GENITOURINARY RADIATION THERAPY - PROSTATE, TESTICULAR, BLADDER CANCER

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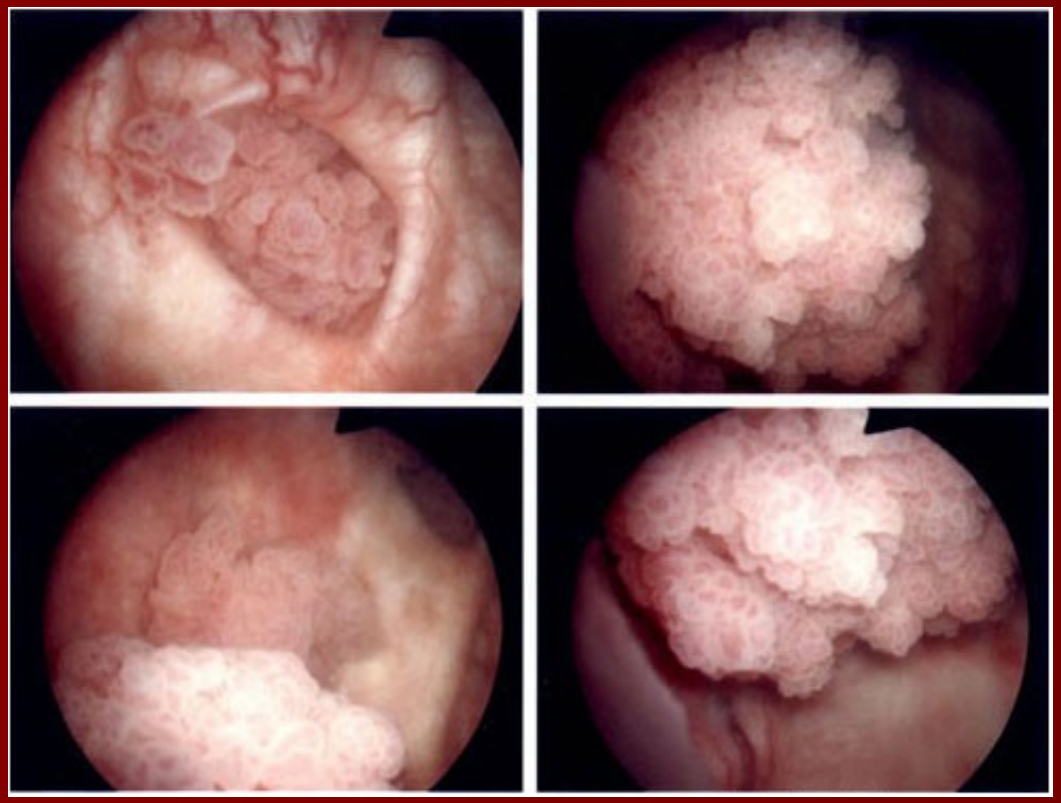
bladder cancer (C 67)



Bladder cancer ranks as the ninth most frequently-diagnosed cancer worldwide, with the highest incidence rates observed in men in Southern and Western Europe, North America, as well in certain countries in Northern Africa or Western Asia. Incidence rates are consistently lower in women than men, although sex differences varied greatly between countries. Diverging incidence trends were also observed by sex in many countries, with stabilising or declining rates in men but some increasing trends seen for women. Bladder cancer ranks 13th in terms of deaths ranks, with mortality rates decreasing particularly in the most developed countries; the exceptions are countries undergoing rapid economic transition, including in Central and South America, some central, southern, and eastern European countries, and the Baltic countries.

Bladder cancer

- 4 times more common in men than in women,
- most often recognized in the 7th decade of life (between 50 and 80 years old),
- bladder cancer has become a common cancer globally, with an estimated 430 000 new cases diagnosed in 2012.

Etiology

- (EXPOSURE WITH COMPOUNDS) exposure to chemicals (eg aromatic amines, aniline dyes, some industries - rubber, chemical, steel, gas,
- (SMOKING DEPENDENT) higher incidence of high-grade cancer; Schistosoma haematobium infection (Africa, Asia Minor) - chronic inflammatory conditions: squamous cell carcinomas (LONG TERM INFLAMMATION, INFECTION),
- (REIRRADIATION) of pelvis minor,
- chronic cyclophosphamide and phenacetin confirmed on animal model (DRUGS INTAKE);

Bladder tumors are a heterogeneous group with different malignancy potential (which should be considered in therapy – VERY HETEROGENOUS GROUP!).

