Oncogynaecological quadruplicity - case report

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Summary

A case of a 54-year-old woman with bilateral breast, endometrial, and ovarian cancer was referred to our clinic by the Oncology Department where she had been treated with chemotherapy for the breast cancer. The clinical aspects of this unique case and follow-up are presented. This is the first such serious case of primary oncogynaecological quadruplicity to be described in the literature. Forty-two months after the initial diagnosis, the patient is in good health with no signs of cancer recurrence.

Key words: Oncogynaecological quadruplicity; Tumorigenesis.

Introduction

Despite uncontestable medical success in diagnostics and therapy of malignant tumours, they have occupied second place in terms of cause of death for many years. The incidence of some types of malignancies in women is decreasing (gastric cancer), but many others are on the increase (colorectal, pulmonary cancer). This stable trend comprehends many civilized countries [1].

Invasive gynaecological malignancies contribute considerably to all female malignant tumours and form almost one-third of the cases [1]. The most frequent malignant tumour of gynaecological localisation is breast cancer, the second is endometrial cancer, the third is ovarian cancer, and the fourth is cervical cancer (without preinvasive forms) [2]. The incidence of cervical cancer is stationary, whereas that of the other three malignancies is increasing [1, 3]. The incidence and mortality in the Czech Republic in 2001 are summarised in Table 1.

A diagnosis of multiple primary cancers is a rare phenomenon, however, it seems that it has been increasing for several years [4]. The most frequent coincidence with female malignancies are those of the digestive system, while the most common gynaecological duplicities are breast and endometrial cancer, and breast and cervical cancer [1]. According to our information (PubMed) primary malignant female quadruplicity has not ever been described [4-6].

Table — *Incidence and mortality of the most common gynaecological cancers in the Czech Republic in 2001. The mortality rate is standardised per European standards.*

Localisation	Incidence 100,000 women	New cases per year	Mortality 100,000 women
Breast cancer	93.5	4,904	27.4
Endometrial cancer	30.8	1,613	4.2
Ovarian cancer	21.5	1,126	11.9
Cervical cancer	19.1	1,003	6.3

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We report a case of a woman who was affected with the three most common gynaecological malignancies, i.e., bilateral breast carcinoma, endometrial carcinoma, and ovarian carcinoma.

Case Report

The patient X.Y., born in 1949, was admitted to our clinic in June 2003, referred by the Oncogynaecology Department where she had been treated with chemotherapy (adriamycin, fluorouracil, cyclophosfamide) for bilateral breast cancer and surgical gonadectomy to exclude hormonal stimuli as a part of a complete therapy. After finishing neoadjuvant therapy, a bilateral mastectomy was planned. She did not tolerate the chemotherapy well and suffered from mild leucopenia and anemia after cytostatics.

History

A tonsillectomy in 1967 and surgery for prolapsed disks in 1978 had been performed. She was on permanent medication: lithium carbonica and Wobenzym, and was allergic to procaine.

Her gynaecological anamnesis included menarche at 15 years old and two spontaneous deliveries in 1971 and 1975. Cryoconisation of the cervix was performed in 1983. Menopause occurred in 2000-2001. She had been feeling extremely exhausted for five years, from the beginning of 2001 and discovered a lump in the right breast by self-examination. Mammography confirmed bilateral breast carcinoma. Initially she was treated by alternative medicine and later by chemotherapy. Her condition was good. She was eupnoic, mobile and well orientated. Somatic findings were normal. She had light sinus tachycardia (106/min). She was able to undergo total anaesthesia and surgery.

Blood count & biochemistry

Haemoglobin was 117 g/l, haematocrit 0.342, erythrocytes 3.82 x 10^{12}/l, leukocytes 3.3 x 10^{9}/l, and thrombocytes 183 x 10^{9}/l. Neutrofil count was 0.732, eosinofils 0.032, basophils 0.008, monocytes 0.012, lymphocytes 0.216. She was blood type B, Rh positive. Glycemia, urea, creatinine, uric acid, liver enzymes, cholesterol, triglycerids, proteinemia, ionts, haemocoagulation, and chemical examination of urine were normal.

Gynaecological examination

External genitalia were normal. The vagina was normal and the cervix was cylindrical with a quiescent transformation zone, purulent secretion but no signs of bleeding.

Palpation of the uterus showed AVF, normal size, and the adnexa had no resistence. Sonography showed endometrial hyperplasia.

After gynaecological examination, the previous plan was changed. We first performed hysteroscopy and curettage before the planned gonadectomy because of the sonographically detected endometrial hyperplasia.

Hysteroscopy and curettage

On 27/6/2003 sondage was 7 cm AVF, dilatation to Hegar 6, and the uterine cavity was symmetrical with a polypus-like endometrium with haemorrhage. Curettage of the cervix showed small areas of mucosa. Curettage of the corpus revealed polypus-like endometrium, macroscopically non suspicious. A minor operation was performed without complications. Histological findings showed chronic cervicitis, focal squamous metaplasia, and endometroid carcinoma (G1).

Surgery

On 4/7/2003 abdominal hysterectomy, bilateral salpingo-oophorectomy, bilateral salpingo-oophorectomy, frozen section peroperatively, and peritoneal lavage were carried out.

Surgery was performed via a lower medial laparotomy; normal macroscopic findings on the internal genitalia were found and there was a small amount of fluid in the Douglas pouch.

