Histological tumour type (Required)

Reason/Evidentiary Support

In concordance with the dataset for Orchidectomy specimens, the World Health Organisation (WHO) 2016 classification of testicular tumours should be used.[1]

Retroperitoneal lymphadenectomy (RPLND) before treatment
The type of tumour identified in an RPLND is crucial information to determine further treatment. The tumour in prechemotherapy RPLNDs (also referred to as primary RPLNDs) generally (but not always) show similar findings to that in the orchidectomy specimen. In primary setting, pathologic N staging is more commonly used to determine the need for adjuvant chemotherapy with pN0 and pN1 leading to surveillance and pN2 and pN3 (rare) leading to adjuvant chemotherapy.

RPLND after treatment
After chemotherapy, and especially in late relapses, the pathology may be substantially different from that seen in primary RPLND.[2] In general terms, after chemotherapy, 40-50% of germ cell tumour cases show pure necrosis with no viable tissue seen. A further 40% show teratoma, while the remaining 10% show a mixture of 'malignant' germ cell elements such as embryonal carcinoma, or yolk sac tumour, and a small number may show somatic transformation. Pure teratomatous metastasis is generally treated by surgical excision alone, whereas patients who have other residual germ cell tumour components are usually treated with additional chemotherapy. Metastatic sex cord-stromal tumours are also occasionally operated upon.[3] Even the type of tumour seen substantially affects the prognostic and therapeutic implications[4] with, for example, certain variants being associated with a good outcome[5] while others are associated with an intermediate[6] or more aggressive course.[7] Diagnosis of these variants may be challenging and require expert consultation. The percentage of 'viable malignant cells' has also shown to be a determinant of prognosis in a number of studies.[8-11] 10% is the most common cut-off used to determine the need for further treatment.

For post-chemotherapy residual masses, particularly in the absence of a biopsy diagnosis prior to treatment, it is often useful to examine areas of necrosis, as ghost outlines of the tumour often remain and allow the distinction between seminoma and non-seminomatous germ cell tumour. The reporting of number and location of lymph nodes involved by necrosis, fibrosis, xanthomatous and fibroxanthomatous reaction is important to the treating physician to evaluate the extent and distribution of tumour in different lymph nodes. There is evidence that fibrosis often represents neoplastic stroma originating from teratoma or yolk sac tumor. The spindle cells in the areas of fibrosis are often reactive to cytokeratin and display allelic loss (85%) and 12p anomalies (33%) characteristic of germ cell tumours. Xanthomatous and fibroxanthomatous reaction may sometimes pose a diagnostic challenge and immunohistochemical staining for evaluation of residual tumour is deemed necessary in occasional cases. It is important to recognise that residual viable malignancy (embryonal carcinoma, yolk sac tumour, classical seminoma or choriocarcinoma) may trigger further chemotherapy and therefore it is important to only report viable elements along with percentage of viable tumour and not semi-viable or non-viable tumour. Necrosis and post-chemotherapy teratoma would not usually trigger further therapy, unless the clinical situation dictates otherwise. In the case of cystic trophoblastic tumour (CTT), an explanatory note should be provided to caution the

physicians against further chemotherapy. Data for CTT are limited but the largest study of 15 patients with follow-up showed that 11 did not recur, three showed late recurrences of possibly unrelated yolk sac tumour and the one patient who did recur with a rise in hCG had unresected residual masses.[5] For post-chemotherapy RPLND, it may be desirable to embed more of the specimen if it is found to contain necrosis or non-viable tumour to exclude small foci of viable tumour.

Secondary somatic malignancy is rare and challenging to diagnose. The tumour typically consists of a pure population of atypical mesenchymal or epithelial cells and occupies at least one low-power field (×4 objective, 5 mm in diameter).[1] Sarcomas are the most common type, though some post-chemotherapy sarcoma-like tumours may be sarcomatoid yolk sac tumours.[12] Primitive neuroectodermal tumour (PNET) is another relatively common somatic-type malignancy which behaves aggressively.[13,14] Most carcinomas are adenocarcinomas, usually Not Otherwise Specified (NOS) type. Occasionally, patients may develop nephroblastoma.[15]

A somatic malignancy in a metastasis increases likelihood of dying from the disease and if it is localized, surgical resection is the optimal treatment.[7] Patients usually respond poorly to the treatment for conventional germ cell malignancy.[16] Some somatic malignancies may respond to a specific chemotherapy that is effective for the specific subtype, so accurate subtyping of the somatic transformation is important.

