USG was performed and a hypoechogenic 6 \times 7 cm solid lesion confined to the right anterolateral part of the uterus and metastatic right external iliac lymphadenopathy (LAP) 2 cm in diameter were detected. She was referred to the Oncology Clinic

with a diagnosis of breast cancer and myoma uteri. The patient received 6 cycles of FAC chemotherapy consisting of 5-fluorouracil (500 mg/m², day 1), adriamycin (50 mg/m², day 1) and cyclophosphamide (500 mg/m², day 1), given every 3 weeks. She had severe vaginal bleeding during chemotherapy, so an abdominal and pelvic MRI was planned. A 6 \times 7 \times 9 cm mass originating from the cervix, invading the rectum and bilateral parametria, lesions in both ovaries which had similar signal characteristics with the cervical mass and, also a metastatic right external iliac LAP 2 cm in diameter were detected (Figure 3A and 3B). The tumor marker levels were as



Figure 3. (A) Sagittal T2-weighted image shows a bulky cervical mass, 7 \times 9 cm in diameter with heterogeneous signal intensity. (B) Coronal T2-weighted image shows loss of fat plane between mass and rectum, metastatic right external iliac lymphadenopathy of 2 cm diameter, and also similar signal intensity lesions in both ovaries.

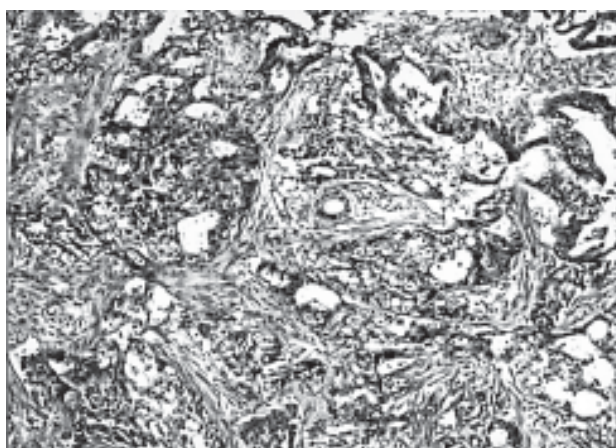


Figure 4. Mucinous adenocarcinoma of the cervix. Well differentiated tumor with desmoplasia and irregular gland formation (H&E $\times 100$).

follows: CEA: 134 ng/ml (normal range 0-2.5 ng/ml), CA12-5: 657 IU/ml (normal range 1.9-16.3 IU/ml). A cervical punch biopsy revealed mucinous adenocarcinoma of the cervix with positive immunostaining for CEA, Alcian blue and acidic mucin (Figure 4). She was considered as FIGO IVA cervical cancer, and was treated by concomitant chemoradiotherapy with cisplatin 40 mg/m²/weekly and external radiotherapy with 70.4 Gy in 38 fractions. By the end of the therapy, a 75% disease regression was detected in repeat MRI. Two weeks after the completion of treatment the patient was admitted to the emergency room complaining of dyspnea and abdominal distention. An abdominal USG revealed metastases in the liver and massive ascites. The patient died soon, due to rapid disease progression. Postmortem examination was not possible due to her family's disagreement.

Discussion

Literature reports show that the polyps accompanying PJS generally become symptomatic in very young age and these patients undergo repeated operations due to ileal obstructions [1]. Our patient was also operated twice when she was 8 and 18 years old because of ileus due to intestinal polyps.

PJS is generally found together with SCTAT. This association was first described by Scully et al. in 1970 [2], and was also shown by many other case reports in the literature [1]. However, some benign (other than SCTAT), or malignant ovarian malignancies accompanying PJS were also defined [3,4]. Gonadoblasto-

ma is one of the mixed sex cord stromal and germ cell tumors of the ovaries, its most important feature being its prevalence in puberty and adolescence. No case report in the literature could be found relating to gonadoblastoma and PJS. Our patient was operated for unilateral gonadoblastoma at the age of 27 and didn't receive any adjuvant therapy.

The incidence of breast, cervical and pancreatic cancers is high in PJS patients. Giardello et al. reported that from 31 PJS patients who were followed between 1973 and 1985, 15 (48%) developed cancer (4 gastrointestinal, 10 non-gastrointestinal) and the observed development of cancer in these patients was 18 times greater compared to normal population [5]. Broadman et al. from the Mayo Clinic reported 26 noncutaneous cancers in 18/34 (53%) of patients between 1945 and 1996. Of these, 10 were gastrointestinal cancers, 16 non-gastrointestinal and 6 were breast cancers. The authors reported that the cancer incidence is 9.9 fold in PJS patients, and the risk of breast and gynecological cancers is 20.3 fold in women with PJS [6]. Synchronous gastrointestinal and breast cancers were reported in the literature [8,9], but no report was found about synchronous cervical and breast cancer in PJS patients like in our case. In the literature, there was only one case report with cervical cancer, bilateral breast cancer and SCTAT metachronously accompanying PJS [10]. In PJS patients, cancers become evident before the age of 50, and these patients die in a rather young age compared to other cancer patients [1,5]. Our patient was 34-year-old when she was diagnosed. Adenocarcinomas of the cervix are characteristically bulky tumors. When they are poorly differentiated or have evidence of nodal spread, they have a very high rate of extrapelvic spread and behave aggressively [11,12]. In our patient, a bulky tumor in the cervix with metastatic LAP were detected and due to rapid extrapelvic disease progression the patient died in a very short time.

Because the cancer incidence is high in patients with PJS, close follow-up of these patients is important. However, no optimal surveillance and follow-up strategy are currently available. Tomlinson and Houlston proposed a follow-up plan for patients with PJS [13]. In this plan, it is advised to begin breast examination and annual abdominal and pelvic USG at the age of 25, and mammography at the age of 35 with annually cervical smear. In the Mayo Familial Cancer Program, a more strict follow-up strategy is being advised including starting pelvic and breast examinations at the age of 20 [14]. In our patient close follow-up wasn't possible in the way it was planned to be, since she was mentally retarded and it was

hard to cooperate with, and on the other hand the family were not conscious of the problem.

We conclude that PJS patients should be under regular follow-up for, at least, early detection of colon, breast, and cervical cancer. However, the ovarian tumors which accompany PJS are generally benign (SCTAT), but rarely other types of ovarian tumors may be detected.

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