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Successful treatment by chemoradiotherapy for locally advanced cervical low-grade endometrial stromal sarcoma. Case report and review of the literature

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Summary. We describe the case of a 51-year-old patient with primary low-grade endometrial stromal sarcoma (ESS) of the uterine cervix (FIGO stage IIB). The patient was diagnosed with the neoplasm in June 2009. No synchronous extra-pelvic metastases were found. She was referred to chemoradiotherapy. Three cycles of AP-scheme (doxorubicin 60 mg/m^2 and cisplatine 50 mg/m^2; one cycle every 28 days) were administrated. External beam irradiation was divided into two steps. In the first step the uterus, both adnexa, parametria, and regional pelvic lymph nodes were irradiated (total dose of 39.6 Gy, 4 fields, 22 fractions of 1.8 Gy per fraction, 5 days/week). Afterwards, only the uterus and both adnexa were irradiated (total dose of 26.0 Gy, 3 fields, 13 fractions of 2.0 Gy per fraction, 5 days/week). As the last part of treatment, intracavitary brachytherapy was administered using a high-dose Ir192 source, with 7 Gy / 2.0 cm being delivered to the vaginal surface in 1 fraction (intrauterine applicator 6 cm in diameter with vaginal cylinder 2.6 cm). Treatment was finished in January 2010. The patient, 57 months after the end of treatment, is still under control in our department. No signs of recurrence have been detected since then. We conclude that patients with primary low-grade ESS of the uterine cervix, even when locally advanced, can be successfully treated with combined chemoradiotherapy.

Key words: low-grade endometrial stromal sarcoma, uterine cervix, treatment

«Il successo del trattamento con radiochemioterapia del sarcoma dello stroma endometriale cervicale di basso grado localmente avanzato. Caso clinico e revisione della letteratura»

Riassunto. Descriviamo il caso di una paziente di 51 anni con sarcoma stromale endometriale (ESS) della cervice uterina (stadio FIGO IIB) di basso grado. La neoplasia fu diagnosticata alla paziente nel giugno del 2009. Non furono trovate metastasi sincrone extra-pelviche. La paziente fu sottoposta alla radiochemioterapia. Le furono somministrati tre cicli di trattamento secondo lo schema AP (doxorubicina 60 mg/m^2 e cisplatino 50 mg/m^2, un ciclo ogni 28 giorni). L'irradiazione a fasci esterni è stata divisa in due fasi. Nella prima fase l'utero, sia annessi, parametria e linfonodi pelvici regionali sono stati irradiati (dose totale di 39,6 Gy, 4 campi, 22 frazioni di 1,8 Gy per frazione, 5 giorni/settimana). In seguito, solo utero ed entrambi annessi sono stati irradiati (dose totale di 26,0 Gy, 3 campi, 13 frazioni di 2,0 Gy per frazione, 5 giorni/settimana). Come ultima parte del trattamento, la brachiterapia endocavitaria è stata somministrata con un'alta dose di Ir192 come sorgente, con 7 Gy/2,0 centimetri somministrati alla superficie vaginale in 1 frazione (applicatore intrauterino di 6 cm di diametro con cilindri vaginali 2,6 cm). Il trattamento è stato terminato nel gennaio 2010. La

paziente, 57 mesi dopo la fine del trattamento, è ancora sotto controllo presso il nostro reparto; non è stata rilevata la presenza di alcun segno di recidiva. Concludiamo, che le pazienti con basso grado di ESS primario della cervice uterina; anche localmente avanzato, possono essere trattati con successo con chemioradioterapia combinata.

Parole chiave: basso grado di sarcoma stromale endometriale, cervice uterina, trattamento

Introduction

Mesenchymal tumors are rare uterine neoplasms with stromal differentiation that enclose an endometrial stromal sarcoma (ESS). ESS accounts for 0.2% of all malignant uterine tumors and represents 10-15% of all types of uterine sarcomas (1, 2). There are three types of ESS: endometrial stromal nodule, low-grade ESS and high-grade ESS, as first described by Norris and Tylor in 1966 (3). ESS is usually diagnosed in the uterine corpus, but other locations in the endocervix, rectovaginal septum, omentum, ovary and peritoneum have been described (4-6). The average age of patients at diagnosis is 40-60 years (1).

