

Simplified Management Policies for Testicular Cancer an Overview Report by Indian Radiation Oncologists!!

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Abstract: Testicular cancer is a rare tumor type accounting for 1% of malignancies in men. Testicular cancer occurs when cancer cells form in one or both the testicles. It is, however, the most common cancer in young men in Western populations. The incidence of testicular cancer is increasing globally, although a decline in mortality rates has been reported in Western countries. It is important to identify whether the variations in trends observed between populations are linked to genetic or environmental factors. We review several clinical studies and summarize the current trends in the management of testicular cancer, As well as how can we simplify radiotherapy and chemotherapy in the testicular cancer treatment. The epidemiologic risk factors for the development of testicular cancer are a history of cryptorchidism or undescended testis, Klinefelter syndrome (increase incidence of mediastinal germ cell tumor) Extra gonadal germ cell tumor found in less than 10% cases were mediastinal and retroperitoneal areas are the most common sites however Pineal gland germ cell tumor more common in children furthermore it has been found that familial history of testicular cancer also present. Increase percentage of cases of germ cell tumors of testis reported among HIV positive persons.

Keywords: Testicular cancer, Radiotherapy, Chemotherapy. Cryptorchidism, Klinefelter Syndrome

1. Introduction

The peak incidence is in the third decade of life for Nonseminoma and in the fourth decade for pure Seminoma. Familial clustering has been observed, particularly among siblings. Germ cell tumors (GCTs) of the testis are rare, but are the most common cancer in young men. GCTs may consist of one predominant histological pattern or may represent a mixture of multiple histological types. For treatment purposes, two broad categories are recognized:

- 1) Pure seminoma and
- 2) Others, which together are termed Nonseminomatous GCTs (NSGCTs).

In general, Seminoma tends to be less aggressive, to be diagnosed at an earlier stage, and to spread predictably along lymphatic channels to the retro peritoneum before spreading hematogenously to the lung or other organs. Compared with NSGCTs, seminoma is exquisitely sensitive to radiation therapy and platinum - based chemotherapy. NSGCTs are usually mixed tumors and teratoma often exists at the sites of metastasis with other GCT elements; cure often requires chemotherapy to kill the chemosensitive - components and surgery to remove the teratomatous components.

The main factors contributing to excellent cure rates of GCTs are careful staging at diagnosis; adequate early treatment using chemotherapeutic combinations, with or without radiotherapy and surgery; and strict follow - up.

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Types of Testicular Cancers:

99% of testicular tumors are malignant in nature, mal descended testes undoubtedly predisposing factor for testicular cancer, and there are five types of testicular tumors as listed below

- 1) Seminoma 40%
- 2) Teretoma 32%
- 3) Both above combined form are 14%
- 4) Lymphoma of testise found in 7% among 65 year and above age group.
- 5) Interstitial tumor in 1.5% cases

Peak incidence of Teretoma is 20 to 35 years of age and peak incidence of Seminoma is 35 to 45 years of age.

Seminoma: Seminoma arises from mediastinum of the testis tumor having solid and cystic component in it and divided by fibrous septa presence of lymphocytes infiltration indicates good host reaction henceforth good prognosis as well, Seminoma mainly metastasis by lymphatic's rarely via blood stream.

Teretoma: They arises from Retetestes of totipotent cells henceforth it contains part of ectoderm, mesoderm as well as endoderm components in the tumors that's why often cartilaginous nodules present in tumor. This tumor mostly spared by blood stream henceforth lung metastasis is the common.

Spermatocytic variety of Seminoma: Usually occurs in elder age exceeding more than 50 years of age, tumor originates from mature spermatogonia these variety of tumors having excellent prognosis, radiotherapy rarely required and surgery remains the choice of treatment.

Lymphatic drainage of testis:

Lymphatic channel of testis runs upwards in spermatic cord through internal inguinal ring to paraaortic lymph node from here it drains into thoracic duct and finally to left supraclavicular lymph node, lymphatic's from medial side of testis drains to pelvic lymph nodes, inguinal lymph nodes gets involved once testicular tumor involving scrotum.

