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Down Syndrome Complicating Synchronous Endometrial and Salpinx Cancer. Presentation of a Rare Case and Mini-Review of the Literature

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Abstract

There are only a few reports of uterine cancers in women with Down syndrome, whose tumor profile is marked by a reduced risk for solid neoplasms.

In our case, an early diagnosis of metastaticsynchronous endometrial cancer stage II in the anatomic area of salpinx and stage III in endometrial cavity was confirmed in a 55-year-old, nulliparous, menopausal, obese woman with Down syndrome, presented with irregular vaginal bleeding.

Although uterine cancers are underrepresented in women with Down syndrome, uterine malignancy should be considered in differential diagnosis of abnormal vaginal bleeding.

Our goal remains, proper diagnosis and treatment followed by assiduous therapeutic mapping.

Keywords: *Down Syndrome, Trisomy 21, Endometrial Cancer, Uterine Cancer*

Introduction

Down syndrome is by far the most common and best known human chromosomal disorder, representing the most common cause of intellectual disability. Originated as trisomy of chromosome 21, leading to multiple and systemic complications. According to recent literature, there is a wide range of phenotypic variation. [1]

Down syndrome represents the most common autosomal abnormality. Incidence isestimated about 1 case in 800 live births. [2]

Uterine cancer is defined as any invasive neoplasm of the uterine corpus. Invasive neoplasms of the female pelvic organs account for almost 15% of all cancers in women. The most common of these malignancies is uterine cancer.

An estimated 54,870 cases are diagnosed annually, leading to 10,170 deaths. It is the fourth most common cancer, accounting for 7% of female cancers, following breast, lung, and colorectal cancer.

Endometrial adenocarcinoma is the most common gynecologic malignancy in United States. However, it has a favorable prognosis because the majority of patients present at an early stage, resulting in only 4% of cancer deaths in women. [3]

There are only a few reports of uterine cancers in women with Down syndrome, whose tumor profile is marked by a reduced risk for solid neoplasms.

Case

A postmenopausal, obese, 55-year-old woman(para 0, gravida 0) with diagnosed Down Syndrome admitted at our Department complaining of episodes of mild uterine bleeding.

Physical examination revealed active hemorrhage arised from the anatomic region of cervix and vagina. Pap smear free of malignancy. Transvaginal ultrasound confirmed the presence of physical examination.

Patient underwent diagnostic curettage. Histologic evaluation revealed endometrial cancer stage

II. (FIGO). As part of disease staging, a thorax and upper-down abdomen CT was performed. No sign of metastatic malignancy, including presence of infiltrated lymph nodes.

Multidisciplinary approach decided surgical staging of the lesion. As gold standard, a total abdominal hysterectomy with bilateral salpingooopherectomy was performed. Inside peritoneal cavity all intraoperative findings were similar to the age of the patient.

All abdominal organs were in a strange correlation bounded followed by acongenital abdominal hernia containing omentum.

Patient underwent total abdominal hysterectomy with bilateral salpingooopherectomy. As additional surgical step, bilateral lymph node dissection was performed.

Finally, there was surgical restoration of the hernia, submitting the dissected omentum for histologic evaluation.

Final histologic analysis confirmed all the preoperative findings, revealing synchronous endometroid adenocarcinoma grade II inside the endometrial cavity and endometroid adenocarcinoma grade III in the anatomic region of right adnexa., including infiltration of the omentum. All lymph nodes were free of malignancy.

Multidisciplinary approach decided episodes of chemotherapy. Patient was discharged from the hospital the 6th pod in good clinical condition.

Discussion

Risk factors concerning the infiltration of endometrial cancer include age of the patient, tumor size, lymph node infiltration, disease grading, deep myometrial invasion, lymphovascular space invasion, cervical involvement, positive cytology, and adnexal or serosal involvement. [4]

According to recent bibliography, surgical pathologic findings create categories of low, moderate, and high risk regarding uterine recurrence. These categories help define proper prognosis and treatment recommendations.

Low Risk

Low risk is defined as grade I or II endometroid tumors with only inner one half myometrial invasion, no cervical extension, no lymphovascular space involvement, and negative findings on cytology and grade IIIendometroid tumors with no myometrial invasion. These patients need no adjuvant therapy, although some gynecologic oncologists administer adjuvant therapy to all patients with grade 3 tumors.

Low risk patients randomized to vaginal brachytherapy versus observation found no significant difference in vaginal recurrence (1.2% vs 3.1%) and no difference in 5 yr OS 96%. [5]

UPSC, clear cell, and carcinosarcoma are considered high risk for recurrence even with only endometrial involvement.

Moderate Risk

Much controversy and research surrounds post-operative management of intermediate risk for recurrence patients with endometrial cancer, which includes low grade (I or II) with deep myometrial invasion or cervical involvement. Guidelines suggest consideration of adjuvant external beam or vaginal brachytherapy or both. Prospective trials have shown a decrease in local recurrence but no change in overall survival. [6-8]

The subset of patients with high-intermediate risk has a significant decrease in local recurrence and would benefit from adjuvant radiation.