Histology

- *urothelial carcinoma in situ* (it often goes to infiltrating type of cancer or both types comes toegether),

- *papillary urothelial carcinoma* - high-grade tumors and low grade malignancy, cells with different atypia,

- *infiltrating urothelial carcinoma* - every infiltrating cancer, evaluation based on a deep cut of the change along with the muscle membrane,

- *urothelial papilloma* - type of epithelial growth with cells difficult to distinguish from normal cells, rare, rarely recurrent;

Symptoms

- macro- or microscopic **hematuria**,
- urinary frequency,
- urinary urgency,
- miction disorders,
- pain of soft tissue, and of bones.

WORKUP

- history and physical (bimanual bladder examination with per rectum/per vaginam!),
- complete blood count with electrolytes and creatinine,
- urinalysis and urine cytology,
- cystoscopy,
- chest X-ray,
- TAUS,
- CT urography,
- abdominal and pelvic CT/MRI with contrast,
- TURbt → pathomorphological confirmation,
- other (in clinically indicated).

TAUS – transabdominal ultrasound, TURbt – transuretheral resection of the bladder tumor

Histology

papillary urothelial neoplasm of low malignant potential, PUNLMP - fast epithelial growth of skin lesions with a slight deviation from normal epithelium, exceeding 6 cell layers, tendency to progression, poor progression

Histology

- about 90% of all bladder cancers are transitional carcinomas,

Squamous carcinomas - 8%, glandular carcinomas - 2%, mixed forms that should be treated as transitional cell carcinomas, 1/3 cases are multifocal changes (often with cancer in situ) - prognosis in coexistence of invasive and pre-invasive lesions is worse (treatment as infiltrating forms),

- assessment of degree of differentiation G, main prognostic factor, next to T feature (poor differentiated carcinomas – 30% IMPORTANT RISK FACTOR !!!

Biology

- hematogenous metastases:
  - ✓ lungs,
  - ✓ liver,
  - ✓ bones of the pelvis and spine,
- lymph nodes metastases:
  - ✓ obturators,
  - ✓ pelvic,
  - ✓ paraaortic.

In patients with a history of hematuria without a reasonable cause, urinalysis with cytological examination and abdominal ultrasonography should be performed.

(with kidney, bladder and prostate evaluation)

- lack of early detection markers and monitoring the effects of treatment,
- cytological examination – not much useful in the diagnosis of malignant hyperplasia, in cases of high malignancy can be found tumor cells,
- urine test - a method used in screening in people who are particularly vulnerable (OCCUPATIONAL EXPOSURE – URINE EXAMINATION, NO MARKERS OF EARLY DETECTION)

Treatment

- it is important for clinical management to determine the extent of bladder wall infiltration,
- non-invasive ca: Ta, Tis or infiltrating only mucosa: T1 is a superficial carcinoma, T2 is the muscular layer infiltration,
- treatment and prognosis depend on the clinical stage of the disease, histopathological malignancy of bladder tumor.

Treatment

- depends on the stage of tumor progression, its differentiation and the nature of growth (superficial and invasive cancer), the treatment consists of prevention of recurrence and progression,
- superficial tumours **(Ta-T1)**: endoscopy (electrocautery and electrocoagulation),
- **T1 G3** - cystectomy is considered, as is in the case of **Tis** after failure of adjuvant treatment),
- in case of invasive infiltrating ca **(T2, T3) cystectomy** and in case of feature of **N+** adjuvant or neoadjuvant treatment is needed.

Surgery

- **transurethral resection (electroresection):** only superficial lesions,
- **partial cystectomy:** tumour removal with 3 cm margin; not in: deep tumour infiltration and high degree of malignancy,
- **cystectomy (radical step):** the primary way of treatment of infiltrating tumours, as well as for intra-bladder, local sparing and radiotherapy failures, the results of radical cystectomy are respectively 20% and 60% of 5-year and 10-year survival.

