Testicular Cancer: Management and Post-Treatment Survivorship

UNC Lineberger Cancer Network
Patient Centered Care
Mary W. Dunn, MSN, RN, OCN, NP-C
Adult Nurse Practitioner
Department of Urology & Department of Medicine, Division of Oncology

UNC LINEBERGER UNC CANCER CARE

1

Objectives

- Identify treatment options for testicular cancer depending on the subtype and stage
- Discuss common treatment-related side effects
- Describe three challenges that patients may face in the post-treatment survivorship phase

UNC UNC

2

Definition

Testicular cancer is a disease in which malignant cells arise in the testicle

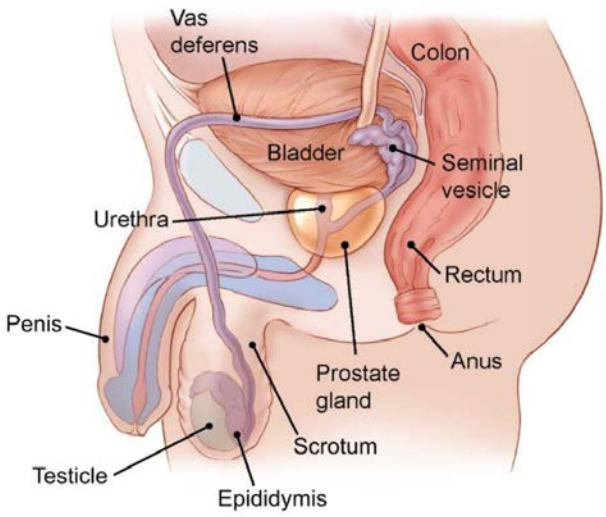
More than 90% of cancers of the testicle develop in germ cells (cells that make up the sperm)

3

Anatomy

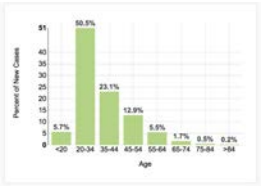
- Testicles are part of the male reproductive system
  - Produce male hormones like testosterone
  - Produce sperm
  - Oval; 4-5 cm in length
- Multi-layered tunica cover the testes
- Seminiferous tubules are the site of spermatogenesis
- Epididymis: Coiled tube attached to the testis where sperm mature
- Vas Deferens: Sperm travel from epididymis via the vas

4



5

Epidemiology



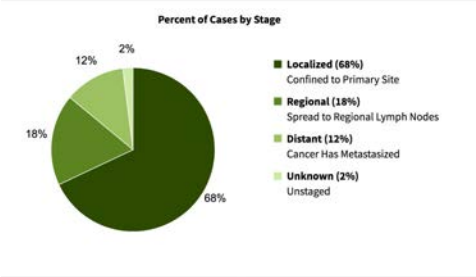
- 2021: 9,470 new cases
- 2021: 440 deaths

- Lifetime risk: 1 in 250
  - Risk of death: 1 in 5,000
- Average age at diagnosis: 33
  - 6% of cases occur in children and teens
  - 8% of cases occur in men over 55

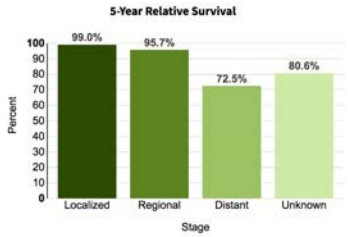
- Accounts for about 0.5-1% of all male cancers
  - ~24th most common
- Most common cancer in boys/men ages 15-35

6

Epidemiology



Percent of cases by stage at diagnosis



5-year relative survival by stage at diagnosis

7

Risk factors

- Cryptorchidism (undescended testicle)
  - 7-10% of patients w/ testicular cancer have cryptorchidism
- Family history
  - Father or brother
  - Only a small # occur in families
- HIV
- Personal history
  - 3-4% of men will develop bilateral tumors
- Caucasian
- Infertility
  - 2.8 x more likely than general population

