Saudi oncology society and Saudi urology association combined clinical management guidelines for testicular germ cell tumors

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Abstract

In this report, updated guidelines for the evaluation, medical, and surgical management of germ cell tumor of testes are resented. They are categorized according the stage of the disease using the tumor-node-metastasis staging system 7th edition. The recommendations are presented with supporting level of evidence.

Key Words: Guidelines, management, Saudi, testicular germ cell tumors

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Testicular cancer is a rare disease. A total of 78 cases have been diagnosed in 2010, with an age standardized rate of 0.8 cases/100,000 representing 1.7% of all diagnosed cancer in Saudi males (www.scr.org.sa). Owing to the rarity of the disease and the need for multidisciplinary approach in managing testis cancer, the group recommended that all testicular cancer cases should be managed in tertiary care centers.

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1. Staging: The American Joint Committee on Cancer tumor-node-metastasis staging for testis cancer (7th edition 2010) was used.
2. Staging evaluation of testicular tumors.
   2.1. Ultrasound of the scrotum is recommended to diagnose the tumor
   2.2. Serum tumor markers includes alpha fetoprotein [AFP], beta human chorionic gonadotropin [beta-hCG], and Lactate Dehydrogenase (LD) should prior to orchiectomy
   2.3. Computed tomography (CT) chest, abdomen and pelvis should performed for confirmed testicular cancer.
3. Risk stratification: The International Germ Cell Cancer Collaborative Group Risk Classification[1] should be used:
   3.1. Good prognosis.
      3.1.1. For patients with seminoma:

3.1.1.1. Any primary site
3.1.1.2. No nonpulmonary visceral metastasis
3.1.1.3. Normal serum AFP, any serum beta-hCG or lactate dehydrogenase (LDH)
3.1.2. For patients with nonseminoma germ cell tumor (NSGCT):
3.1.2.1. Testicular or retroperitoneal primary tumor.
3.1.2.2. No nonpulmonary visceral metastasis.
3.1.2.3. Serum AFP <1000 ng/mL, beta-hCG <5000 mIU/mL, and LDH <1.5 times the upper limit of normal.
3.2. Intermediate prognosis:
3.2.1. For patients with seminoma:
3.2.1.1. Any primary site
3.2.1.2. Nonpulmonary visceral metastasis
3.2.1.3. Normal serum AFP, any beta-hCG or LDH
3.2.2. For patients with NSGCT:
3.2.2.1. Testicular or retroperitoneal primary.
3.2.2.2. No nonpulmonary visceral metastasis.
3.2.2.3. Any of the following: serum AFP 1,000-10,000 ng/mL; beta-hCG 5000-50,000 mIU/mL; LDH 1.5-10 times the upper limit of normal.
3.3. Poor prognosis:
3.3.1. For NSGCT only, any of the following:
3.3.1.1. Mediastinal primary site.
3.3.1.2. Nonpulmonary visceral metastasis.
3.3.1.3. Serum AFP >10,000 ng/mL; serum beta-hCG >50,000 mIU/mL; LDH more than 10 times the upper limit of normal

4. Treatment: All patients who will undergo treatment with chemotherapy, RPLND or Radiotherapy should offered sperm banking. The treatment will depend on the histological subtype as follow:
4.1. Seminoma: All stages should undergo urgent inguinal orchiectomy. Trans-scrotal biopsy or orchiectomy for any intra-testicular lesion is absolutely contra-indicated. Further treatment will depend on the stage:
4.1.1. Stage I: Patient could offered one of the following options:
4.1.1.1. Chemotherapy: Single agent carboplatin: 1-2 doses at area under the curve 7[2] (Evidence Level EL-1)
4.1.1.2. Radiotherapy: Infradiaphragmatic para-aortic ± ipsilateral iliac nodes[3,4] (EL-1)
4.1.1.3. Surveillance: This should be done only in compliant patients with primary tumors <4 cm and <pT2[5] (EL-1)
4.1.2. Stage is: The patients should offered radiotherapy to infradiaphragmatic para-aortic lymph nodes (EL-3)
4.1.3. Stage IIA and IIB:
4.1.3.1. Radiotherapy to infradiaphragmatic para-aortic and ipsilateral Iliac nodes[6] (EL-2)
4.1.3.2. For Stage IIB, chemotherapy with four cycles of etopodice and cisplatin (EP) or three cycles of bleomycin, etoposide, and cisplatin (BEP) could be given in a case where the radiotherapy toxicity is high (EL-2)
4.1.4. Stage IIC and III: Treatment will depend on the risk classification:
4.1.4.1. Good risk: Chemotherapy with four cycles of EP (for patients with compromised lung function), or three cycles of BEP[7,8] (EL-1)
4.1.4.2. Intermediate risk: Chemotherapy with four cycles of BEP[9] (EL-1).
4.1.5. Management of postchemotherapy residual nodes/masses seen on CT scan: This depend on the size and the level of tumor markers (hCG).
4.1.5.1. If size <3 cm and normal markers: Surveillance.
4.1.5.2. If more than 3 cm and normal markers: Do positron emission tomography scan:[10]
4.1.5.2.1. If negative: Surveillance (EL-2).
4.1.5.2.2. If positive consider one of the following options:
4.1.5.2.2.1. Surgical resection.
4.1.5.2.2.2. Second-line chemotherapy if positive for residual disease (See item 3.2.5.3.2)
4.1.5.2.2.3. Radiotherapy