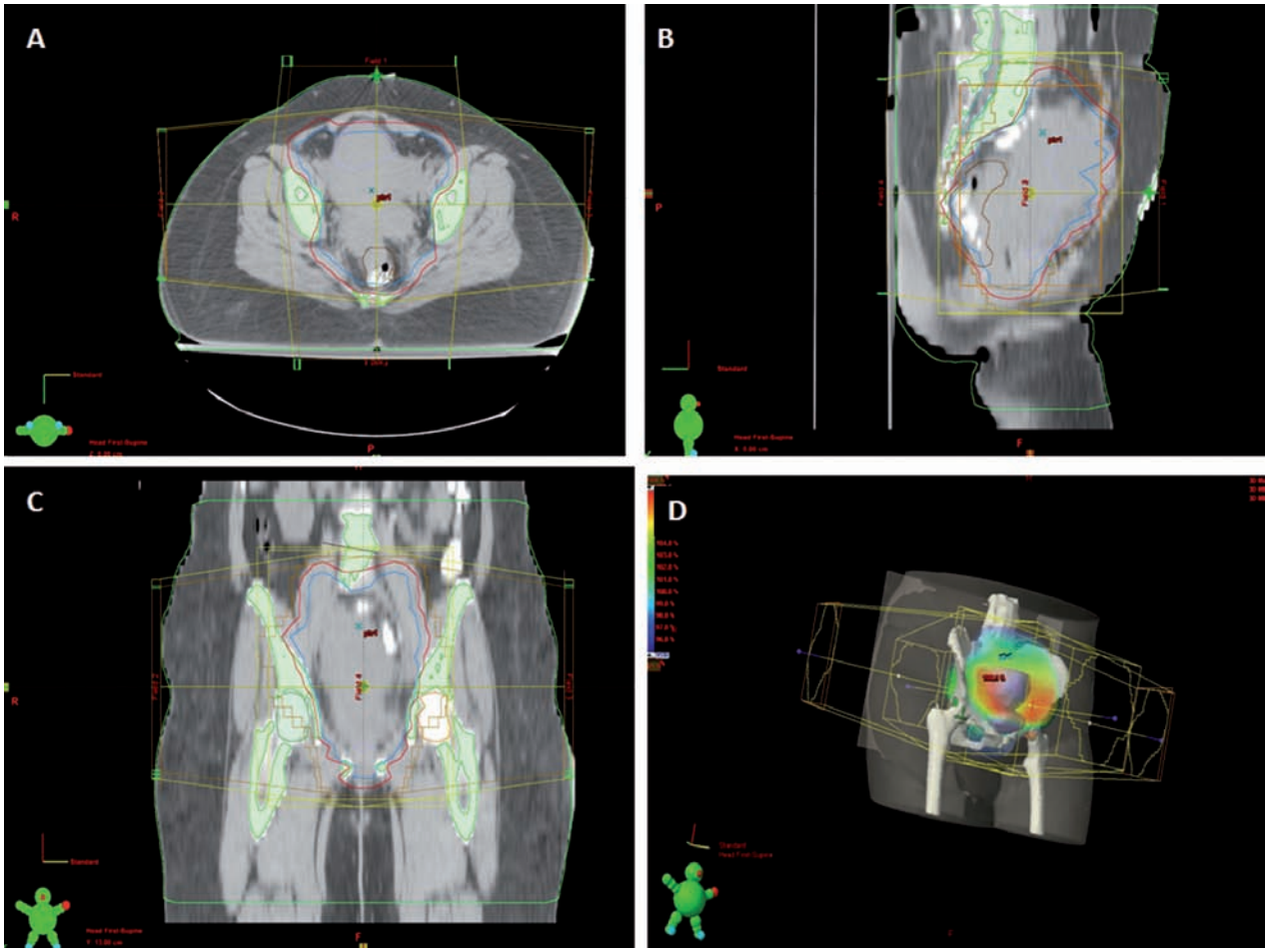

Figure 1. A-D: Dose distribution plan of the first step of EBRT. Planning tumor volume 1 (PTV1) covered the whole uterus, both adnexa, the parametria, and the regional pelvic lymph nodes.

