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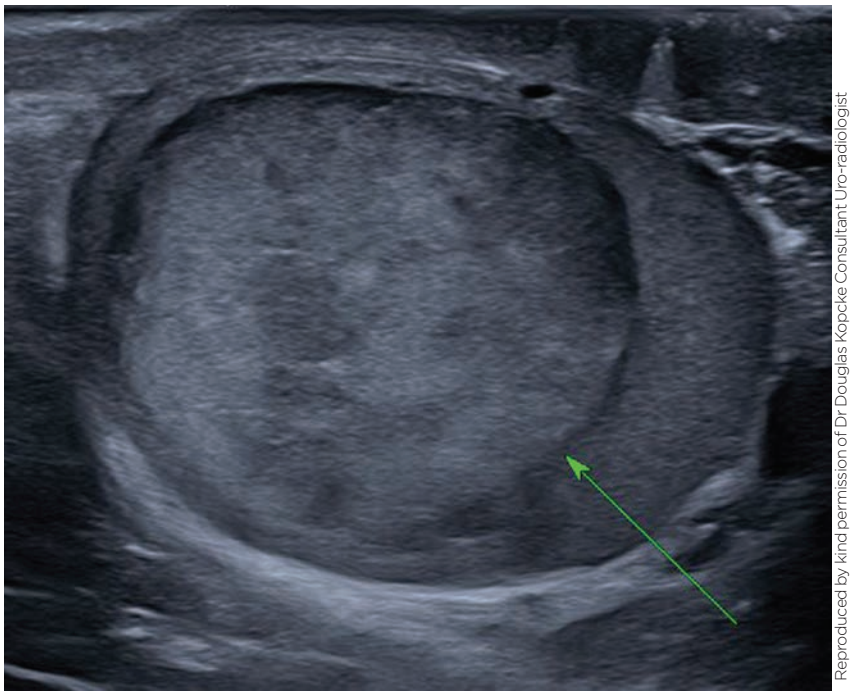

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FIGURE 1
Ultrasound image of right testicle showing a testicular tumour

What are the risk factors?

How should men be assessed and examined?

How should patients be followed up?

TESTICULAR CANCER ACCOUNTS FOR 1% OF MALE CANCERS OVERALL AND IS THE MOST COMMON solid cancer in men aged between 15 and 49 years old. The estimated lifetime risk of testicular cancer for men born after 1960 is 1 in 215 in the UK. Around 2,300 new diagnoses are made each year in the UK.[1]

At present a full time GP is likely to diagnose one or two new cases of testicular cancer during their career. However, it is important to recognise that the incidence rates for testicular cancer have risen 24% since the early 1990s and are projected to rise by a further 12% in the UK between 2014 and 2035.[1]

Early diagnosis of testicular cancer is associated with excellent outcomes and as such GPs should maintain a high level of suspicion for this disease.

The precise aetiology of testicular cancer is unknown but recognised risk factors include:

- A history of undescended testicles (cryptorchidism). Boys born with their testicles inside their abdomen are 3-6 times more likely to develop testicular cancer than those whose testicles have descended into the scrotum by birth.[2] The risk is higher in both testes although more so on the affected side.[3]

  Even if boys have an early orchidopexy to fix the affected testis in the scrotum there remains a two-fold higher risk compared with the general population[4]
- A family history. Men whose father or brother has had testicular cancer have a four- or eight-fold higher risk of developing the disease, respectively[5]
- Previous testicular cancer. Men with a history of testicular cancer have at least a twelve-fold increased risk of developing cancer in their other testicle compared with the general population[5]
- Testicular cancer is up to three times more common in Caucasians and Northern Europeans than non-Caucasians
- A history of subfertility[6]
- HIV increases the risk of developing testicular seminoma[7]

'Usually the scrotal swelling will be painless, however around 20% of patients may report pain as the first symptom'

PRESENTATION

Most men will attend their GP to discuss a lump that they have identified in their scrotum, which may or may not be related to their testicle.