Radiotherapy

- used in the absence of consent for surgical treatment or when there are no indications for this treatment,
- teletherapy with radical doses: **45 Gy na miednicę + BOOST na guz pęcherza do 65 Gy**,
- better results together with chemotherapy,
- neoadjuvant and adjuvant radiotherapy requires modern technics of planning.

Chemotherapy

- in radical treatment is associated with other methods: intrabladder (superficial tumours, bCG, mitomycin, doksorubicin, epirubicin (induction of inflammation, immunostimulation - increase of probability of progression reduction),
- neoadjuvant: (20% CR, 20-45% PR) – no influence on OS,
- postoperative,
- alone only in paliative treatment.

Prognosis

- PUNLMP and papillary carcinomas with high maturity: 80 – 90%,
- 5-year OS in 0, I, II clinical stages: 50 -70%,
- in III clinical stage: 20-30%, and in IV-th average length of life from several to several months),
- best resorts get about 75% 5-year survival after cystectomy in low-level cases and 20% in advanced ones.

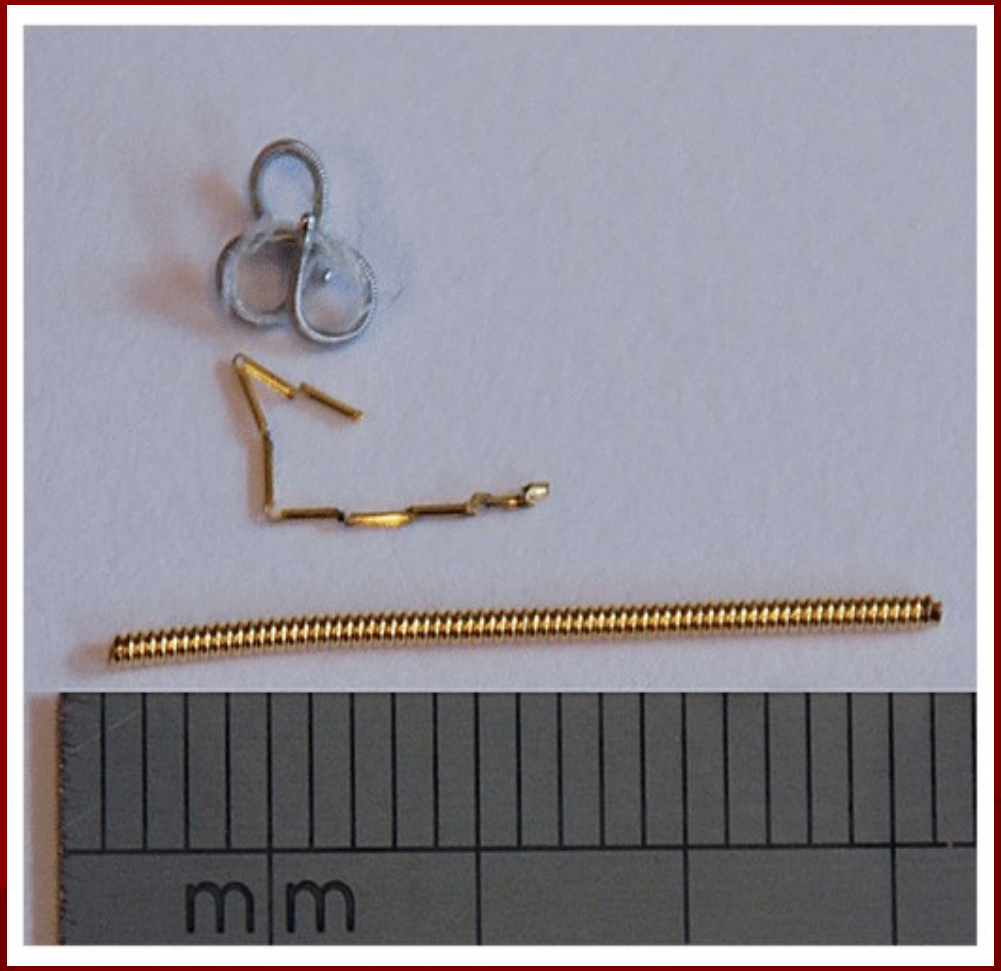
prostate cancer (C 61)

Symptoms

- asymptomatic,
- problems with urination,
- bone pain (in metastatic disease)