8

Clinical Presentation

- Most often, painless mass/lump in the testicle
- Heaviness, aching in lower abdomen or scrotum
- Gynecomastia, breast tenderness
  - Caused by high levels of human chorionic gonadotropin (hcg)
- Advanced disease
  - Low back pain (RPLN mass)
  - SOB, CP, cough (pulm mets)
  - Abdominal pain
  - 10-12% present w/ distant mets disease
  - 1-2% have bil disease at diagnosis

9

Work-up & Diagnosis

- Physical exam
- Scrotal ultrasound
  - Sensitivity near 100% when combined with PE
  - Typically well defined and hypoechoic
- Tumor markers
  - Pre-orchiectomy
  - Post-orchiectomy
    - Should be a predictable decline
  - Post-chemo/XRT
    - Therapeutic lag
  - CXR

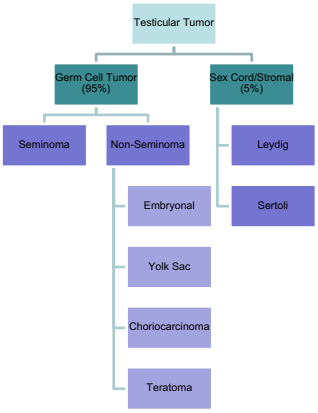
10

Serum Tumor Markers

Alpha-Fetoprotein	• Pure embryonal, yolk sac, mixed; not chorio or pure seminoma • Half life 5-7 days
Beta-human chorionic gonadotropin	• All chorios, 40-60% embryonal, 5-10% seminoma • Half life 24-36 hours
Lactate Dehydrogenase	• Low specificity for GCT; many false + • Half life 4-5 days

11

Histologic Variants



12

NSGCT vs Seminoma

1. Mixed Tumor
   1. Mixture of seminoma and nonseminoma
2. Embryonal Carcinoma
   1. Grey/white fleshy mass, papillary projections
   2. AFP and HCG
3. Yolk sac Tumor
   1. Yellow/pale grey, Schiller-Duvall bodies
   2. AFP and HCG
4. Choriocarcinoma
   1. Grey/white, syncytiotrophoblasts and cytotrophoblasts
   2. Never AFP, always HCG
   3. Worst prognosis of all testis tumors
5. Teratoma
   1. Cystic with multiple germ cell layers in different stages of maturation
   2. No AFP or HCG
   3. Chemo and radiation resistant

1. Classic
   1. 95% of Seminomas
   2. Large uniform cells with clear cytoplasm and distinct cell borders, lobulated and pale
2. Spermatocytic
   1. 5% of Seminomas
   2. Low metastatic potential

13

Age/STMs/Treatment Response

Tumor	Age	AFP	HCG	XRT	Chemo
Yolk Sac	<10	Maybe	Maybe	Resistant	Sensitive
Chorio	20-30	Never	Always	Resistant	Sensitive
Embryonal	25-35	Maybe	Maybe	Resistant	Sensitive
Teratoma	25-35	Never	Never	Resistant	Resistant
Seminoma	30-40	Never	Maybe	Sensitive	Sensitive

14

Radical Orchiectomy

- Inguinal approach
  - Testis removed with the surrounding tunica vaginalis, spermatic cord up to the level of the internal inguinal ring
- Avoid seeding the scrotum and disrupting the lymphatics
  - Trans-scrotal biopsy and trans-scrotal orchiectomy increase risk of local recurrence
- 1 hour operation
- Day op or overnight

15

Post-orchiectomy evaluation

- Post-orchiectomy markers
  - It takes > 5 half-lives to eliminate circulating markers
  - 1-2 weeks for HCG; 3 weeks for LDH; 5 weeks for AFP
  - S stage is determined using the nadir value of post-orch markers
- CT abdomen and pelvis (chest if abnormal CXR or CT AP)
  - CT cannot differentiate between cancer, teratoma, necrosis, fibrosis
  - Abdominal CT has a 30% false negative rate