Usually the scrotal swelling will be painless, however around 20% of patients may report pain as the first symptom they notice. A dull or dragging ache in the testicle or a heaviness in the scrotum may be described alone and 10% of men presenting with testicular pain will have a delayed diagnosis of a testicular tumour made.[8,9]

Rarely men may present with signs of metastatic testicular cancer which include: an abdominal mass, cervical or supraclavicular lymphadenopathy, back pain, weight loss, cough, shortness of breath, nausea, vomiting, gastrointestinal bleeding, central or peripheral nervous system symptoms.

Despite testicular cancer awareness campaigns explaining the importance of routine self-examination and the need to present to a GP if any abnormality »

is found or suspected when they check themselves; many men still feel embarrassed and frightened when they talk about their reason for consulting.

Men should be reassured during their consultation that testicular cancer is one of the most treatable cancers and currently at least 95% of men will survive at least five years after their diagnosis.[1]

EXAMINATION

A thorough history should be taken and full abdominal examination should be performed on every patient who presents with suspected testicular cancer. The abdominal examination should be performed in a warm room where the patient's privacy can be maintained.

'The patient should always be asked to check that where you are palpating is consistent with where he palpated any perceived abnormality'

The examination should include visual inspection and palpation of the abdomen for abdominal masses and scars.

Orchidopexy is performed through a small groin and scrotal incision. It is important to look for these scars as patients may not recall the surgery being performed as it is usually carried out when boys are very young, after the age of 8 months.

A scrotal examination should be performed lying and standing to elicit whether left and right testicles are present in the scrotum and palpate any abnormalities of the testicle.

Whether or not the healthcare professional performing the examination detects a testicular abnormality; the patient should always be asked to check that where you are palpating during the examination is consistent with where he palpated any perceived abnormality.

Important negative differential diagnoses which can clearly be identified at examination should be looked for and include: inguinal hernia, varicocele, epididymal cyst and orchitis.

If metastatic disease is suspected, it is appropriate to perform respiratory and neurological examinations.

INVESTIGATION

NICE guidance recommends that all men who have non-painful enlargement or a change in shape or texture of their testis should be referred urgently to urology using the two-week wait pathway for suspected cancer referrals.[10]

In men who have unexplained or persistent testicular symptoms an urgent direct access testicular ultrasound scan should be requested. An ultrasound should also be requested if the patient has significant risk factors for testicular cancer or a previous history of testicular cancer in the contralateral testicle and the healthcare professional has a high suspicion that testicular cancer may be an underlying diagnosis. If the option of a direct access ultrasound scan is not available then consider referring the patient to urology under the two-week wait pathway.[10]

A recent large study of the clinical features of testicular cancer in primary care highlighted other findings that GPs should be alert to. Men with persistent testicular pain or unresolving epididymo-orchitis should be referred for urgent review. Men aged under 50 years old with a new clinically significant hydrocele should also be referred for review.[11]

CONFIRMING DIAGNOSIS

Scrotal ultrasound is the key investigation to determine whether there is a solid tumour within the testicle (see figure 1, p11). This is performed urgently in all men with suspected testicular cancer. The sensitivity and specificity of testicular ultrasound is 92-99% and 95-98% respectively.[12]

All men diagnosed with testicular cancer on ultrasound should have a testicular tumour marker blood test performed at diagnosis. Alpha-fetoprotein (AFP), beta-human chorionic gonadotrophin (β-hCG) and lactate dehydrogenase (LDH) are the testicular tumour markers measured.

The levels of the tumour markers at diagnosis can help indicate what type of testicular cancer is present and can also be used to evaluate response to treatment.

Testing for testicular tumour markers can be carried out in the community if clinically GPs have a high suspicion of a testicular cancer diagnosis but this should not delay referral to urology.

In secondary care all men diagnosed with a testicular cancer will be booked to undergo an urgent CT scan of the chest, abdomen and pelvis to exclude metastatic spread.