4.1.5.3. If the residual mass is enlarging or markers increasing: Second-line chemotherapy (EL-2) - See item 3.2.5.3.2.

4.1.6. Management of patients failing 1st line chemotherapy: Patients will receive second line chemotherapy; options are

4.1.6.1. Four cycles of vinblastin, ifosfafide and cisplatin (VeIP) regimen[11] (EL-2) or

4.1.6.2. Four cycles of paclitaxel, ifosfamide and cisplatin (TIP) regimen[12] (EL-2).

4.1.7. Management of patients failing second-line chemotherapy: Patients will be treated with combination paclitaxel and Gemcitabine for those who did not receive paclitaxel before.[13]

4.2. Nonseminoma: All stages will undergo urgent inguinal orchiectomy. Trans-scrotal biopsy or orchiectomy for any intra-testicular lesion is absolutely contra-indicated. Further treatment will depend on the stage as follow:

4.2.1. Stage I:

4.2.1.1. Treatment will depend on the presence of any the following risk factors:[14]

4.2.1.1.1. Lymphovascular invasion.

4.2.1.1.2. Presence of emberyonal histology (50% or more).[15]

4.2.1.1.3. Absence of yolk sac histology.

4.2.1.1.4. Tumor stage > T1.

4.2.1.2. Stage I with no risk factors: Options are:

4.2.1.2.1. Surveillance: Should be reserved in compliant patients[16,17] (EL-2).

4.2.1.2.2. Two cycles of adjuvant chemotherapy with BEP regimen[16-18] (EL-1).

4.2.1.2.3. Open nerve sparing retroperitoneal lymph node dissection (RPLND): To be done only in high volume tertiary care centers[18] (EL-2): Further therapy will depend on the pathological result as follow:

4.2.1.2.3.1. pN0: Surveillance.

4.2.1.2.3.2. pN1: Surveillance in compliant patients or two cycles of chemotherapy with BEP in noncompliant patients (EL-3).

4.2.1.2.3.3. pN2-3: Three cycles of chemotherapy with BEP regimen (EL-3).

4.2.1.3. Stage I with any risk factor of above: Options are:

4.2.1.3.1. Two cycles of adjuvant chemotherapy with BEP regimen.[16]

4.2.1.3.2. Open nerve sparing RPLND: To be done only in high volume tertiary care centers[19] (EL-2): Further therapy will depend on the pathological stage as in item 4.2.1.2.3.

4.2.1.4. Stage Is: Patient should receive three cycles of systemic chemotherapy with the BEP regimen (EL-3).

4.2.2. Stage IIA and IIB: Options of therapy will depend if markers (AFP and hCG) are normal or elevated:

4.2.2.1. Normal markers: Options are:

4.2.2.1.1. Primary chemotherapy with three cycles of BEP.[8]

4.2.2.1.2. Open nerve sparing RPLND,[20,21] if the nodal metastasis is in the primary landing zone in selected patients. It should be done only in high volume center by experienced uro-oncologist. Further therapy will depend on the pathological stage as in item 4.2.1.1.3.

4.2.2.2. Elevated markers: Systemic chemotherapy depending on the international risk classification group:

4.2.2.2.1. Low risk: Three cycles of BEP.[7,8]

4.2.2.2.2. Intermediate and high risk: Four cycles of BEP.[9]

4.2.3. Stage IIC and III: Treatment will be with chemotherapy depending on the international risk classification.

4.2.3.1. Low risk: Three cycles of BEP chemotherapy.[7,8]

4.2.3.2. Intermediate and high risk: Four cycles of BEP chemotherapy.[9]

4.2.4. Management of postchemotherapy:

4.2.4.1. No residual disease and normal markers: Surveillance.[22]

4.2.4.2. No residual disease and elevated markers (AFP and hCG): Second line chemotherapy. See item 4.2.4.3.2.

4.2.4.3. Residual disease by CT scan (>1 cm): This depend on the level of serum markers:

4.2.4.3.1. Normal markers: RPLND and resection of all residual disease if technically feasible: [23,24] further therapy will depend on pathology result:

4.2.4.3.1.1. Mature teratoma, necrosis, or fibrosis: no further therapy.

4.2.4.3.1.2. Residualgerm cell tumor: Two cycles of chemo therapy[25] with EP, VIP or TIP (see below) (EL-2).

4.2.4.3.2. Elevated markers: Second line chemo therapy; options are

4.2.4.3.2.1. Four cycles of VeIP regimen.[11]

4.2.4.3.2.2. Four cycles of TIP regimen.[12]

4.2.5. Management of patients failing second line chemotherapy: Patients will be treated with paclitaxel and Gemcitabine if did not receive paclitaxel before.[13]

4.2.6. Management of patients failing all lines of chemotherapy: In the case of markers progression after salvage treatment and exhaustion of all possible chemotherapeutic options, resection of residual tumors (desperation surgery) should be considered if complete resection of all tumors seems technically feasible.[26]

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