WORKUP

- history and physical (with DRE!),
- PSA,
- prostate biopsy (histopathology, GS),
- pelvic CT/MRI,
- bone scan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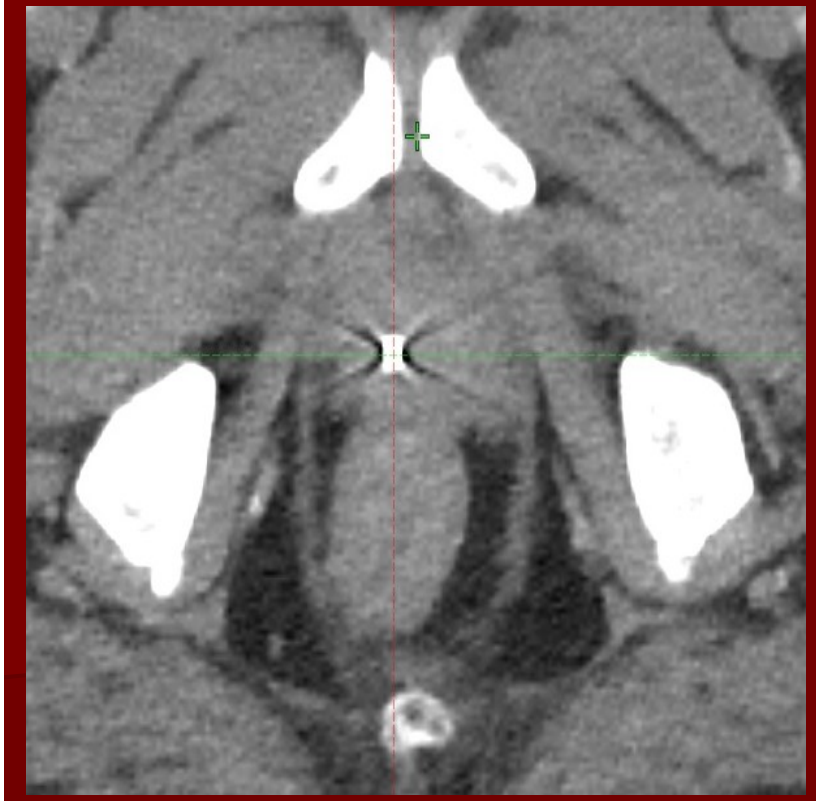


Prostate cancer

- more than 1.1 million cases of prostate cancer were recorded in 2012, accounting for around 8 per cent of all new cancer cases and 15 per cent in men.

- it is usually diagnosed at 60 years of age, the average age at diagnosis is 70 years,

- THE MAJOR RISK FACTOR IS AGE.

Prostate cancer

- 2-3 times more often in people whose relatives in the first line he was suffering from cancer; 2 cases increase risk 9-fold,
- Nutrition Facts: foods with large amounts of meat and saturated fats, low in selenium content and vitamin E (protective effect is attributed to diet high in soy, vegetables and fruits, cereal products),
- Race factors: most common among African Americans, the most common among the yellow, known role of hormones both in development as well and treatment.

Early detection

- per rectum examination - every year in men over 50 years old,
- determination of serum PSA in men with dysuria or suspicion in per rectum, PSA growth may occur in inflammation and benign prostatic hyperplasia,
- in case of abnormal result of one of these tests, the biopsy of the gland.

Histology

- the most common form is **adenocarcinoma** of varying degrees of differentiation, which is significant in prognosis,

- precancerous disease is intraepithelial neoplasia (PIN), prostatic intraepithelial neoplasia (PIN); High and low malignancy, PIN 2 and PIN 3 - high probability of coexistence (50%) or later onset of invasive cancer.

Histology

- Gleason score (correlates with prognosis and clinical grade, is based on the assessment of the architecture of hyperplasia, scale scores correspond to 5 types of histoarchitecture: type 1 - well differentiated to type 5 - low-grade cancer, 2 types are rated: dominant and next in relation to the area occupied, the sum of the points gives the final grade,
- from 2 to 10; The risk of metastases is: G1 (2-4 points) - 20%, G2 (5-7 points) – 40%, G3 (8-10 pts) – 75%,
- risk of death within 15 years depending on Gleason scale: 2-4 points - risk 4-7%; in the case of 8-10 points, up to 87% in a 55-year-old man.