MANAGEMENT

The primary treatment for testicular cancer is usually a radical orchidectomy where the entire abnormal testicle is removed through an inguinal incision. This is normally performed as an urgent procedure as soon as possible after diagnosis.

All patients should be offered the opportunity to bank sperm prior to orchidectomy. There will be local protocols in place but all men choosing to bank sperm will have to undergo blood tests to exclude hepatitis B, C and HIV. If these blood tests come back positive, sperm banking can only be offered at two highly specialised centres in the UK.

'All patients should be offered the opportunity to bank sperm prior to orchidectomy'

From 12 months after treatment patients may be offered sperm analysis to determine whether continued sperm storage is necessary.

During the consent process for radical orchidectomy men should be offered a testicular prosthesis. This artificial implant is placed in the empty scrotum at the end of the operation to give the appearance of a testicle being present in the scrotum. There is a small risk of prosthesis related infection after surgery (0.6-2%) so patients should be given the option of having an implant inserted at a later date.[13]

There are certain circumstances when radical orchidectomy is not carried out or a more nuanced approach is considered. These are when:

- The tumour is present in the patient's only testis or both testicles – in these cases partial orchidectomy may be possible
- There is a small non palpable mass < 50% of testicular volume on ultrasound scan – in these cases partial orchidectomy may be considered
- There is reduced androgen function
- Men have symptoms and signs and are unwell with metastatic testicular cancer. In these cases chemotherapy may be required prior to orchidectomy

MONITORING AND FOLLOW-UP

All patients diagnosed with testicular cancer are managed by a multidisciplinary team (MDT) including cancer nurse specialists, radiologists, urologists and

oncologists. Once radical orchidectomy has been performed the pathological tissue diagnosis is combined with the staging imaging information and used by the MDT to advise patients on whether additional treatment is recommended and what should constitute appropriate follow-up.

Testicular tumours are broadly subclassified into seminoma and non seminomatous germ cell tumours. The Union for International Cancer Control clinical staging system is used to form prognostic groups and guide further management.[14] Depending on the stage of their tumour, after radical orchidectomy patients may be offered active surveillance, chemotherapy, radiation or further surgery to remove lymph nodes located at the back of the abdomen in the form of a retroperitoneal lymph node dissection.

The minimum recommended follow-up based on European guidelines for patients diagnosed with early and advanced disease are illustrated in tables 1, 2 and 3, below.[15] »

Table 1

Recommended minimal follow-up for seminoma clinical stage I on active surveillance or after adjuvant treatment (carboplatin or radiotherapy)[15]

Modality	Year 1	Year 2	Year 3	Years 4 & 5	After 5 years
Tumour markers ± doctor visit	2 times	2 times	2 times	Once	Further management according to survivorship care plan
Chest X-ray	-	-	-	-	
Abdominopelvic CT/MRI	2 times	2 times	Once at 36 months	Once at 60 months	

Table 2

Recommended minimal follow-up for non seminoma clinical stage I on active surveillance[15]

Modality	Year 1	Year 2	Year 3	Years 4 & 5	After 5 years
Tumour markers ± doctor visit	4 times***	4 times	2 times	1-2 times	Further management according to survivorship care plan
Chest X-ray	2 times	2 times	Once, in case of LVI+*	At 60 months if LVI+*	
Abdominopelvic CT/MRI	2 times	At 24 months****	Once at 36 months**	Once at 60 months**	

* LVI+: Lymphovascular invasion present
** Recommended by 50% of European Association of Urology consensus group members
*** In case of high-risk (LVI+) a minority of the consensus group members recommended six times
**** In case of high-risk (LVI+) a majority of the consensus group members recommended an additional CT at eighteen months

Table 3

Recommended minimal follow-up after adjuvant treatment or complete remission for advanced disease (excluded: patients with poor prognosis and no remission)[15]