16

Staging

AJCC Staging System for Testicular Cancer

T: Primary Tumor Staging	
pTx	Primary tumor cannot be assessed
pT0	No evidence of primary tumor
pTis	Intratubular germ cell neoplasia (carcinoma in situ)
pT1	Tumor limited to testis and epididymis without LVI; tumor may invade tunica albuginea but not tunica vaginalis
pT2	Tumor limited to the testis and epididymis with LVI or tumor extending through the tunica albuginea with involvement of the tunica vaginalis
pT3	Tumor invades the spermatic cord with or without LVI
pT4	Tumor invades the scrotum with or without LVI

N: Regional LN Clinical Staging (cN)		N: Regional LN Pathologic Staging (pN)	
cNX	Regional LN cannot be assessed	pNX	Regional LN cannot be assessed
cN0	No regional LN metastasis	pN0	No regional LN metastasis
cN1	LN mass ≤2cm in greatest dimension; or multiple LN, none >2cm	pN1	Metastasis with a lymph node mass ≤2cm in greatest dimension and ≤5 lymph nodes positive, none >2cm
cN2	LN mass >2cm but not >5cm in greatest dimension; or multiple LN, any mass >2cm but not >5cm	pN2	Positive LN >2cm but not >5cm in greatest dimension; or >5 positive LNs, none >5cm; or evidence of extranodal extension
cN3	LN mass >5cm in greatest dimension	pN3	LN mass >5cm in greatest dimension

M: Metastatic Disease Staging		S: Serum Tumor Markers Staging	
Mx	Distant metastasis cannot be assessed	Sx	Markers not available or not performed
M0	No distant metastasis	S0	Marker levels normal
M1a	Non-regional LN or pulmonary metastasis	S1	LDH <1.5 × ULN and B-hCG <5,000 and AFP <1,000
M1b	Non-pulmonary visceral metastases	S2	LDH 1.5–10 × ULN, or B-hCG 5,000–50,000, or AFP 1,000–10,000
		S3	LDH >10 × ULN or B-hCG >50,000 or AFP >10,000

Stage Grouping	TNMS
0	pTis, N0, M0, S0
IA	pT1, N0, M0, S0
IB	pT2-T4, N0, M0, S0
IS	Any pT/Tx, N0, M0, S1-3
IIA	Any pT/Tx, N1, M0, S0-1
IIB	Any pT/Tx, N2, M0, S0-1
IIC	Any pT/Tx, N3, M0, S0-1
IIIA	Any pT/Tx, Any N, M1a, S0-1
IIIB	Any pT/Tx, Any N, M1a, S2 Any pT/Tx, N1-3, M0, S2
IIIC	Any pT/Tx, N1-N3, M0, S3 Any pT/Tx, Any N, M1a, S3 Any pT/Tx, Any N, M1b, Any S

17

Risk categories

Risk Status	Nonseminoma	Seminoma
Good Risk	All of the following: -testicular or retroperitoneal primary tumor -M0 or M1a -S0 or S1	All of the following: -Any primary site -M0 or M1a -Normal AFP
Intermediate Risk	All of the following: -testicular or retroperitoneal primary tumor -M0 or M1a -S2	All of the following: -Any primary site -M1b -Normal AFP
Poor Risk	Any of the following: -Mediastinal primary tumor -M1b -S3	No patients are classified as poor risk

International Germ Cell Consensus Collaborative Group

18

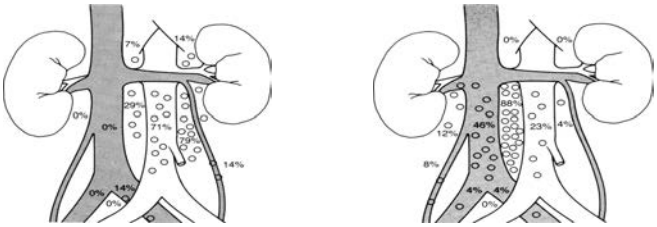
Metastasis from Testis Tumors

- Usually lymphatic spread
  - Chorio and yolk sac may metastasize hematogenously
- Retroperitoneal LN are the most common site of metastasis
- When normal lymphatic flow has not been altered, lymphatic spread occurs in a predictable and stepwise pattern
  - Right→ interaortocaval RPLN
  - Left→ left para-aortic RPLN
  - Often spread from right to left, and rarely left to right

