

Testicular cancer



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UROLOGY

Incidence and mortality



Primary testicular cancer (TC) is the most common solid cancer in men aged 20 to 45; rare below 15 years and above 60 years. Constituting 1 to 2% of all male cancers, the lifetime risk of developing testicular cancer is 1 in 500. It is also considered the most curable cancer

Epidemiology and aetiology



Age: the most common affected age group is 20 to 45 years, with germ cell tumours; teratomas are more common at ages 20 to 35; while seminoma is more common at ages 35 to 45 years. Rarely, infants and boys below 10 years develop yolk sac tumours and 50% men >60 years with TC have lymphoma.

Race: white people are three times more likely to develop TC than black people in the USA.

Cryptorchidism: 10% of TC occur in undescended testes: the risk increases by 3 to 14 times compared to men with normally descended testes. Ultrastructural changes are present in these testes by age 3 years, although earlier orchidopexy does not completely eliminate the risk of developing TC. 5 to 10% of patients with a cryptorchid testis develop malignancy in the normally descended contralateral testis



Intratubular germ cell neoplasia (IGCN):

synonymous with carcinoma in situ, although the disease arises from malignant change in spermatogonia. 50% of cases develop invasive germ cell TC within 5 years. The population incidence is 0.8%. Risk factors include cryptorchidism, extra-gonadal germ cell tumour, previous or contralateral TC (5%), atrophic contralateral testis, 45XO karyotype, and infertility.

Human immunodeficiency virus (HIV): patients infected with the HIV virus are developing seminoma more frequently than expected.

Genetic factors appear to play a role, given that first-degree relatives are at higher risk, but a defined familial inheritance pattern is not apparent.

Maternal oestrogen ingestion during pregnancy increases the risk of cryptorchidism and TC in the male offspring.

Testicular cancer: clinical presentation



Symptoms

Most patients present with a scrotal lump, usually painless or slightly aching. Delay in presentation is not uncommon, particularly those with metastatic disease. This may be due to patient factors (fear, self-neglect, ignorance, denial) or earlier misdiagnosis. Occasionally (5%) acute scrotal pain may occur, due to intra-tumoural haemorrhage, causing diagnostic confusion. The lump may have been noted by the patient, sometimes after minor trauma, or by his partner. In 10%, symptoms suggestive of advanced disease include weight loss, lumps in the neck, chest symptoms, and bone pain.

Signs



Examination of the genitalia should be carried out in a warm room with the patient relaxed. Observation may reveal asymmetry or slight scrotal skin discolouration.

Using careful bimanual palpation, the normal side is first examined, followed by the abnormal side. This will reveal a hard, non-tender, irregular, non-transilluminable mass in the testis, or replacing the testis. Care should be taken to assess the epididymis, spermatic cord, and overlying scrotal wall, which may be normal or involved in 10 to 15% of cases.

Rarely, a secondary hydrocoele may be present if the tunica albuginea has been breached. General examination may reveal cachexia, supraclavicular lymphadenopathy, chest signs, hepatomegaly, lower limb oedema, or abdominal mass "all suggestive of metastatic disease. Gynaecomastia is seen in ~5% of patients with TC, due to endocrine manifestations of some tumours.

Differential diagnosis



Testicular torsion, epididymo-orchitis, hydrocoele, epididymal cyst, hernia, haematoma, or syphilitic gumma (rare).

The majority of scrotal lumps are harmless lesions, but no risks should be taken. Every patient who is concerned should be seen, examined, and if any doubt persists, should be investigated further.

Investigations

Ultrasound is an extension of the physical examination and will confirm that the palpable lesion is within the testis, distorting its normally regular outline and internal echo pattern. Any hypoechoic area within the tunica albuginea should be regarded with suspicion. It may distinguish a primary from a secondary hydrocoele. Ultrasound may also be used to identify occult primary impalpable lesions as small as 1 to 2mm tumour in a patient presenting with systemic symptoms and signs or an incidental finding.

Abdominal and chest CT scans are usually obtained for staging purposes if the diagnosis of TC is confirmed or considered likely.

Testicular cancer: serum markers



Onco-fetal proteins

Alpha-fetoprotein (AFP) is expressed by trophoblastic elements within 50 to 70% of teratomas and yolk sac tumours. With respect to seminoma, the presence of elevated serum AFP strongly suggests a non-seminomatous element. Serum half-life is 3 to 5 days; normal <10ng/ml.

Human chorionic gonadotrophin (hCG) is expressed syncytiotrophoblastic elements of choriocarcinomas (100%), teratomas (40%), and seminomas (10%). Serum half-life is 24 to 36h. Assays measure the beta-subunit; normal <5mIU/ml.

When used together, 90% of patients with advanced disease have elevation of one or both markers; less among patients with low-stage tumours.

Cellular enzymes



Lactate dehydrogenase (LDH) is an enzyme, elevated in serum for various causes, therefore less specific. It is elevated in 10 to 20% of seminomas, correlating with tumour burden, and is most useful in monitoring treatment response in advanced seminoma.