Modality	Year 1	Year 2	Year 3	Years 4 & 5	After 5 years
Tumour markers ± doctor visit	4 times	4 times	2 times	2 times	Further management according to survivorship care plan**
Chest X-ray	1-2 times	Once	Once	Once	
Abdominopelvic CT/MRI	1-2 times	At 24 months	Once at 36 months	Once at 60 months	
Thorax CT	*	*	*	*	

* Same time points as abdominopelvic CT/MRI in case of pulmonary metastases at diagnosis
** In case of teratoma in resected residual disease: the patient should remain with the uro-oncologist

key points

SELECTED BY

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Testicular cancer accounts for 1% of male cancers and is the most common solid cancer in men aged between 15 and 49 years old. Around 2,300 new diagnoses are made each year in the UK. The estimated lifetime risk of testicular cancer for men born after 1960 is 1 in 215 in the UK. The precise aetiology of testicular cancer is unknown but recognised risk factors include cryptorchidism, family history, previous testicular cancer, Caucasian ethnicity, subfertility and HIV.

Most men present with a lump that they have identified in their scrotum. Although the scrotal swelling is usually painless, pain is the first symptom in around 20% of patients, typically a dull or dragging ache in the testicle or a heaviness in the scrotum. Rarely men may present with signs of metastatic testicular cancer which include: an abdominal mass; cervical or supraclavicular lymphadenopathy; back pain; weight loss; cough; shortness of breath; nausea; vomiting; gastrointestinal bleeding; central or peripheral nervous system symptoms.

Examination should include visual inspection and palpation of the abdomen for abdominal masses and scars. Orchidopexy is performed through a small groin and scrotal incision and it is important to look for these scars as patients may not recall the surgery being performed in early life. A scrotal examination should be performed lying and standing to determine whether left and right testicles are present in the scrotum and palpate any abnormalities of the testicle. The differential diagnosis includes inguinal hernia, varicocele, epididymal cyst and orchitis.

NICE recommends that all men who have a non-painful enlargement or change in shape or texture of their testis should be referred to urology using the two-week wait pathway. In men who have unexplained or persistent testicular symptoms, an urgent direct access testicular ultrasound scan should be requested.

Scrotal ultrasound is the key investigation to determine whether there is a solid tumour within the testicle. All men diagnosed with testicular cancer on ultrasound should have a testicular tumour marker blood test. The levels of the markers at diagnosis can help indicate what type of testicular cancer is present and can also be used to evaluate response to treatment. An urgent CT scan of the chest, abdomen and pelvis is necessary to exclude metastatic spread.

The primary treatment for testicular cancer is usually a radical orchidectomy and all patients should be offered the opportunity to bank sperm beforehand. Postoperatively, depending on the tumour stage, patients may be offered active surveillance, chemotherapy, radiation or further surgery to remove retroperitoneal lymph nodes. Following treatment GPs should routinely evaluate men for symptoms of hypogonadism and assess hormonal status accordingly.

The risk of a second contralateral tumour is 1% so all patients should continue self-examination routinely after treatment for testicular cancer.

POTENTIAL FUTURE COMPLICATIONS

Although testicular cancer has a high survival rate, some men may suffer irreversible morbidity from their treatment. Men treated with radiotherapy and chemotherapy are at increased risk of leukaemia and solid organ cancers compared with the general population. Cisplatin based chemotherapy can be associated with ototoxicity, peripheral neuropathy, or nephrotoxicity. Bleomycin chemotherapy can cause pulmonary toxicity.[16]

Despite the availability of sperm banking, infertility may be a significant survivorship issue for men who have undergone treatment. Patients with testicular cancer have abnormal semen parameters prior to treatment in up to 50% of cases.[17] Radical orchidectomy followed by chemotherapy or radiotherapy may cause testicular dysgenesis syndrome. Retroperitoneal lymph node dissection is associated with the risk of retrograde ejaculation.

Assisted reproduction techniques may be required after testicular cancer treatment to achieve successful conception.