19

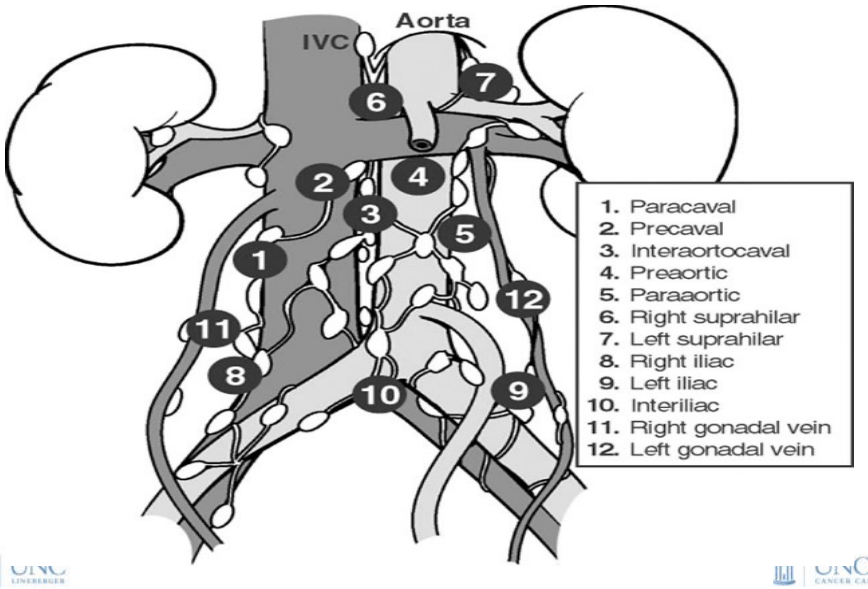
Metastasis from Testicular Tumors

- Inguinal nodes
  - If tumor invades through tunica vaginalis or into scrotum
  - Previous scrotal or inguinal surgery
- Pelvic nodes
  - If tumor invades into the epididymis or spermatic cord
- Distant non-node (most to least common)
  - Lung, liver, brain, bone, kidney, adrenal, GI tract, spleen



20

Retroperitoneum



21

Treatment after Orchiectomy

22

Primary Chemotherapy

- Cisplatin is the most effective agent against GCT
- Bleomycin/Etoposide/Cisplatin (BEP) or Etoposide/Cisplatin (EP)
- Bleomycin: Antitumor antibiotic that binds to and breaks DNA
  - SE: Pneumonitis, pulmonary fibrosis, nail/skin change
- Etoposide: Alkylating agent
  - SE: Myelosuppression, mucositis, vomiting, alopecia
- Cisplatin: Cross links DNA
  - SE: Nephrotoxicity, neurotoxicity, ototoxicity, nausea, vomiting
- Carboplatin: Cross links DNA
  - SE: Myelosuppression, nausea, vomiting, neuropathy
  - One cycle is a tx option for stage IA or IB pure seminoma
  - Carbo should not be substituted for Cis in good risk patients because it results in a lower complete remission rate

23

Other chemotherapy

- **Salvage Chemotherapy**
  - Indication: Progression on primary chemo or relapse after primary chemo
  - Regimens: Usually 4 cycles
    - Etoposide, Ifosfamide, Cisplatin (VIP)
    - Vinblastine, Ifosfamide, Cisplatin (VeIP)
    - Taxol, Ifosfamide, Cisplatin (TIP)
  - CR: 50%; sustainable DR: 25%
- **HD Chemotherapy and Auto Bone Marrow Transplant**
  - Indication: Extremely poor prognosis or poor response to standard chemo
  - Auto transplant after HDC because HDC kills marrow
  - 10-20% achieve durable remission
  - 5-10% mortality