Clinical features:

- 1) Patient usually does not seek medical advice up to four to six month after the first symptoms which is enlargement of testis.
- 2) Sensation of heaviness complained by patients once testis's has enlarged two to three times of its normal size.
- 3) In 10% cases history of trauma is reported by patients, secondary hydrocoel being found among 10% cases of testicular tumor, in 7% to 10% cases patients of testicular tumor presented with features of Epididymo-orchitis

Examination findings: Patients complains of heaviness in his testis, loss of testicular sensation found, along testicular swelling but greatest gentleness required to elicit signs of testicular sensations for fear dissemination of malignant cells, spermatic cord found to be thickened on involved side, supraclavicular lymph node to be examinations, hepatic examination to be done to rule out liver enlargement, x - ray chest carried out to rule out lung metastasis particularly in case of Teratoma,

Investigations:

- 1) Collect blood specimen for β HCG, α fetoprotein, lactic dehydrogenase (LDH) useful in diagnosis as well as assessing the response of treatment.
- 2) Chest X - ray in order to rule out lung Mets as well as, lateral view to rule out mediastinal lymph node.
- 3) Confirmation by orchiectomy surgery to get detail histopathological test done
- 4) Sonography whole abdomen along scrotum to find out testicular enlargement as well as to find out pelvic and Retroperitoneal / Paraortic lymphadenopathy and furthermore to rule out the liver Mets.
- 5) Intravenous pyelography (IVP) done in order to rule out two things first doing it before radiation treatment planning to avoid kidney from radiation portals the second advantage of doing IVP is to detecting displacement of Ureter and renal pelvic pressure caused by enlarged paraortic lymphadenopathy.

Histological Classification of Testicular Cancers: By WHO

- 1) Germ cell tumors
 - a) Seminoma:
 - Classical/typical seminoma.
 - Spermatocytic seminoma.
 - b) Teratoma:
 - Mature.
 - Immature.
 - Malignant transformation in mature or immature variety.
 - c) Embryonal carcinoma.
 - d) Yolk sac tumor (Endodermal sinus tumor).
 - e) Choriocarcinoma
- 2) Sex cord tumors (Interstitial cell tumors) usually chemo resistant and radio resistant kind of testicular tumors they divided into three types as given below
 - a) Leydig cell tumors, secretes excess Androgen hormone
 - b) Sertoli cell tumors.
 - c) Granulosa cell tumors secretes excess Estrogen hormone,
- 3) Lymphoma.
- 4) Metastatic deposit in testis from different tumors like primary may be in prostate, lung, melanoma, renal cell carcinoma.

Seminomas and Non Seminomas Germ Cell Tumors of Testis

- 1) Seminomas germ cell tumor categorize as given below
 - A. Seminoma,
 - Anaplastic seminoma usually in 30 to 40 years of age.
 - Spermatocytic seminoma.
- 2) Non seminomas germ cell tumors of testis divided in two
 - Teratoma
 - Choriocarcinoma.
 - Yolk sac tumors (Endodermal sinus tumor)
 - Infantile Embryonal cell Carcinoma.

Royal Marsadan Hospital Staging system of testicular cancer

Stage - 1, Lesion limited to testis only no evidence of spread of disease.

Stage - 2, Lymph node involves below diaphragm

2a - Nodes less than 2cm

2b - Nodes 2 - 5 cm in size

2c - Nodes more than 5cm.

Stage - 3, Nodes present above the diaphragm,

Stage - 4, Pulmonary or hepatic metastasis.

