UTERINE SARCOMAS

Deni Karelović

Department of Gynecology and Obstetrics
University Hospital Split

UTERINE SARCOMAS

- Originate from mesenchymal tissue, i.e. smooth muscle or connective tissue of the uterus
- *Sarcoma* (greek 'sarx' = meat)
- Fast progression
- Bad prognosis
- Most commonly an accidental finding after myoma operation

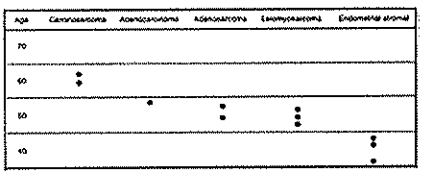
EPIDEMIOLOGY

- Rare tumors that make for:
- 1 % of malignant tumors of female genital tract
- 3 % - 7 % of malignant tumors of the uterus

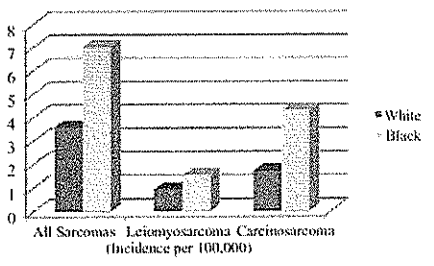
RISK FACTORS

Age

- Average age ~ 60 years



RISK FACTORS



Pelvic radiation therapy

RISK FACTORS

High-energy (ionizing) radiation used to treat some cancers can damage cells' DNA, sometimes increasing the risk of developing a second type of cancer. If you have had pelvic radiation, your risk for developing uterine sarcomas is increased. These cancers usually are diagnosed 5 to 25 years after exposure to the radiation.

RISK FACTORS

RB gene changes

Women who have had a type of eye cancer called *retinoblastoma* that was caused by being born with an abnormal copy of the *RB* gene have an increased risk of getting uterine leiomyosarcomas.

Tamoxifen use

10 year period
2000. – 2010. year - 47

17 year period
1993. – 2010. god. - 103

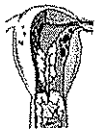
Average age= 58 (39 – 94 ± 12,4)

Department of Gynecology and Obstetrics
University Hospital Split

PATHOLOGY CLASSIFICATION

MAIN HISTOLOGIC TYPES

- 40-50 % CARCINOSARCOMAS (MIXED MESODERMAL SARCOMAS)
- 30 % LEYOMIOSARCOMAS
- 15 % ENDOMETRIAL STROMAL SARCOMAS



University Hospital Split

- 56 % - mixed mesodermal sarcoma
- 32 % - leyomiosarcoma
- 11 % - endometrial stromal sarcoma

UTERINE SARCOMAS
GOG CLASSIFICATION

GYNECOLOGIC ONCOLOGY GROUP

I. Non-epithelial neoplasms

- a. Endometrial stromal tumors
  - I. Stromal nodule
  - II. Low grade stromal sarcoma
  - III. High grade stromal sarcoma
- b. Smooth muscle tumor of uncertain malignant potential
- c. Leiomyosarcoma
  - I. Epithelioid
  - II. Myxoid
- d. Mixed endometrial stromal and smooth muscle tumor
- e. Poorly differentiated (undifferentiated) endometrial sarcoma
- f. Other soft tissue tumors
  - I. Homologous
  - II. Heterologous

II. Mixed epithelial-non-epithelial tumors

- a. Adenosarcoma
  - I. Homologous
  - II. Heterologous
  - III. With high-grade stromal overgrowth (see notes)
- b. Carcinosarcoma (malignant mixed mesodermal tumor or malignant mixed müllerian tumor)
  - I. Homologous
  - II. Heterologous

UTERINE SARCOMAS
CLASSIFICATION (WHO 2003.)

International Society of Gynecologic Pathologists
and the
World Health Organization

- Mesenchymal tumors
- Endometrial stromal and related tumors
  - Endometrial stromal sarcoma, low grade
  - Endometrial stromal nodule
  - Undifferentiated endometrial sarcoma
- Smooth muscle tumors
  - Leiomyosarcoma
    - Epithelioid variant
    - Myxoid variant
  - Smooth muscle tumor of uncertain malignant potential
  - Leiomyoma, not otherwise specified
    - Histologic variants
    - Mitotically active variant
    - Cellular variant
    - Hemorrhagic cellular variant
    - Epithelioid variant
    - Myxoid
    - Atypical variant
    - Lipoleiomyoma variant
  - Growth pattern variants
    - Diffuse leiomyomatosis
    - Dissecting leiomyoma
    - Intravenous leiomyomatosis
    - Metastasizing leiomyoma
- Miscellaneous mesenchymal tumors
  - Mixed endometrial stromal and smooth muscle tumor
  - Perivascular epithelioid cell tumor
  - Adenomatoid tumor
  - Other malignant mesenchymal tumors
  - Other benign mesenchymal tumors
- Mixed epithelial and mesenchymal tumors
  - Carcinosarcoma (malignant müllerian mixed tumor, metaplastic carcinoma)
  - Adenosarcoma
  - Carcinofibroma
  - Adenofibroma
  - Adenomyoma
  - Atypical polypoid variant