24

Radiation and RPLND

- **External Beam Radiation Therapy (XRT)**
  - Treatment for Stage I, IIA, or IIB pure seminoma
  - Toxicities = Nausea, vomiting, fatigue, bone marrow suppression, gastritis, peptic ulcer, secondary cancers
  - Prior abdominal XRT, IBS, should consider surveillance
- **Retroperitoneal Lymph Node Dissection (RPLND)**
  - Modified Template: Avoids RP dissection on contralateral side
  - Nerve sparing preserves nerves within the template
  - Right & left templates
  - If a palpable nodal met is discovered during a modified template, a full bilateral template should be performed
  - Margins of resection should not be compromised to maintain the template or preserve ejaculatory function
  - Morbidity is higher for post-chemo RPLND

25

Pure Seminoma

- Stage IA or IB:
  - pT1-pT2: Observation, Carboplatin x 1 or XRT
  - pT3-pT4: Carboplatin x1 or XRT
  - XRT 20 Gy or 25.5 Gy
- Stage IIA, IIB
  - XRT or
  - BEP x 3 or EP x 4
- Stage IIC or III: Chemotherapy
  - Good risk: BEP x 3 or EP x 4
  - Intermediate risk: BEP x 4 or VIP x 4

26

NSGCT

- Stage I (no risk factors)
  - Surveillance, NS-RPLND or BEP x 1
- Stage I (with risk factors; LVI, spermatic cord)
  - Surveillance or BEP x 1 or NS-RPLND
- After NS-RPLND
  - pN0: Observe
  - pN1 or pN2: Observe or EP x 2
  - pN3: EP x 4 or BEP x 3
- Stage IIC or III: Chemotherapy
  - Good Risk = BEP x3 or EP x 4
  - Intermediate and Poor Risk = BEP x 4
  - Complete Response= observe
  - Partial Response = NS-RPLND
  - Poor Response = Salvage therapy

27

5-year Overall Survival

Stage	Risk Status	Seminoma	Nonseminoma
I	-	>98%	>98%
IIA or IIB	-	>95%	>95%
IIC or III	Good	86%	94%
	Intermediate	72%	83%
	Poor	-	71%

28

Question 1

Which of the following is a treatment option for good risk stage IIC NSGCT?

1. Surveillance
2. Radiation plus 1 cycle of Carboplatin
3. Radiation only
4. BEP x 3 cycles

29

Treatment Complications

- Hypogonadism
  - Usually not caused by unilateral orchiectomy alone
  - Bilateral orchiectomy
  - Cisplatin-based chemotherapy has severe dose-dependent effects on spermatogenesis
  - Complications related to hypogonadism: Osteoporosis, metabolic syndrome, type II diabetes, cardiovascular disease
  - Associated with diminished QOL
  - Screening
  - Treatment
- Infertility (SPERM BANK!)
  - Chemotherapy: Affect endocrine testicular function v direct impact on spermatogenesis
  - RPLND: Retrograde ejaculation resulting in infertility
    - Nerve sparing
  - Radiation therapy: Improper delivery
  - Spermatogenesis recovery: 50% in 2 years, 80% in 5 years
  - Fertility Preservation Programs
  - Psychosocial support

30

Treatment Complications

- Neuropathy
  - Chemotherapy induced
  - Protect hands and feet
  - Medical management
  - Loose clothing, good shoes
- Fatigue
  - Treatment induced, hypogonadism, depression
  - Treat underlying cause(s)
  - Good sleep hygiene
  - Regular exercise
- Anxiety/Depression
  - Caused by cancer experience or pre existing
  - Mental health providers
  - Medical management
  - Encourage participation in support groups

31

Treatment Complications

- Ototoxicity
  - Tinnitus/high frequency hearing loss, 4-8MHz (~20% of patients)
  - Assess noise exposure
  - Audiometry
- Nephrotoxicity
  - Decrease in GFR may not improve over time
  - Long-term renal function
- Pulmonary toxicity
  - Bleomycin toxicity
  - Smoking cessation
  - PFTs prior to bleomycin and as needed
- Pain
  - Chronic pain related to post-operative complications