Hypogonadism resulting from treatment is common.[16] GPs should routinely evaluate men post treatment for symptoms and assess hormonal status accordingly. Decisions to administer testosterone replacement therapy should be made based on clinical symptoms and initiated in secondary care. GPs should refer men with confirmed low testosterone levels and symptoms of hypogonadism to secondary care according to their local protocols.

CONCLUSION

Although uncommon, testicular cancer is one of the most treatable cancers with excellent survival rates. GPs have a key role to play in the early diagnosis of testicular cancer and supporting men diagnosed with the disease. Most men will live a long life after treatment and GPs must be alert to these men's holistic needs and identify and manage men's long term survivorship needs.

Competing interests: None

REFERENCES

1 Cancer Research UK Testicular cancer statistics www.cancerresearchuk.org/health-professional/cancer-statistics/statistics-by-cancer-type/testicular-cancer [Last accessed 17 April 2021]
2 Akre O, Pettersson A, Richiardi L. Risk of contralateral testicular cancer among men with unilaterally undescended testis: a meta analysis. *Int J Cancer* 2009;124(3):687-89
3 Lip SZ, Murchison LE, Cullis PS et al. A meta-analysis of the risk of boys with isolated cryptorchidism developing testicular cancer in later life. *Arch Dis Child* 2013;98(1):20-26
4 Pettersson A, Richiardi L, Nordenskjold A et al. Age at surgery for undescended testis and risk of testicular cancer. *N Engl J Med* 2007;356(18):1835-41
5 Hemminki K, Li X. Familial risk in testicular cancer as a clue to a heritable and environmental aetiology. *Br J Cancer* 2004;90(9):1765-70
6 Walsh TJ, Croughan MS, Schembri M et al. Increased risk of testicular germ cell cancer among infertile men. *Arch Intern Med* 2009;169(4):351-56
7 Manecksha RP, Fitzpatrick JM. Epidemiology of testicular cancer. *BJU Int* 2009;104(9 pt B):1329-33
8 Germa-Lluch JR, Garcia del Muro X, Maroto P et al. Clinical pattern and therapeutic results achieved in 1490 patients with germ-cell tumours of the testis: the experience of the Spanish Germ-Cell Cancer Group (GG). *Eur Urol* 2002;42:553-62
9 Moul J. Timely diagnosis of testicular cancer. *Urol Clin North Am* 2007;34:109-17
10 National Institute for Health and Care Excellence. NG12. Suspected cancer: recognition and referral. NICE. London. 2015. www.nice.org.uk/guidance/ng12 Updated 2021 [Last accessed 17 April 2021]
11 Shephard EA, Hamilton WT. Selection of men for investigation of possible testicular cancer in primary care: a large case-control study using electronic patient records. *Br J Gen Pract* 2018;68:e559-65
12 Coursey Moreno C, Small WC, Camacho JC et al. Testicular tumors: what radiologists need to know — differential diagnosis, staging, and management. *Radiographics* 2015;35(2):400-15
13 Marshall S. Potential problems with testicular prostheses. *Urology* 1986;28:388-90
14 Brierley JE et al. The TNM classification of malignant tumours 8th edition. 2016. www.uicc.org/resources/tnm/publications-resources
15 The European Association of Urology Guidelines on Testicular Cancer 2020: https://uroweb.org/guideline/testicular-cancer
16 Travis LB, Fossà SD, Schonfeld SJ et al. Second cancers among 40,576 testicular cancer patients: focus on long-term survivors. *J Natl Cancer Inst* 2005;97(18):1354-65
17 Djaladat H, Burner E, Parikh PM et al. The association between testis cancer and semen abnormalities before orchiectomy: a systematic review. *J Adolesc Young Adult Oncol* 2014;3(4):153-59

Useful information

The British Association of Urological Surgeons
www.baus.org.uk

Orchid
www.orchid-cancer.org.uk

Cancer Research UK
www.cancerresearchuk.org

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