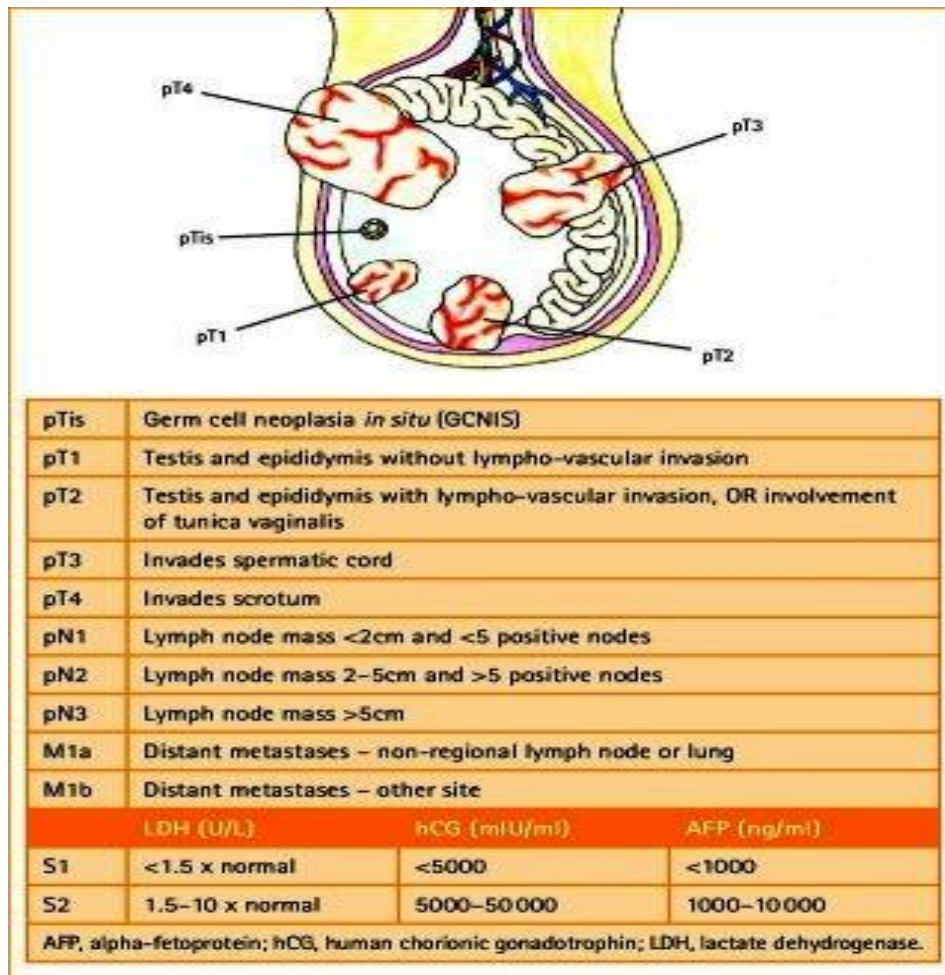


Figure 1: TNM Classification of Testicular tumors (drawn by Beth Goddard)

Testicular serum tumor markers according to Tumor Types

- Serum α fetoprotein, Access by enzyme linked immune sorbent assay (ELISA) Normal value is 15ng/ml, In stage - 1 serum α fetoprotein raised among 10 - 20% cases, stage - 2 serum α fetoprotein raised among 20 - 40% cases, stage - 3/4 serum α fetoprotein raised among 40 - 60% cases.
- Serum HCG it is a glycoprotein having two sub units α and β secreted by Syncytiotrophoblast cells α sub unit is identical to LH, FSH, TSH hormones, β Sub unit increased concentrations found in pure seminoma as well as in Nonseminomas germ cell tumors false positive reports found since antibody of β hcg shows cross reactivity with LH hormone, pituitary gland production of β hcg has also been reported.
- Serum LDH It reflects the tumor burden in advance seminoma 80% cases shows increased value of serum LDH, and in case of Non seminomas 60% shows increased value of serum LDH level.

Stage wise treatment of testicular tumor

Seminoma:

Early Stage Treatment

Being very radiosensitive tumor for stage1&2 Radiotherapy is a treatment of choice after getting high Orchidectomy done radiotherapy for above mention stage provides five year survival rate at 95%. Radiotherapy dose for early stage

disease is 25Grey in 20 fractions, followed by 10Grey boost to involved Para aortic lymph node area radiotherapy portal use as **Dog leg technique** (upper border taken at 10th thoracic vertebra D10,) and low limit taken floor of obturator foramen, lateral boundary taken involved site 1.5cm lateral to true bony pelvic brim, medial boundary is taken 1 cm to opposite pelvic infield involved site of renal hilum is taken in Dog leg technique, When lower Para aortic lymph node involvement is present chances of retrograde lymphatic metastasis to opposite side of pelvis is high than we prefer to give radiotherapy as **Inverted Y Field technique**. Its boundary is like upper limit is same as dog leg technique means at 10th thoracic vertebra D10, and lower limit is involving both side of pelvic lymph node up to floor of obturator foramen. Refer to given below figures for both techniques.