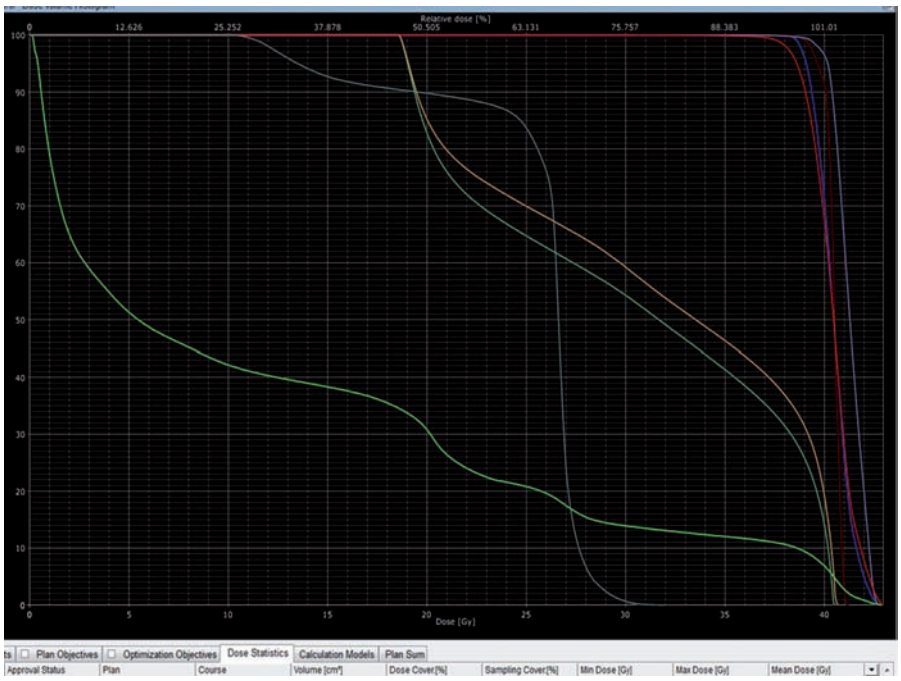

Figure 2. Histogram for the first part of treatment: red – PTV1, blue – clinical tumor volume 1 (CTV1), brown – rectum, bright green – spinal cord, dark green – femoral heads, violet - urinary bladder.

Cervical low-grade ESS is a very rare infiltrating tumor, characterized by indolent growth and late recurrences, classically described as arising in foci of cervical endometriosis (5-7). It is typically densely cellular and characterized by the presence of oval to spindle-shaped cells, that resemble the cells of the endometrial stroma, without evidence of significant atypia, rare mitotic figures (less than 10 MF/10 HPF, usually less than 3 MF/10 HPF), and pleomorphism. A wide network of thin-walled small vessels supports the cells (2, 7, 8). A review of the English literature on Medline produced by searching for the item cervical low-grade ESS showed few such cases (2, 4, 6).