FIGO clasification

Carcinosarcomas – as endometral carcinoma

IA Tumor invades ≤ half myomerium
IB Tumor invades > half myometrium

IIIA Tumor invades serose tissue of uterus and/or adnexa
IIIB Tumor spreads to vagina and/or parametria
IIIC1 Invades pelvic lymph nodes
IIIC2 Invades paraaortal lymph nodes

FIGO staging for uterine sarcomas. *Int J Gynaecol Obstet 2009; 104: 179.*

FIGO classification

Leyomiosarcomas

IA Tumor ≤ 5cm
IB Tumor > 5 cm

IIA Tumor invades adnexa
IIB Tumor invades extrauterine pelvic stuctures

IIIA Single site
IIIB Multiple sites
IIIC Invades pelvic and/or paraaortal lymph nodes

FIGO staging for uterine sarcomas. *Int J Gynaecol Obstet 2009; 104: 179.*

FIGO classification

Endometral stromal sarcomas and adenosarcomas

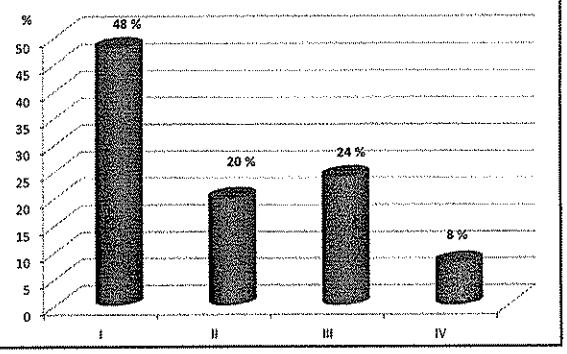
IA Tumor limited to endometrium without myometrium invasion
IB Tumor invades ≤ half myometrium
IC Tumor invadira > half myometrium

IIA Tumor invades adnexa
IIB Tumor invades extrauterine pelvic structures

IIIA Single site
IIIB Multiple sites
IIIC Invades pelvic and/or paraaortal lymph nodes

FIGO staging for uterine sarcomas. *Int J Gynaecol Obstet 2009; 104: 179.*

FIGO - University Hospital Split



CARCINOSARCOMAS
MIXED MESODERMAL SARCOMAS

- **40-50 % of all sarcomas**
- **Average age 62-65 / adenosarcoma: 57**
- **Signs and symptoms: metrorrhagia, polipoid tumor mass in the uterus, often prominating from the cervix and falling out from vagina**
- **Muscle, cartillage, bone**
- **Often metastazes into the lymph nodes and paraaortally 20-30 %**
- **The worst prognosis**
- **Survival: middle 2 years, early stage 50 %, advanced stage insignificant**

Leiomyosarcoma

- 1/3 of uterine sarcomas
- Average age 52 years.
- Multiple chnges in genes and kariotype
- in 5-10 % originates from myoma
- SIGNS AND SYMPTOMS: metrorrhagia, pain, ubrzan fast growing tumor (6-9 cm) o the uterus
- Metastases: liver, lungs, kidney, brain, bones
- Responds better to chemotherapy, it is resistant to irradiation
- Relapse mostly within 2 years
- 5-year survival
  - Total 15-25 %
  - For I and II st 40 – 70 %

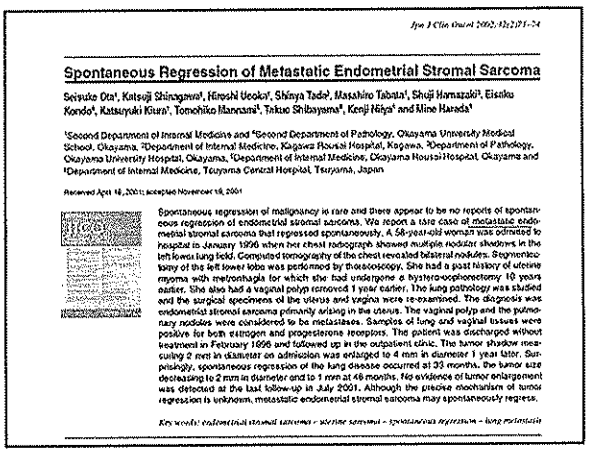
Stenford (PH)

- **Atypic cells**
- **≥10 mitosis /10 VPV**
- **Focuses of coagulation necrosis**

ENDOMETRIAL STROMAL SARCOMA

- **rares 15 %**
- **weak malignant potential <10 mytoses /10 VPV**
- **Average survival 11 years**
- **5-year survival in I st 80 %**
- **Hormonal th is effective**

- **High malignant potential**
- **5-year survival for I st 50 %**
- **Hormonal th is not effective**