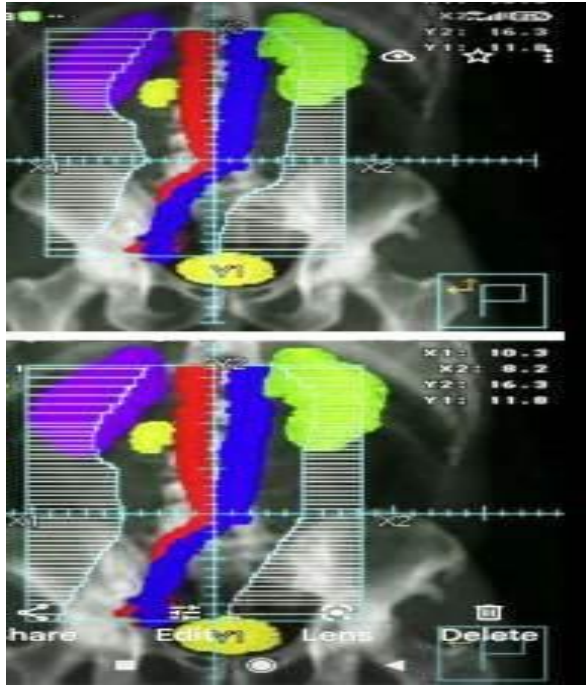


Figure 2: Multi Leaf Collimator block based Dog leg radiotherapy planning Source Red Journal International Journal of Radiation Oncology, Biology. Physics, Critical Review volume 83, Issue4, E445 - E452 July15, 2022.

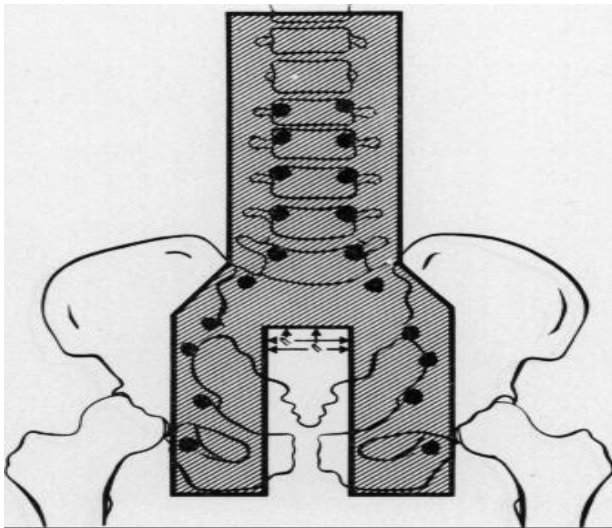


Figure 3: Inverted Y Field technique

Source: HOWARD JACOBS professor EMERITUS University College of London Hospitals, NHS Foundation Trust

Higher stage seminoma treatment means patients are in stage 2B, C/ Stage - 3/4:

In these cases four cycle of chemotherapy as BEP regimen given and then if patient is in stage 2, B or C / Stage 3 chemotherapy followed by adjuvant radiotherapy 20 to 30 Grey dose. In seminoma if metastasis is present survival rate is still very good but it drops down to 75%.

Treatment of Nonseminomatous Germ Cell Tumor

Stage - 1 After high inguinal orchidectomy we adopt the policy of follow up as surveillance because of two reasons: first due to presence of reliable tumor marker and second reason is we don't have to follow up the patients for long

period because non seminomatous tumors almost in 90% cases if at all relapse they relapse within two years.

Stage 2/3 we give 4 cycle of chemotherapy as standard regime is BEP regime followed by retroperitoneal lymph node dissection.

Treatment of Residual Or Recurrent Germ Cell Tumor of Testis

After completion of treatment if CECT shows residual node less than 3cm then policy is to keep the patient on follow up but if node is more than 3cm then we have treatment options as Salvage chemotherapy in form of Carboplatin 450mg/m² Day - 1 and Etoposide 150mg/m² D1 to D3 only two cycles are recommended because mortality rate with this regime is 10 to 12% particularly in BEP resistant cases above regime having 30% response rate.

Conflict of Interest: None

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