Placental alkaline phosphatase (PLAP) is a fetal isoenzyme, elevated in up to 40% of patients with advanced germ cell tumours. It is not widely used as it is non-specific. May be elevated in smokers.

Clinical use



These markers are measured at presentation, 1 to 2 weeks after radical orchidectomy, and during follow-up to assess response to treatment and residual disease.

Normal markers prior to orchidectomy do not exclude metastatic disease; normalization of markers post orchidectomy cannot be equated with absence of disease; and persistent elevations of markers post-orchidectomy may occur with liver dysfunction and hypogonadotrophism, but usually indicate metastatic disease.

WHO histopathological classification of testicular tumours

Germ cell tumours (90%)

Seminoma (48%)

Spermatocytic, classical, and anaplastic subtypes

Non-seminomatous GCT (42%)

Teratoma:

Differentiated/mature

Intermediate/immature

Undifferentiated/malignant

Yolk sac tumour

Choriocarcinoma

Mixed NSGCT

Mixed GCT (10%)

Other tumours (7%)

Epidermoid cyst (benign)

Adenomatoid tumour

Adenocarcinoma of the rete testis

Carcinoid

Lymphoma (5%)

Metastatic, from another site (1%)

Sex cord stromal tumours (3%) (10% malignant)

Leydig cell

Sertoli cell

Mixed



90% of testicular tumours are malignant germ cell tumours (GCT), split into seminomatous and non-seminomatous (NS) GCTs for clinical purposes.

Seminoma, the most common germ cell tumour, appears pale and homogeneous. NSGCTs are heterogeneous and sometimes contain bizarre tissues such as cartilage or hair. Metastases to the testis are rare, notably from the prostate (35%), lung (19%), colon (9%), and kidney (7%).



The right testis is affected slightly more commonly than the left; synchronous bilateral TC occurs in 2% of cases. TC spreads by local extension into the epididymis, spermatic cord, and, rarely, the scrotal wall.

Lymphatic spread occurs via the testicular vessels, initially to the para-aortic nodes. Involvement of the epididymis, spermatic cord, or scrotum may lead to pelvic and inguinal node metastasis. Blood-borne metastasis to the lungs, liver, and bones is more likely once the disease has breached the tunica albuginea.

TNM staging of testicular germ cell tumours



Tx The primary tumour has not been assessed (no radical orchidectomy)

To No evidence of primary tumour

Tis Intratubular germ cell neoplasia (carcinoma in situ)

T1 Tumour limited to testis and epididymis without vascular invasion; may invade tunica albuginea but not tunica vaginalis

T2 Tumour limited to testis and epididymis with vascular/lymphatic invasion, or tumour involving tunica vaginalis

T3 Tumour invades spermatic cord with or without vascular invasion

T4 Tumour invades scrotum with or without vascular invasion

Nx Regional lymph nodes cannot be assessed

No No regional lymph node metastasis

N1 Metastasis with a lymph node less than 2cm or multiple lymph nodes, none >2cm

N2 Metastasis with a lymph node size 2 to 5cm or multiple lymph nodes, collected size 2 to 5cm

N3 Metastasis with a lymph node mass >5cm

Mx Distant metastasis cannot be assessed

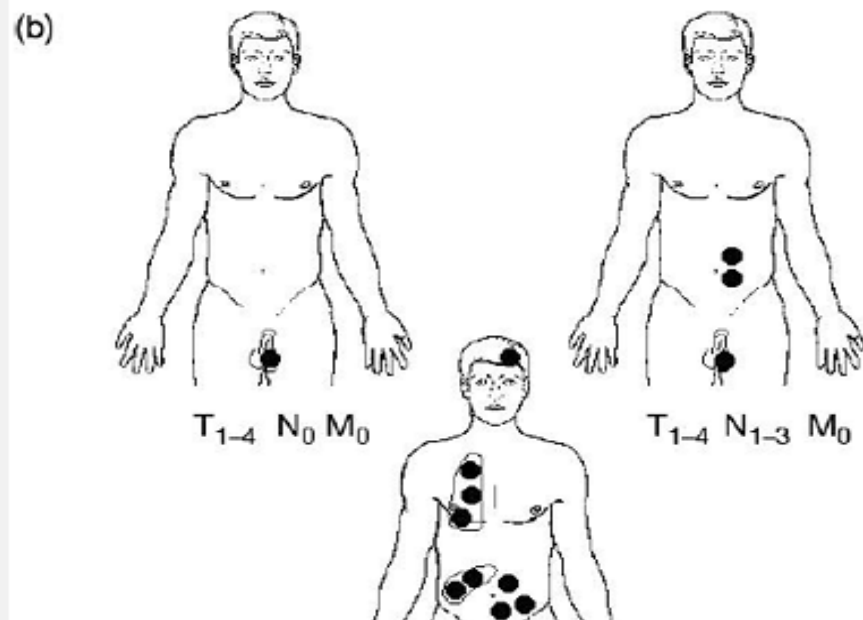
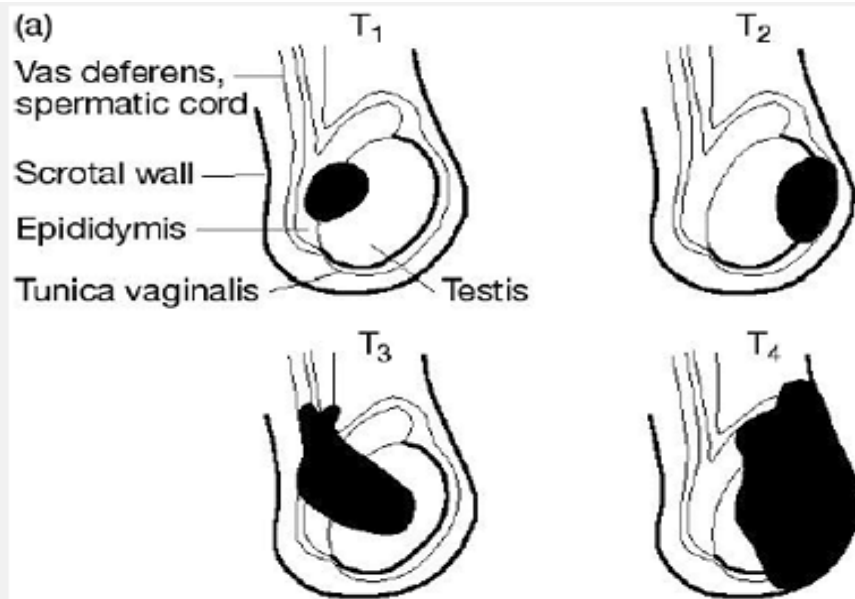
Mo No distant metastasis