WHO classification of tumours of the testis and paratesticular tissue[a1]

Descriptor	**ICD-O codes**
Germ cell tumours derived from germ cell neoplasia in situ (GCNIS)	
Non-invasive germ cell neoplasia	
Germ cell neoplasia in situ	9064/2
Specific forms of intratubular germ cell neoplasia *Tumours of one histological type (pure tumours)*	
Seminoma	9061/3
Seminoma with syncytiotrophoblast cells	
Non-seminomatous germ cell tumours	
Embryonal carcinoma	9070/3
Yolk sac tumour, postpubertal-type	9071/3
Trophoblastic tumours	
Choriocarcinoma	9100/3
Non-choriocarcinomatous trophoblastic tumours	
Placental site trophoblastic tumour	9104/3
Epithelioid trophoblastic tumour	9105/3
Cystic trophoblastic tumour	
Teratoma, postpubertal-type	9080/3
Teratoma with somatic-type malignancies	9084/3
Non-seminomatous germ cell tumours of more than one histological type	
Mixed germ cell tumours	9085/3
Germ cell tumours of unknown type	

Descriptor	ICD-O codes
Regressed germ cell tumours	9080/1
Germ cell tumours unrelated to germ cell neoplasia in situ	
Spermatocytic tumour	9063/3
Teratoma, prepubertal type	9084/0
Dermoid cyst	
Epidermoid cyst	
Well-differentiated neuroendocrine tumour (monodermal teratoma)	8240/3
Mixed teratoma and yolk sac tumour, prepubertal-type	9085/3
Yolk sac tumour, prepubertal-type	9071/3
Sex cord-stromal tumours	
Pure tumours	
Leydig cell tumour	8650/1
Malignant Leydig cell tumour	8650/3
Sertoli cell tumour	8640/1
Malignant Sertoli cell tumour	8640/3
Large cell calcifying Sertoli cell tumour	8642/1
Intratubular large cell hyalinizing Sertoli cell tumour	8643/1
Granulosa cell tumour	
Adult granulosa cell tumour	8620/1
Juvenile granulosa cell tumour	8622/0
Tumours in the fibroma-thecoma group	8600/0
Mixed and unclassified sex cord-stromal tumours	
Mixed sex cord-stromal tumour	8592/1
Unclassified sex cord-stromal tumour	8591/1
Tumour containing both germ cell and sex cord-stromal elements	
Gonadoblastoma	9073/1

a The morphology codes are from the International Classification of Diseases for Oncology (ICD-O). Behaviour is coded /0 for benign tumours; /1 for unspecified, borderline, or uncertain behaviour; /2 for carcinoma in situ and grade III intraepithelial neoplasia; and /3 for malignant tumours.

References

1 World Health Organization (2016). *World Health Organization (WHO) Classification of tumours. Pathology and genetics of the urinary system and male genital organs*. Moch H, Humphrey PA, Reuter VE, Ulbright TM. IARC Press, Lyon, France.

2 Daneshmand S, Albers P, Fossa SD, Heidenreich A, Kollmannsberger C, Krege S, Nichols C, Oldenburg J and Wood L (2012). Contemporary management of postchemotherapy testis cancer. *Eur Urol* 62(5):867-876.

3 Hendry J, Fraser S, White J, Rajan P and Hendry DS (2015). Retroperitoneal lymph node dissection (RPLND) for malignant phenotype Leydig cell tumours of the testis: a 10-year experience. *Springerplus* 4:20.

4 Riggs SB, Burgess EF, Gaston KE, Merwarth CA and Raghavan D (2014). Postchemotherapy surgery for germ cell tumors--what have we learned in 35 years? *Oncologist* 19(5):498-506.