PSA

- **tPSA score: 0,4 – 4,0 ng/ml** (2,5 ng/ml to 50 years, 4,0 ng/ml to 60 years, 5,4 ng/ml to 54 years, 6,6 ng/ml to 74 years),
- free fraction **fPSA** (P grows, when fPSA is low, if tPSA 4,0 – 10,0 ng/ml and fPSA < than its 10%, means that P of cancer is higher 50%; if fPSA > than its 30%, P of cancer minimal),
- if tPSA > 10,0 ng/ml and DRE is ok => biopsy under TRUS,
- if tPSA is ok and DRE is not => biopsy under TRUS,

Symptoms

- in case of limited prostate cancer - symptoms are often not present !!!,
- in case of local disease: dysuria, urinary frequency, hematuria,
- at the spread: bone pain (bone metastases) or lower extremity oedema (pelvic lymph node metastasis).

Prognostic and predictive factors

- clinical stage,
- age of the patient (higher mortality for young men),
- Gleason score (2-4 pts = good prognosis, survival time similar to that in the corresponding age without cancer diagnosis,> 7 = unfavorable prognosis),
- concentration and dynamics of PSA growth.

Diagnosis

- DRE,
- PSA level,
- TRUS (*transrectal ultrasonography*),
- TAUS (*transabdominal ultrasonography*),
- MRI of pelvis minor,
- Chest X-ray,
- Bone scintigraphy,
- CT of abdomen.

ADVANCES OF RADIOTHERAPY

Non-invasive

Similar outcomes to surgery

Easy to tolerate

Minimal impact on quality of life

DISADVANTAGES OF RADIOTHERAPY

- Time commitment
- Irritative symptoms
- Side effects

Keys to Successful Treatment

Goal: high dose to prostate, spare surrounding normal tissue (ie, precision)

Treatment Planning

Treatment Delivery

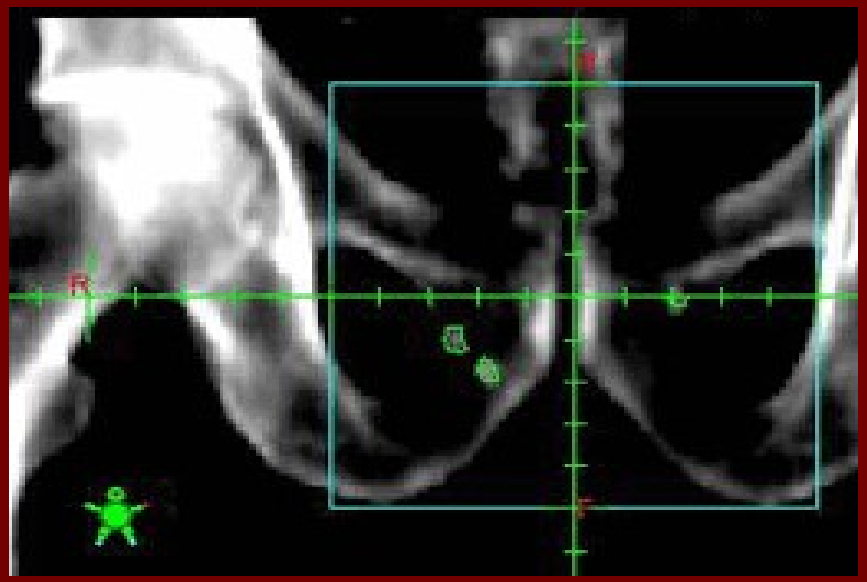
Buzz words: 3D Conformal, IMRT, IGRT

Treatment planning

Treatment planning:

- Fiducial marker placement
- CT scan + MRI

(molds, tattoos)



Side effects

Short term:

- bladder irritation: increased frequency
- rectal irritation: diarrhea
- fatigue

Long term:

- erectile dysfunction
- rectal irritation

Treatment

- cancer limited to organ (T1, T2),
- cancer in pelvis minor (locoregional, T3N1),
- dissemination.

- prostatectomy with/without lymphadenectomy,
- radiotherapy (teletherapy and/or brachytherapy, high doses).