32

Treatment Complications

- Cardiovascular Toxicity
  - **Direct hypothesis**: Chemo causes diffuse endothelial damage, including coronary arteries, gradually leading to cardiovascular disease
    - Raynaud's phenomenon: 25-61% of survivors
    - Microalbuminuria: Present in 12% of patients treated with chemo and in <1% of those treated with orchiectomy or healthy age-matched controls.
    - Laboratory markers of inflammation: von Willebrand factor, fibrinogen, tissue-type plasminogen activator, CRP
    - Circulating endothelial cells
    - Platelet aggregation caused by Cisplatin thought to explain increased incidence of MI in young patients with no other risk factors.
  - **Indirect hypothesis**: Chemo leads to an increased incidence of cardiovascular disease risk factors including hypertension, hyperlipidemia, and the metabolic syndrome, which increase risk of cardiovascular disease.
    - Hyperlipidemia (32-82%)
    - Hypertension (50%)
    - Obesity (48%) BMI > 25
- Cardiac workup should be based on clinical presentation
- Evidenced-based screening guidelines do not exist

33

Treatment Complications

- Second Malignant Neoplasms
  - Testicular Cancer survivors experience a 1.7-3.5 fold increased overall risk for Second Malignant Neoplasms compared to the general population
  - Risks After Radiotherapy
    - Leukemia: Absolute risk is low, ~9 cases per 10,000 patients per year followed for 15 years after 25Gy of a/p radiotherapy
    - Solid Cancers: Risks increase 5 years after treatment. Melanoma, lung*, thyroid, esophagus*, pleura*, stomach, pancreas, colon, rectum, kidney, bladder, connective tissue
      - *Supradiaphragmatic XRT rarely used anymore
    - Limit total amount of radiation without compromising cure rate
  - Risks After Chemotherapy
    - Leukemia: Absolute risk is low ~16 cases per 10,000 patients per year followed for 15 years
    - Solid Cancer: Related to prolonged accumulation on cisplatin?
  - Prior treatment may limit therapeutic options
  - Diagnostic radiation exposure
    - Conflicting results

34

Question 2

You are counseling a patient about toxicity associated with Bleomycin. What side effect is unique to this chemotherapy agent used for testis cancer treatment?

1. Restless leg syndrome
2. Pulmonary toxicity (e.g., pneumonitis)
3. Dry mouth
4. Lower extremity edema

35

Post-treatment

- After completion of treatment(s), patients transition into a surveillance program
- NCCN Guidelines
- "Usual practice" for all cancers
  - Most followed by primary oncology provider
  - Focus on monitoring for cancer recurrence and evaluating for persistent toxicity
- Challenges
  - Survivors can get lost in the shuffle in busy practice, where focus may be on patients who are undergoing active treatment
  - Underutilization of developing comprehensive follow-up plan that includes monitoring for late-term effects and optimizing use of specialty services
  - Ownership of care when patient has seen multiple oncology specialists

36

Models of Survivorship Care

- Community-based, shared-care model
  - Most adult cancer survivors are treated in a community setting
  - Extensively studied in chronic diseases
    - E.g. Diabetes managed by both PCP and endocrinology
  - Oncology provider
    - Delivers cancer therapy
    - Keeps PCP informed
    - Guidance in long-term survivorship care (including Survivorship Care Plan)
    - Transition care back to PCP at appropriate time
    - Available for questions, consults, referrals
  - Primary care provider
    - Address physical and emotional needs
    - Assume care of aspects that are feasible in primary care setting
    - Refer for problems/periodic evaluations
    - Consult in areas of uncertainty

37

Models of Survivorship Care

- Academic Medical Centers
  - Disease-specific cancer survivor programs
    - Earliest iteration of models for adult cancer survivorship care
  - Comprehensive Survivor Programs
    - Consultative model
      - Primary oncologist refers patient for a one-time visit with the survivor-program staff
      - Oncology summary, surveillance plan, counseling re: late effects, psychological needs, risk reduction
    - Nurse practitioner-led survivor clinic
      - Embedded within the treatment team
      - Survivors are transitioned to the NP for formal follow up
    - Specialized multidisciplinary survivor clinic
      - MDs, APPs, SWs, RNs, psychologists, network of consultative specialists, all of whom specialize in the care of cancer survivors