M1a Non-regional lymph node or pulmonary metastasis

M1b Distant metastasis other than to non-regional lymph node or lungs

Radical orchidectomy

The final investigation and the primary treatment for all testicular tumours, unless tissue diagnosis has been made from a metastasis. This involves excision of the testis, epididymis, and cord, with their coverings, through a groin incision. The cord is clamped, transfixed, and divided near the internal inguinal ring before the testis is manipulated into the wound, preventing inadvertent metastasis. A silicone prosthesis may be inserted at the time or at a later date. This treatment is curative in ~80% of patients. Fertility prophylaxis by freezing sperm should be offered to patients without a normal contralateral testis. Contralateral testis biopsy should be considered in patients at high risk for IGCN



Testicular cancer: management of non-seminomatous germ cell tumours (NSGCT)



Following radical orchidectomy and formal staging, the patient is normally managed by the oncologist, though the urologist may be asked to perform retroperitoneal lymph node dissection (RPLND) in selected cases. In the presence of elevated AFP, a seminoma would be managed as for teratoma. Combination chemotherapy, introduced in the 1980s, revolutionized the treatment of metastatic testicular teratoma, which was hitherto virtually untreatable.

Non-metastatic disease



T 1 to 4NoMoSo: surveillance or chemotherapy (bleomycin, low-dose etoposide, cisplatin) depending on risk factors for relapse (lymphatic or vascular invasion, (T2 to 4); surveillance in presence of risk factors results in 25% relapse rate, most <1 year post orchidectomy.

Metastatic disease



Good prognosis: chemotherapy (bleomycin etoposide and cisplatin 1 to 3 cycles), residual or recurrent mass; salvage chemotherapy if histology confirms tumour.

Intermediate and poor prognosis: chemotherapy (bleomycin, etoposide, cisplatin 1 to 4 cycles); RPLND for residual or recurrent mass; salvage chemotherapy if histology confirms tumour.

Surveillance and follow-up after treatment



Surveillance requires the following:

Year 1: monthly clinic visit with serum markers and chest X-ray, abdominal CT months 3,6,9, and 12 months

Year 2: 2-monthly clinic visit with serum markers and chest X-ray, abdominal CT month 24

Years 3,4, and 5: 3-monthly clinic visit with serum markers and chest X-ray

Annual clinic visit with serum markers and chest X-ray, thereafter to 10 years

Testicular cancer: management of seminoma, IGCCN, and lymphoma



Of all seminomas, 75% are confined to the testis at presentation and are cured by radical orchidectomy; 10 to 15% of patients harbour regional node metastasis; and 5 to 10% have more advanced disease. Following radical orchidectomy and formal staging, the patient is managed by the oncologist. Treatment and follow-up depends largely on disease stage according to presence of metastases and size of nodal disease, as follows

Non-metastatic disease



T1NoMoSo 1: risk of subsequent para-aortic node relapse is 20%. Adjuvant radiotherapy (RT) 20Gy in 10 fractions reduces risk to 1%. RT includes para-aortic nodes.

Spermatocytic subtype usually warrants surveillance

Metastatic disease



T1to3 N1 MoSo : RT

T1to3 N2 Mo So : RT; chemotherapy if nodes near kidneys.

T1to4 N3 Mo So : chemotherapy (either bleomycin, etoposide, and cisplatin or etoposide and cisplatin); if residual node mass >3cm (rare), retroperitoneal lymph node dissection (RPLND) considered; if histology reveals tumour (30%), salvage chemotherapy.

T1to4No M1: chemotherapy; if residual node mass (rare), RPLND considered; if histology reveals tumour (30%), salvage chemotherapy.