Perioperatively histological findings from the frozen section revealed well differentiated endometroid carcinoma with the start of invasion maximally into one-third of the myometrium (2.5 mm invasion vs 2.5 cm of the whole wall thickness). No signs of angioinvasion were seen but chronic cervicitis and koilocytosis were found.

The postoperative course was without complications and the patient was released on the seventh day after surgery. Extraction of the sutures was done in the outpatient department after ten days.

Cytology of lavage was performed on 7/7/2003 showing benign hyperplasia of the mesothelium.

Oncological examination

On 10/7/2003 the patient was advised to continue chemotherapy starting the next day and brachyradiotherapy was ordered.

On 11/7/2003, complete histological findings included the ovaries and fallopian tubes. The left tube and ovary were without pathological changes. The right tube was thin with small thin-paratubal cysts with flattened linings.

The right ovary was macroscopically 4 x 3 x 2.5 cm with a smooth surface and a small thin-walled cyst with gelatinous contents. Microscopically small foci of endometroid adenocarcinoma were distinguished and in some areas small papillary formations and squamous metaplasia were present. Tumour did not invade the ovarian surface. The final diagnosis was primary ovarian carcinoma. The patient was oncologically reevaluated on 15/7/2003. An examination and further oncological therapy were recommended.

Follow-up

The patient had undergone standard brachytherapy and the value of CA-125 was normal. She subsequently underwent bilateral mastectomy with exenteration of the axilla.

On 3/11/2003 the histopathological type showed infiltrating ductal and partially infiltrating lobular carcinoma, G2, pT2 N2 MO (of 15 nodes five were infiltrated). Estrogen receptors were positive in 80% and progesterone receptors were positive in 30%. Her-2/neu positivity was grade 2 and Ki-67 was positive in 10%.

On 13/11/2003, the histopathological type revealed infiltrating ductal carcinoma, G1, pT1 N1 MO. Estrogen receptors were positive in 90% and progesterone receptors were positive in 20%. Her-2/neu was negative and Ki-67 showed 10% positivity.

Actinotherapy on both chest walls, axilla and supraclavicular regions was applied during August and September 2004. Adjuvant therapy with paclitaxel (Taxol infusion), adriamycin and cyclophosfamide was finished at the end of October 2004. The end of September 2004 the patient was in a relatively good state on hormonal therapy with tamoxifene (20 mg once daily orally), and was released from hospital.

In December 2006 the last control in the Oncology Department was performed. The status of the patient was very good. No signs of recurrence were found on CT of the chest and abdomen and the values of CA-125 and CA 15-3 were normal. Gynaecological examination showed normal findings after surgery and cytology of the vaginal stump was negative. The patient continues using tamoxifene orally at the same dose.

Discussion

Oncological diagnosis is a serious, often fatal event in human life. Invasive gynaecological malignancies contribute to all female malignant tumours with a considerable part being played in almost one-third of them. Generally, the a etiology of gynaecological tumours is partially caused by the increase of sexually transmitted infections (STIs), and especially by the proliferation of STIs of the second generation, whose somewhat causative agents bring about a certain oncogenic potential, partially by the cycling and periodicity of tissue transformation in fertile age under the influence of sex hormones. The incidence of malignant tumours is substantially influenced by nutrition and lifestyle, e.g., the abuse of alcohol, cigarettes and drugs [3, 7]. There are some hereditary syndromes called "cancer family syndromes" that are connected with a higher risk of gynaecological and other malignant development: ataxia teleangiectatica (Louis-Bar, Boder-Sedgwick), Li-Fraumeni (Frederick-Fraumeni), Peutz-Jeghers (Peutz-Touraine, Hutchinson-Weber-Peutz), Muir-Torre (Lynch II), Cowden (Lloyd, m. Lloyd-Dennis) and inherited mutation in the BRCA-1 and BRCA-2 genes. Ataxia teleangiectatica is autosomally recessive, whereas the others are autosomally dominant [7-9]. Many reasons for tumorigenesis are at this time unknown.

In this case report a 54-year old woman was diagnosed with four independent primary malignant tumours of gynaecological etiology at one time. The patient was affected with the three most common gynaecological malignancies, i.e., bilateral breast carcinoma, endometrial carcinoma, and ovarian carcinoma. Prognosis for

each may be terminal. The gravest tumour seemed to be the invasive bilateral breast carcinoma which was distinguished as the first. Neoadjuvant therapy should favour the efficacy of planned radical surgical therapy and ameliorate the prognosis of the disease.

Endometrial carcinoma with staging pT1b NO MO (IB - according to FIGO staging) and grading G1 can be therapeutically managed [10]. Hysterectomy with bilateral salpingo-oophorectomy and lavage for cytology is a sufficient operative procedure [2].

Ovarian carcinoma with staging pT1a NO MO (IA) should be operated on more radically, i.e., with omentectomy, appendectomy, lavage for cytology, and random biopsies [2, 10]. Normal value of CA-125 after surgery is prognostically positive.

Carcinoma of the breast with a staging of pT2 N2 MO (IIIA) was the worst of the patient's tumours, and a crucial item for the whole therapeutical strategy [10].

Breast carcinoma with a staging of pT1 N1 MO (IIA) as well as high positivity of hormonal receptors and low positivity of proliferative factors are prognostically favourable [10]. Human epidermal growth factor receptor 2 is an oncoprotein, and an independent prognostic factor in which higher expression is observed in 20-25% of invasive breast cancers [11]. Histopathological and histochemical examination of the breast tumours and lymphatic nodes were the crucial items in carrying out the therapeutical management.

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