38

Models of Survivorship Care

- Unclear which models of survivorship care translate to improved patient outcomes
- Debate about who should be responsible for developing and providing a personalized plan for posttreatment care (even among groups in the same institution)
- Based on setting, resources, cancer diagnosis/treatment

39

Components of Survivorship Care

- Coordination
  - Communication among patients, cancer team, PCP
  - Treatment summaries
  - Care Plans
- Prevention and Detection
  - Promoting healthy behaviors (physical activity, diet, substance use, sun protection)
  - Age appropriate screening procedures
- Surveillance
  - Assessment for recurrence
  - Late effects
- Intervention for consequences of cancer and treatment
  - Physical
  - Psychological
  - Social
  - Spiritual

Based on IOM report

40

Survivorship Care Plan (SCP)

- Incorporates treatment summary
- Oncology follow-up schedule
  - Based on NCCN Guidelines
  - Interval and what is being done at each visit
- Health maintenance and promotion
  - General
  - Exercise
  - Nutrition
  - Smoking
- Possible late effects of cancer and cancer treatment
- Support services
- Resources

41

Testicular Cancer Treatment Summary

- Surgical procedures (date, surgeon)
  - Orchiectomy: Laterality, pathology
  - RPLND: Template, pathology
- Chemotherapy (end date, medical oncologist)
  - Name, dose, number of cycles
- Radiation (end date, radiation oncologist)
  - Fields, fractions

42

Why does survivorship care matter for testis cancer patients?

- Immediate and long-term treatment-related toxicities
  - Sexual health
    - Infertility
    - Hypogonadism
    - Retrograde ejaculation
  - Chemotherapy-induced toxicity
    - Ototoxicity
    - Nephrotoxicity
    - Neuropathy
    - Fatigue
    - Cardiovascular toxicity
  - Mental health
    - Depression, anxiety
    - Body image
  - Secondary malignancies
- Extensive follow up schedules

43

Testicular Cancer Survivorship Clinic

- History
  - Established in 2008 as a vision of Liz Sherwood, NP and Paul Godley, MD
  - The LIVESTRONG Survivorship Center of Excellence at UNC Lineberger was formed with a $1.5 million grant and charged with developing survivorship programs and services
  - Was one of seven National LIVESTRONG Centers of Excellence
  - Prior to this, patients followed with either urologist or medical oncologist, sometimes both.
    - Before revision of NCCN guidelines, could be seeing a patient upwards of every 2 months
- Current
  - Monthly, Nurse practitioner-led clinic
  - Transitioned to this model in ~2011

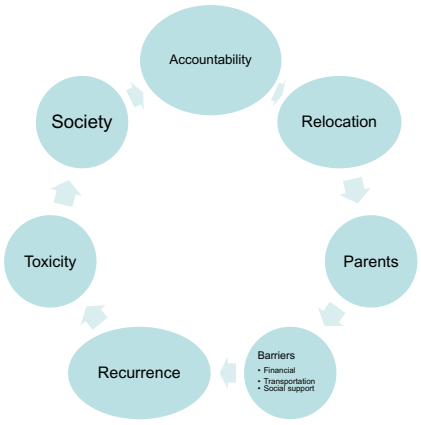
44

Testicular Cancer Survivorship Clinic

- Transition into clinic following definitive treatment
  - Provider-dependent
  - Usually happens after first surveillance visit following chemo or surgery
- If patient has not received his SCP, I will review and provide with a copy
  - Used to be a Word document that I wrote for each patient!
- History, PE
- Review diagnostics
- Side effect management
- Discussion of health maintenance issues and priorities
  - Exercise, balanced diet, substance use, sexual practices, body image concerns
  - Referrals as needed
- Assessment of any issues relating to uncertainty
  - Fear, anxiety, worry

45

Challenges



46

Benefits

- Consistent, high quality expert care
  - Provision of care plans
  - Management of late and long-term SE
  - Counseling on general health promotion strategies
  - Coordination/communication of care among members of the health-care team
  - Continuity
- Frees up MD schedules to see new patients or patients in active treatment
- Helps meet need since shortage of oncologists
- Fosters communication between NP and PCP
- Sustainable and cost-effective

47

Question 3

Testicular cancer survivors may have unique needs as compared to pediatric patients and older adults. What are some challenges that they may face?