Case report

A 51-year-old patient presented in July 2009 to the Gynecologic Cancer Outpatient Clinic at the Regional Cancer Center in Lodz with histologically proven cervical low-grade ESS. The patient, gravida 0, was 1 year postmenopausal. She had a familial cancer history, her mother having had cervical cancer. The patient reported 3 month-long vaginal bleeding. She did not have decreased body weight and presented no other suspect general symptoms. She did not have any significant past medical history of note and there were no other complaints. The patient had no history of prior abdomino-pelvic surgery. On physical examination, she was in good general condition. Gynecological examination revealed an exophytic tumor of the uterine cervix, and an enlarged uterine corpus (fibroids, nearly 150 mm) and bilateral parametria, penetrating the pelvic bones. No synchronous extra-pelvic metastases were found. Abdomino-pelvic ultrasound and CT revealed a pathologic lesion, 119 x 81 mm in diameter, penetrating from the lower part of the uterus bilaterally into the parametria, no signs of extra-pelvic dissemination of the ESS, and left hydronephrosis. Chest X-ray showed clear lung fields. Rectoscopy excluded infiltration of the rectum. The locally advanced neoplasmic disease in the pelvis, but not extra-pelvic, was confirmed by PET-CT, as well. The disease was classified as stage IIB according to the FIGO 2009 staging system (9). Blood investigations including full blood counts: electrolytes, renal function tests, serum proteins and total bilirubin, were within normal limits.

The patient was treated with combined sequential chemoradiotherapy. Three cycles of AP-scheme (doxorubicin 60 mg/m^2 and cisplatine 50 mg/m^2; one