Treatment

- cancer limited to prostate (T1, T2) – **radical treatment**: **radical prostatectomy or radiotherapy** => **PARALLEL METHODS** (among patients with unfavorable prognostic factors prostatectomy goes with lymphadenectomy +/- radiotherapy +/- hormone therapy,
- strict PSA control, in case of rise analogs LHRH and/or antiandrogens,
- *watchful waiting ?*.

Treatment

- cancer limited to pelvis minor (T3), radical treatment: radical hormone therapy, to consider prostatectomy with lymphadenectomy with continuation of hormonal treatment.

Treatment

- cancer limited to pelvis but advanced ! as (T4 lub N1, lub M0): **androgens ablation with radiotherapy,**
- **disseminated** (T4 lub N1, lub M1): **androgens ablation.**

Treatment

- palliative surgical procedures: TURP, PPN = percutaneous renal fistula,
- in case of ureteral infiltration, palliative radiotherapy for lesions, also for metastatic lesions,
- bisphosphonates,
- radioactive isotope (Strontium).

Treatment: **hormone therapy**

- surgical castration: orchidectomy, the cheapest treatment, comparable efficacy and quality of life of people with castration,
- antiandrogens: eg. finasteride, flutamide, cyproterone acetate, bicalutamide,
- pharmacological suppression: agonist drugs = gonadoliberin analogs (LHRH) used alone or in combination with antiandrogens, eg. Goserelin,
- estramustine: combination of estrogen with an alkylating agent, eg. estradiol + chlormethine - lack of efficacy from other hormonal treatments; 2nd line: gestagens, ketoconazole, aminoglutethimide.

testicular cancer (C 62)

Testicular cancer

- INCREASING INCIDENCE OF TESTICULAR CANCER WORLDWIDE, testicular cancer is the most common malignancy in 20 to 34-year-old men. Numerous publications have shown an increase in the incidence of testis cancer in the last 40 years with substantial differences among countries,
- >95% are germ cell tumours=seminomas and non-seminomas,
- seminomas is the most common single histology
- risk factors: undescended testicle, polivinyl chloride exposure, advanced maternal age, Down's syndrome, Klinefelter's syndrome, perinatal estrogen exposure but rather no data on the importance of environmental.

Worldwide we observed a clear trend toward an increased TC incidence in the last 30 years in the majority of industrialized countries in North America, Europe and Oceania. Nevertheless, surprising differences in incidence rates were seen between neighboring countries (Finland 2.5/100,000 cases versus Denmark 9.2/100,000) as well as among regions of the same country (2.8 to 7.9/100,000 according to various regional French registers). In addition, substantial differences in the TC incidence and trends were observed among ethnic groups. The increase in the TC incidence was significantly associated with a birth cohort effect in the United States and in European countries. To date except for cryptorchidism no evident TC risk factor has been clearly demonstrated, although the environmental hypothesis with a key role of endocrine disrupters has been put forward by several groups.

Testicular cancer

- 90% of testicular cancers are germ cell tumors, the remaining 10% are sex cors tumours and lymphomas,
- germ cells tumours: seminomas and non-seminomas,