5 Ulbright TM, Henley JD, Cummings OW, Foster RS and Cheng L (2004). Cystic trophoblastic tumor: a nonaggressive lesion in postchemotherapy resections of patients with testicular germ cell tumors. *Am J Surg Pathol* 28(9):1212-1216.

6 Howitt BE, Magers MJ, Rice KR, Cole CD and Ulbright TM (2015). Many postchemotherapy sarcomatous tumors in patients with testicular germ cell tumors are sarcomatoid yolk sac tumors: a study of 33 cases. *Am J Surg Pathol* 39(2):251-259.

7 Rice KR, Magers MJ, Beck SD, Cary KC, Einhorn LH, Ulbright TM and Foster RS (2014). Management of germ cell tumors with somatic type malignancy: pathological features, prognostic factors and survival outcomes. *J Urol* 192(5):1403-1409.

8 Berney DM, Shamash J, Hendry WF, Arora A, Jordan S and Oliver RT (2001). Prediction of relapse after lymph node dissection for germ cell tumours: can salvage chemotherapy be avoided? *Br J Cancer* 84(3):340-343.

9 Fox EP, Weathers TD, Williams SD, Loehrer PJ, Ulbright TM, Donohue JP and Einhorn LH (1993). Outcome analysis for patients with persistent nonteratomatous germ cell tumor in postchemotherapy retroperitoneal lymph node dissections. *J Clin Oncol* 11(7):1294-1299.

10 Fizazi K, Tjulandin S, Salvioni R, Germa-Lluch JR, Bouzy J, Ragan D, Bokemeyer C, Gerl A, Flechon A, de Bono JS, Stenning S, Horwich A, Pont J, Albers P, De Giorgi U, Bower M, Bulanov A, Pizzocaro G, Aparicio J, Nichols CR, Theodore C, Hartmann JT, Schmoll HJ, Kaye SB, Culine S, Droz JP and Mahe C (2001). Viable malignant cells after primary chemotherapy for disseminated nonseminomatous germ cell tumors: prognostic factors and role of postsurgery chemotherapy--results from an international study group. *J Clin Oncol* 19(10):2647-2657.

11 Fizazi K, Oldenburg J, Dunant A, Chen I, Salvioni R, Hartmann JT, De Santis M, Daugaard G, Flechon A, de Giorgi U, Tjulandin S, Schmoll HJ, Bouzy J, Fossa SD and Fromont G (2008). Assessing prognosis and optimizing treatment in patients with postchemotherapy viable nonseminomatous germ-cell tumors (NSGCT): results of the sCR2 international study. *Ann Oncol* 19(2):259-264.

12 Magers MJ, Kao CS, Cole CD, Rice KR, Foster RS, Einhorn LH and Ulbright TM (2014). "Somatic-type" malignancies arising from testicular germ cell tumors: a clinicopathologic study of 124 cases with emphasis on glandular tumors supporting frequent yolk sac tumor origin. *Am J Surg Pathol* 38(10):1396-1409.

13 Michael H, Hull MT, Ulbright TM, Foster RS and Miller KD (1997). Primitive neuroectodermal tumors arising in testicular germ cell neoplasms. *Am J Surg Pathol* 21(8):896-904.

14 Giannatempo P, Pond GR, Sonpavde G, Albany C, Loriot Y, Sweeney CJ, Salvioni R, Colecchia M, Nicolai N, Raggi D, Rice KR, Flack CK, El Mouallem NR, Feldman H, Fizazi K, Einhorn LH, Foster RS, Necchi A and Cary C (2015). Treatment and clinical outcomes of patients with teratoma with somatic-type malignant transformation: an International collaboration. *J Urol*.

15 Michael H, Hull MT, Foster RS, Sweeney CJ and Ulbright TM (1998). Nephroblastoma-like tumors in patients with testicular germ cell tumors. *Am J Surg Pathol* 22(9):1107-1114.

16 Motzer RJ, Amsterdam A, Prieto V, Sheinfeld J, Murty VV, Mazumdar M, Bosl GJ, Chaganti RS and Reuter VE (1998). Teratoma with malignant transformation: diverse malignant histologies arising in men with germ cell tumors. *J Urol* 159(1):133-138.