1. Long-term effects of treatment on fertility
2. Difficulty discussing emotional aspects of their cancer experience given societal standards
3. Barriers to adhering to surveillance schedule due to relocation due to college graduation, marriage, military deployment, career moves, etc.
4. All of the above

48

Summary

- Testicular cancer has an overall low incidence, but most common in ages 15-40
- Highly treatable and curable; but delay in treatment can decrease overall survival
- Treatment options depend on subtype and stage
- Toxicities can be immediate or long-term
- Post-treatment surveillance care should include all aspects components of survivorship care

49

Resources for Patients

50

References

- Amin MB, Edge SB, Greene F, et al., eds. AJCC Cancer Staging Manual, 8th ed. New York: Springer International Publishing; 2017
- Gospodarwicz MK, Sturgeon JF, Jewett MA. Early stage and advanced seminoma: role of radiation therapy, surgery, and chemotherapy. Semin Oncol 1998; 25: 160-173.
- Hewitt, M, Greenfield, S, & Stovall, E. From Cancer Patient to Cancer Survivor-Lost in transition. 2006. Washington, DC. National Academics Press.
- Huddart RA, Norman A, Shahidi M, et al. Cardiovascular disease as a long-term complication of treatment for testicular cancer. J Clin Oncol 2003; 21: 1513-1523.
- International Germ Cell Consensus Classification: a prognostic factor-based staging system for metastatic germ cell cancers. International Germ Cell Cancer Collaborative Group. J Clin Oncol. 1997: 15 (2): 594-603. Landmark
- Kollmannsberger C, Tandstad T, Bedard PL, et al. Patterns of relapse in patient with clinical stage I testicular cancer manded with active surveillance. J Clin Oncol 2015; 33: 51-57.
- Mortenson MS, Bandak M, Kier MG, et al. Surveillance versus adjuvant radiotherapy for patients with high-risk stage I seminoma. Cancer 2017; 123: 1212-1218.
- Nekhyudov L, Ganz PA, Arora NK, and Rowland JH. Going Beyond Lost in Transition: A Decade of Progress in Cancer Survivorship. J Clin Oncol. 2017;35(18). 1978-1981.
- Oliver RT, Mason MD, Mead GM, et al. Radiotherapy versus one dose carboplatin in adjuvant treatment of stage I seminoma: a randomized trial. Lancet 2005; 366: 293-300. Landmark
- SEER Cancer Statistics Factsheets: Testicular Cancer. National Cancer Institute. Bethesda, MD. 2021. Available at: https://seer.cancer.gov/statfacts/html/testis.html. Accessed November 12, 2021
- Soper MS, Hastings JR, Cosmatos HA, et al. Observation versus adjuvant radiation or chemotherapy in the management of stage I seminoma: clinical outcomes and prognostic factors for relapse in a large US cohort. Am J Clin Oncol 2014; 37: 356-359.

51

References

- Sweeney CJ, Hermans BP, Hellman DK, et al. Results and outcome of retroperitoneal lymph node dissection for clinical stage I embryonal carcinoma-predominant testis cancer. J Clin Oncol 2000; 18: 358-362. Landmark.
- Tandstad T, Stahl O, Hakansson U, et al. One course of adjuvant BEP in clinical stage I nonseminoma mature and expanded results from the SWENOTECA group. Ann Oncol 2014; 25:2167-2172.
- Zenerling F, Kunath F, Jensen K, et al. Prognostic factors for recurrence in patients with clinical stage I seminoma undergoing surveillance-a systemic review. Urol Oncol 2017; 36: 448-458

52