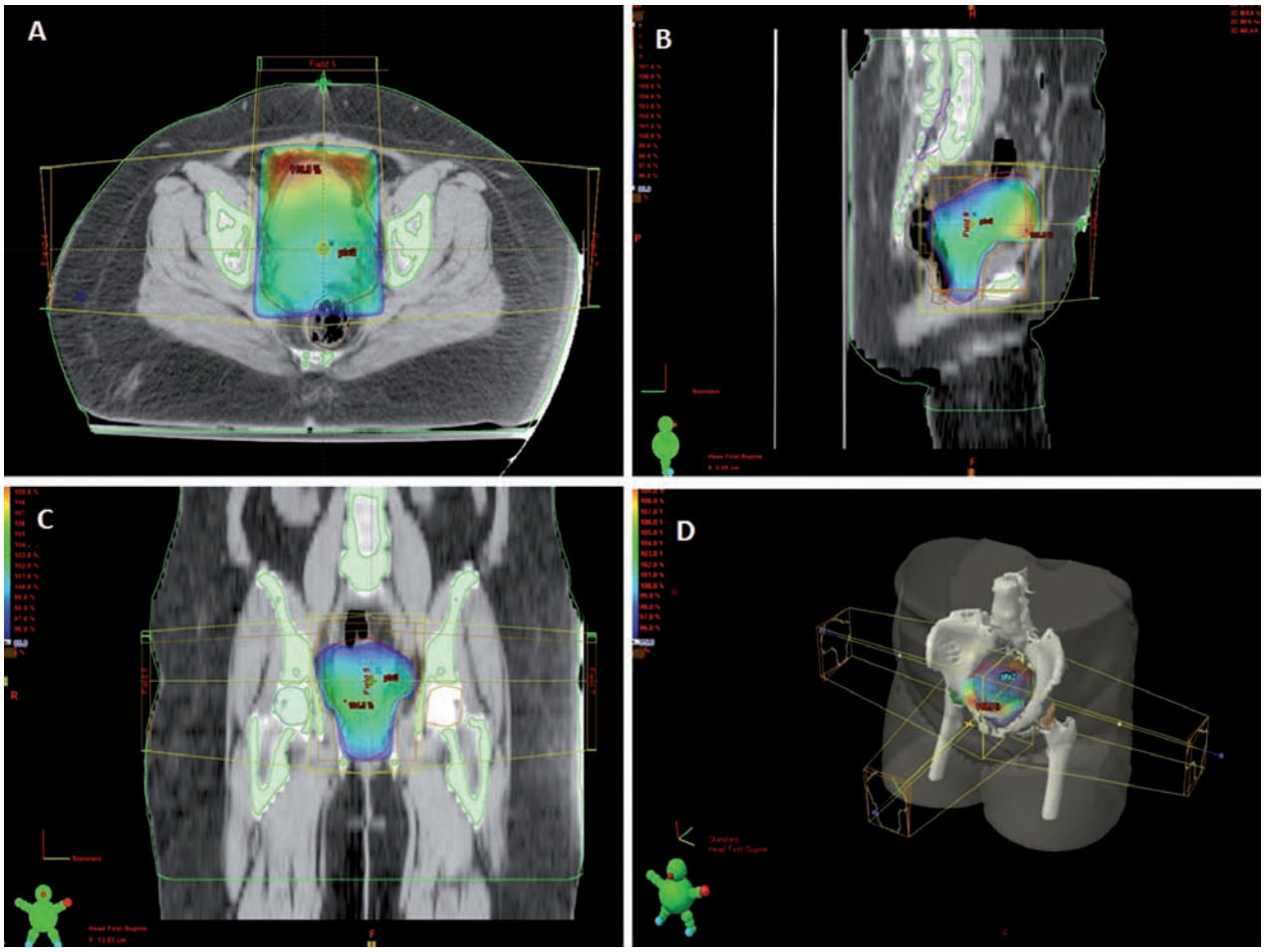

Figure 3. Dose distribution plan of the second step of EBRT. Planning tumor volume 2 (PTV2) covered only the uterus and both adnexa.

cycle every 28 days) were administered. Afterwards, external beam radiotherapy (EBRT) was given by linear Clinac 2300 accelerator (Varian Medical Systems, Inc., USA) at an energy of 15 MV in two steps. First, EBRT was delivered to the pelvic organs (a total dose of 39.6 Gy, 4 fields, 22 fractions of 1.8 Gy per fraction, 5 days/week). Planning tumor volume 1 (PTV1) covered the whole uterus, both adnexa, the parametria, and the regional pelvic lymph nodes. The dose distribution plan of the first step of EBRT is presented in Figures 1-2.

In the control CT examination, an 80-90% decrease in the tumor volume was observed and no signs of the left hydronephrosis. A second part of EBRT was carried out, PTV2 covering only the uterus and both adnexa (total dose of 26.0 Gy, 3 fields, 13 fractions of 2.0 Gy per fraction, 5 days/week). The dose distribution plan of the second step of EBRT is presented in Figures 3-4. Afterwards, intracavitary brachytherapy was administered using a high-dose-rate Ir192 source, with a single dose of 7 Gy specified 2.0 cm from the midline being delivered to the vaginal surface in 1 fraction (intrauterine applicator 6 cm in diameter with vaginal cylinder 2.6 cm). Treatment was conducted in January 2010. No side effects were observed in the rectum, urinary bladder or other pelvic structures during treatment or follow-up. The patient, 57 months after the end of treatment, is still under control in our department. No clinical or radiological signs of recurrence have been detected since then (Figure 5). The patient has been professionally active for one year now.