Testicular cancer

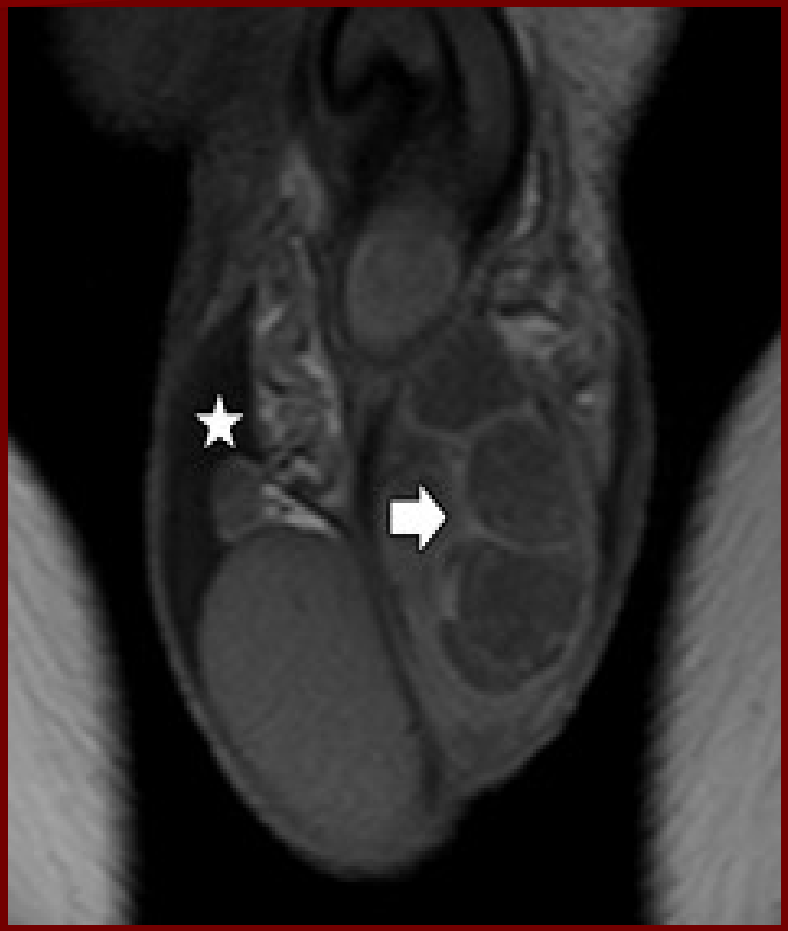
- the most common type of histology occurs alone or in combination with other types of weaning - it can produce beta-hCG and LDH but never AFP; The spermatocyte seminoma subtype is present in older men with lower metastatic potential and normal levels of markers,

Symptoms

- one sided, painless enlargement of a part or whole testis,
- red scrotum
- inflammation or testicular pain in 25% of the patients.

WORKUP

- history and physical examination (manual testicular examination!),
- testicular ultrasound,
- AFP, beta-hCG, LDH,
- chemistry profile,
- chest X-ray,
- **pathomorfological confirmation – radical inquinal orchidectomy**,
- abdominal and pelvic CT,
- chest CT,
- repeat AFP, beta-hCG, LDH 7 up to days after orchidectomy, chorionic gonadotropin
- other (brain MRI, bone scan, PET-CT – if clinically indicated).



Diagnosis

- the most important is microscopic examination of the entire testicle removed from the inguinal canal - no needle biopsy is required !!! NO BAC !!!,

- U-sound test - allows you to recognize change, does not differentiate the nature of the tumor !!!,

-no screening examination.

Treatment: **seminomas**

- ORCHIDECTOMY any clinical stage,
- I clinical stage: **radiotherapy:** postresection to lymph nodes chain – paraaortic +/- pelvic, 20-30 Gy or carboplatin 2 cycles,
- II clinical stage: II A, II B (large lymph nodes, 5 cm) – **radiotherapy to paraaortic + pelvic lymph nodes, 30-36 Gy** , II C (lymph nodes larger than 5 cm) - **chemiotherapy –** BEP, 3 – 4 cycles (bleomycin, etoposide, cisplatin) with radiotherapy to remnants changes after chemotherapy,
- III clinical stage: **chemiotherapy** – 3 - 4 - 5 cycles of BEP.

Treatment : **non seminomas**

- ORCHIECTOMY AND CHEMO- !!!
- I clinical stage: observe lub **lymphadenectomy** (if risk factors) lub or 2 shedules of BEP,
- II clinical stage:
  - II A: **lymphadenectomy** retroperitoneal,
  - II B, II C: **chemiotherapy -** BEP 2-3 cycles,
- III clinical stage: **chemiotherapy** - 4-5 cycles BEP.

Prognosis: **nonseminomas**

1. **good prognosis** – 5-year OS: 90%,
   AFP<1000 ng/ml, βHCG 5000 IU/l, LDH ponad 1,5 x N,
2. **mediocre prognosis – 5-year OS**: 80%
   AFP 1000-10 000 ng/ml, βHCG 5000-50 000 IU/l, LDH < 10 x N,
3. **poor prognosis** – 5-year OS: 70%
   AFP> 10 000 ng/l, βHCG > 50 000 IU/l, LDH > 10x N.

Prognosis: **seminomas**

I clinical stage - almost 100%,

II clinical stage - 70-90%,

III clinical stage - about 70%.

- 15-20% relapse without tratment
- 5% of relapses after radiotherapy