This category includes patients who have any II of the following III risk factors: grade III histology, age older than 60-year-old, or deep invasion to outer one half of the myometrium. [6-8]

PORTEC-2 compared vaginal brachytherapy versus pelvic external beam radiation for high-intermediate risk patients, finding no statistic difference in vaginal recurrence, DFS, or OS at 5 years, with significantly less bowel toxicity and better quality of life. [9-11]

High Risk

Patients with grade III disease with any myometrium invasion, stage II or greater, have lymphovascular or low uterine segment involvement, or clear cell and papillary serous histology.

These patients need adjuvant radiation, chemotherapy, or both. While some recommend whole-pelvic radiation therapy, others advocate only vaginal brachytherapy if the tumor is fully staged without evidence of extracorporeal spread.

Management will need to be individualized depending on grade, histology, and depth of invasion. Management may include close follow-up, returning to the operating room for full staging, vaginal radiation, or pelvic radiation.

A shift toward the use of more systemic chemotherapy over radiation for the treatment of extra-uterine metastatic endometrial cancer has occurred. A Gynecologic Oncology Group (GOG) prospective trial found a survival benefit for patients with stage III or IV disease with the use of systemic chemotherapy with doxorubicin and cisplatin (AP) when compared to whole-abdominal pelvic radiation (WART). [12]

Another GOG trial found a survival advantage with the addition of paclitaxel to cisplatin and doxorubicin (TAP), and was the standard for those patients who can tolerate the treatment. [13]

An increasingly popular alternative regimen is carboplatin and paclitaxel, which has shown efficacy in retrospective trials, and was found in randomized trial (GOG 209) to be no inferior to TAP for PFS or OS . [14-16]

After tumor reductive surgery for extra pelvic/ advanced disease at the time of laparotomy, adjuvant/ adjunctive therapy is individualized. Localized radiation therapy is administered for CNS and symptomatic bone metastases. Otherwise, these patients are treated with chemotherapy and/or progestin or antiestrogen therapy. Medroxyprogesterone acetate and megestrol therapy is efficacious for those low-grade tumors that are estrogen and/or progesterone receptor–positive.

Tamoxifen is another alternative when progestin therapy is contraindicated or has failed. A 75-80% objective response occurs with estrogen and/or progesterone receptor–positive tumors compared to less than 5% in the absence of estrogen and/or progesterone receptor–positive tumors.

Unfortunately, the tumors that tend to have intra-abdominal metastases are high grade and are less likely to be estrogen and/or progesterone receptor–positive tumors (15-41%).

In cases of advanced disease, sending tissue, specifically from metastatic sites, for receptor analysis is useful. Metastases are receptor positive in 25% of metastatic tumors compared to 60% of primary tumors.

The major curative treatment of uterine sarcomas is TAH/BSO with or without surgical staging.

However, a significant number of these tumors are diagnosed intraoperatively and postoperatively.

Subsequently, postoperative therapy usually is necessary, although disagreement generally exists regarding its efficacy in terms of survival.

At times, reoperation for removal of remaining gynecologic organs with surgical staging may be necessary.

In terms of adjuvant therapy, whole-pelvic radiation or progestin therapy can be offered depending on surgical and pathologic findings. stage I low grade ESS can be observed after surgery.

NCCN guidelines recommend that stage II or higher patients receive hormonal treatment given high ER/ PPR positivity.

Megestrol acetate or medroxyprogesterone can improve DFS but not OS. Pelvic radiation can also be offered for advanced stage disease. Whole-pelvic radiation also improves local control for HGESS, especially stage I disease.

However, if advanced disease is present, progestin therapy and doxorubicin-based chemotherapy have a role.

Undifferentiated ESS and leiomyosarcoma have a poor prognosis with tendency for hematogenous spread and recur at distant/extra pelvic sites, thus whole-pelvic radiotherapy is relatively ineffective.

Chemotherapy with oxorubicin, ifosfamide, etoposide, and/or cisplatin may be used with LMS. Recently, gemcitabine and docetaxel (Taxotere) combination therapy has shown promise in unresectable LMSs of different sites. Patients with MMT that is limited to the pelvis benefit from whole-pelvic radiation with respect to local control.

Those patients with evidence of extra pelvic disease may respond to additional postoperative therapy with doxorubicin, cisplatin, and/or ifosfamide.

Conclusion

Down Syndrome represents a rare entity with specific clinical figures. There are few cases in recent bibliography demonstrating correlation and clinical adjustment of this lesion with gynecologic cancer and especially synchronous.

Further clinical studies must be conducted in order to establish the pathophysiologic pathways of this pathologic status. Our scope remains proper diagnosis and treatment of such cases strongly associated with increased quality of life of the patient.

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