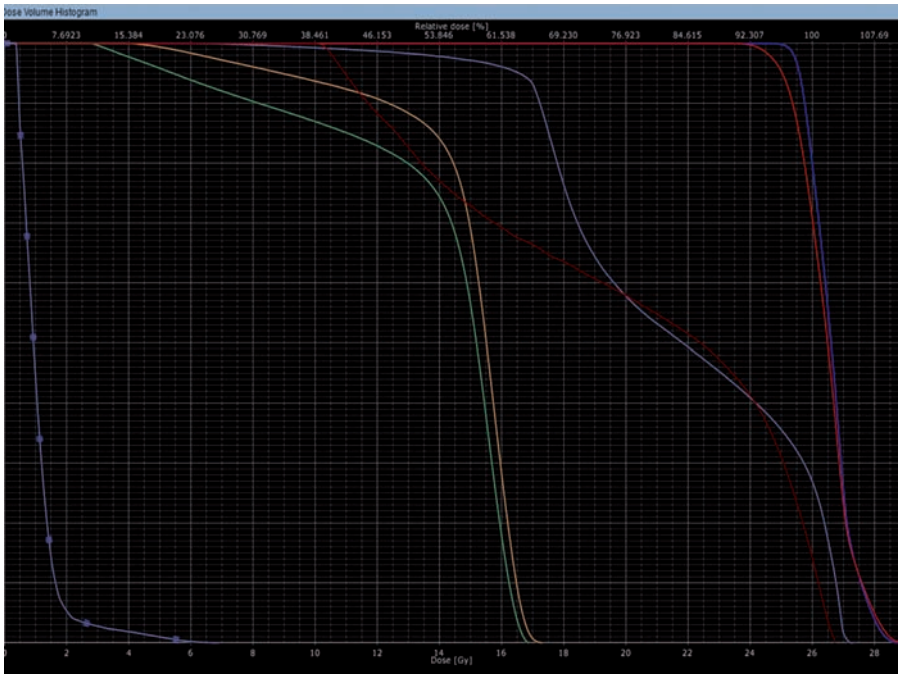

Figure 4. Histogram for the second part of treatment: red – PTV2, blue – clinical tumor volume 2 (CTV2), brown – rectum, bright green – spinal cord, dark green – femoral heads, violet - urinary bladder.

Discussion

Our report presented in the previous section is valuable for two main peculiar features: 1) an extremely rare case of primary cervical low-grade ESS diagnosed at stage IIB; and 2) its successful treatment with combined chemoradiotherapy, which is an unusual feature in such cases.

Due to the limited number of cases reported, the natural history of cervical ESS is not clearly defined. The symptomatology is non-specific, and abnormal vaginal bleeding in many reports is found to be the leading symptom (2, 6, 10). In our patient, post-menopausal vaginal bleeding was the only presenting symptom of the tumor. Hasiakos *et al.*, analyzing the case of a 44-year-old patient with low-grade ESS of the endocervix, reported pelvic and abdominal pain as a possible subsequent symptom, but this was not present in our case (6). Again, Martin *et al.* described a foul-smelling vaginal discharge as a possible additional symptom of cervical ESS (10). Nearly 25% of cervical ESS patients remain asymptomatic, and especially in such cases very rare primary cervical ESS may cause difficulty in reaching a prompt diagnosis (2, 6, 11).

The prognosis in patients with uterine ESS depends on the extent of the tumor at the time of diagnosis but is usually favorable (8, 12). Because of the rarity of low-grade cervical ESS cases, a common suitable treatment regimen cannot be established and treatment needs to be tailored to each patient. The choice of treatment is based on the medical condition, extension of the disease, and clinical stage of disease, and usually includes surgery and/or radiotherapy with or without hormonal therapy, as well as chemotherapy in select cases (13). According to Hasiakos *et al*, surgery is restricted to select early-stage low-grade cervical ESS patients (6). In our case, stage IIB with left hydronephrosis was diagnosed according to the 2009 FIGO Classification. The patient was disqualified from surgery, and successfully treated with chemoradiotherapy. Nowadays, it is postulated that patients with poor prognostic factors such as higher stages, large tumors, involvement of regional lymph nodes and older age should be considered for treatment with additional chemotherapy and/or radiotherapy, similarly to the case presented above (2, 8, 12). According to results by the French Study Group with localized uterine sarcomas (SARCGYN study), the most effective chemo-