Spontaneous Regression of Metastatic Endometrial Stromal Sarcoma

Seisuke Ota[1], Katsuji Shinagawa[2], Hiroshi Ueoka[3], Shinya Tada[2], Masahiro Tabata[1], Shuji Hamazaki[3], Eisaku Kondo[4], Katsuyuki Kiura[1], Tomohiko Maesawa[5], Takuo Shibayama[6], Kenji Niiya[4] and Mine Harada[1]

[1]Second Department of Internal Medicine and [2]Second Department of Pathology, Okayama University Medical School, Okayama, [3]Department of Internal Medicine, Kagawa Rousai Hospital, Kagawa, [4]Department of Pathology, Okayama University Hospital, Okayama, [5]Department of Internal Medicine, Okayama Rousai Hospital, Okayama and [6]Department of Internal Medicine, Tsuyama Central Hospital, Tsuyama, Japan

Received April 18, 2001; accepted November 19, 2001

Spontaneous regression of malignancy is rare and there appear to be no reports of spontaneous regression of endometrial stromal sarcoma. We report a rare case of metastatic endometrial stromal sarcoma that regressed spontaneously. A 58-year-old woman was admitted to hospital in January 1996 when her chest radiograph showed multiple nodular shadows in the left lower lung field. Computed tomography of the chest revealed bilateral nodules. Segmentectomy of the left lower lobe was performed by thoracotomy. She had a past history of uterine myoma with metrorrhagia for which she had undergone a hysterosalpingectomy 10 years earlier. She also had a vaginal polyp removed 1 year earlier. The lung pathology was studied and the surgical specimens of the uterus and vagina were re-examined. The diagnosis was endometrial stromal sarcoma primarily arising in the uterus. The vaginal polyp and the pulmonary nodules were considered to be metastases. Samples of lung and vaginal tissues were positive for both estrogen and progesterone receptors. The patient was discharged without treatment in February 1996 and followed up in the outpatient clinic. The tumor shadow measuring 2 mm in diameter on admission was enlarged to 4 mm in diameter 1 year later. Surprisingly, spontaneous regression of the lung disease occurred at 33 months. The tumor size decreasing to 2 mm in diameter and to 1 mm at 48 months. No evidence of tumor enlargement was detected at the last follow-up in July 2001. Although the precise mechanism of tumor regression is unknown, metastatic endometrial stromal sarcoma may spontaneously regress.

Key words: Endometrial stromal sarcoma – uterine sarcoma – spontaneous regression – lung metastasis

DIAGNOSTICS

- **Medical history: bleeding 80 %, pain 15-50 %**
- **Physical exam: palp. TM**

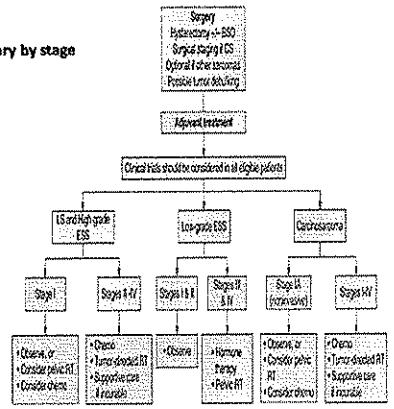
- **TVUltrasound - vaskularization, flow- ↓RI 0,37**
- **Probatory curretage (12/21)/ histeroscopy**
- **CA125 – no use**

- **Thoracic X ray / CT**
- **abdominal CT**

- **Definitive = PHD**
- **Determining the receptor status ...**

TREATMENT

Treatment summary by stage



- Abdominal washing for citology
- Histerectomy and bilateral adnexectomy – most important
- (selective lymphadenectomy – stage?)
  - Routinely NO in leyomiosarcomas abd endometrial stromal sarcomas

- Chemoth. - leyomiosarcomas (gemcytabine+docetaxel)
- Hormonal (medroksiprogesteron) - endometrial stromal sarcoma
  – low malignant potential (rec. status)
- Irradiation – leyomiosarcoma
- Reop. – secondary citoreduction

PROGNOSIS

Prognostic factors:

- FIGO stage
- Age
- Histologic type
- Histologic grade
- Nuclear grade
- Myometrial invasion
- Vascular/lymphatic invasion
- Size of tumor
- Peritoneal citology
- Hormone receptor status
- DNA ploidia and other biologic markers
- Treatment

FIVE-YEAR SURVIVAL AND PH TYPE OF SARCOMA

Overall Survival of Uterine Sarcomas (All Stages)	
Type	**5-Year Survival**
Malignant mixed mullerian tumor	35%
Leiomyosarcoma	25%
Endometrial stromal tumors	
Endometrial stromal sarcoma	60%
High-grade undifferentiated sarcoma	25%

Acharya, 2005

PROGNOSIS

worse in comparison to other gynecologic malignancies

FIVE-YEAR SURVIVAL IN FIGO:

- I stage - 76 %
- II stage - 60 %
- III stage - 45 %
- IV stage - 29 %

best prognosis is for endometral stromal sarcomas and worse for leyomiosarcomas

FIGO	I 57 %
	II 29 %
	III 35 %
	IV16 %