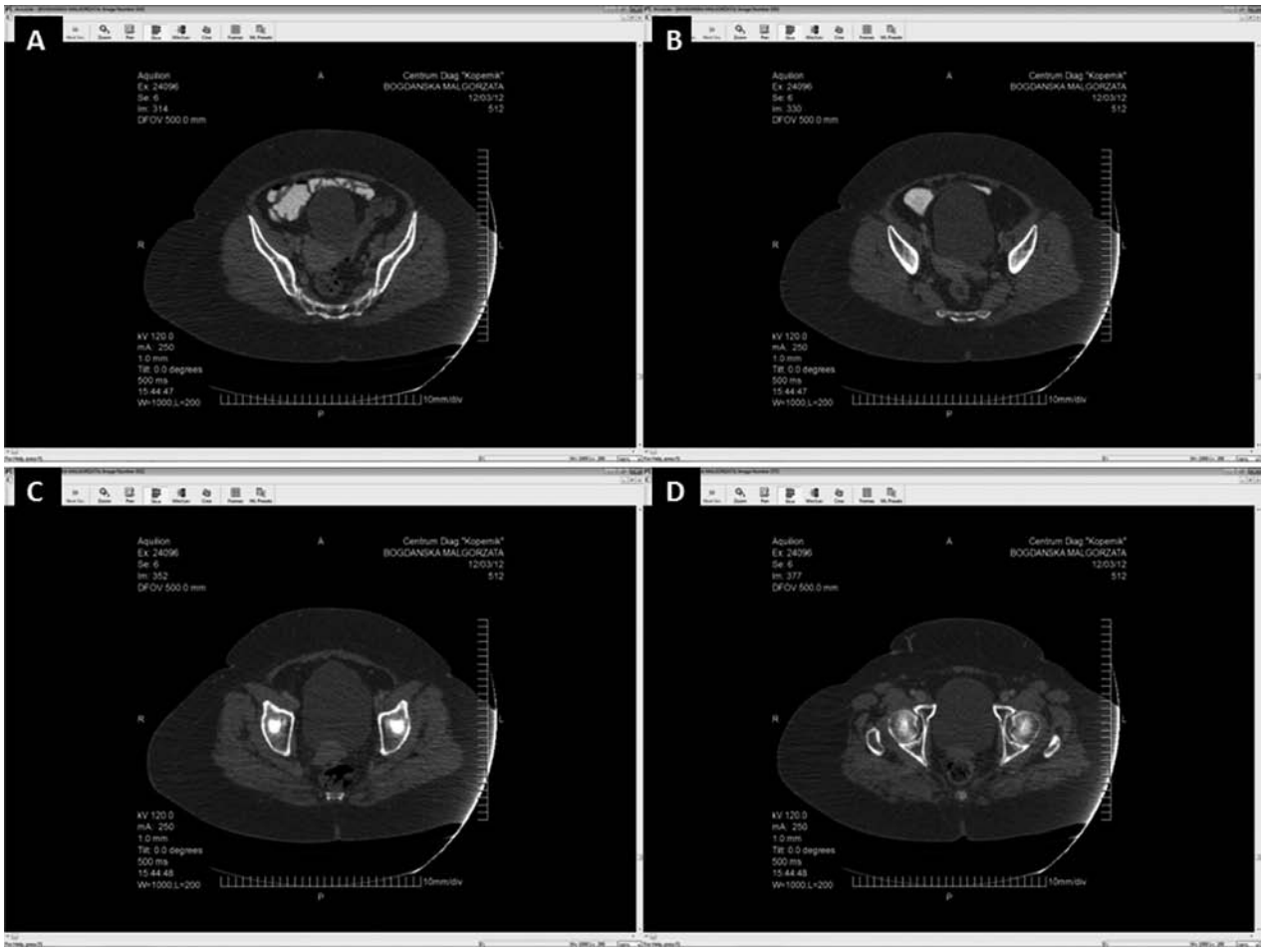

Figure 5. Follow-up: successive CT scans of the pelvis 26 months after treatment, showing complete remission of the low-grade cervical ESS.

therapy in uterine ESS is doxorubicin, cisplatin and ifosfamide (13). In our case doxorubicin 60 mg/m^2 and cisplatine 50 mg/m^2 were given to the patient. ESS patients may receive adjuvant hormonal treatment with progestational agents or aromatase inhibitors, as well (14). Despite treatment, about one third of patients develop recurrences, usually in the pelvis and abdomen, less frequently in the lungs and another locations (12).

In analyzing the case of our 51 year-old patient with low-grade cervical ESS we conclude that chemoradiotherapy given to patients diagnosed with locally advanced tumor can increase their quality of life and prolong survival.

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