Clinical dilemmas in local and regional testis cancer

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Abstract

At the Canadian Testis Cancer Workshop, the multidisciplinary management of testis cancer care was discussed. The two-day workshop involved urologists, medical and radiation oncologists, pathologists, radiologists, physician's assistants, residents, fellows, nurses, patients, and patient advocacy group members.

This review summarizes the discussion regarding clinical dilemmas in local and regional testis cancer. We present cases that highlight the need for a coordinated approach to individualize care. Overarching themes include the importance of a multidisciplinary approach to testis cancer, willingness to involve a high-volume experienced center, and given that the oncological outcomes are excellent, a reminder that clinical decisions need to prioritize selecting a strategy with the least treatment-related morbidity when safe to do so.

Introduction

Testis cancer is the most common solid organ malignancy in men aged 15-29 years. There are approximately 1100 new cases diagnosed in Canada per year. The net 5 year survival from testis cancer in Canada is 96% [1]. Although 70-80% present as clinical stage 1 disease and the majority of these undergo surveillance, the remaining cases often present as clinical dilemmas in which there are a number of treatment options available [2]. These cases lead to lengthy discussions between uro-oncology, medical oncology and radiation oncology and often result in a challenging decision making process for the patient.

In November 2018, The Canadian Testis Cancer Workshop was convened. This two-day meeting was comprised of urologists, medical and radiation oncologists, pathologists, radiologists, physician's assistants, residents and fellows, nurses, patients and patient advocacy group members – all with an interest in testis cancer. One of the goals of the workshop was to discuss the challenging areas of testis cancer care – areas in which the guidelines are not necessarily clear or do not cover. The objective was to distill through discussion around cases, expert approach to working through these challenges.
Herein we present local/regional disease dilemmas and address distant disease dilemmas in a separate manuscript.

Case 1

A 25-year-old man presented with a 1-month history of a painless left testis mass.

- Medical History- Nil
- Social History- Accountant, Single, No children
- Tumor markers- Alpha feto-protein (AFP) 1.7 ng/mL, Human Chorionic Gondatropin (HCG) 1 IU/L Lactate Dehydrogenase (LDH) 230 microkat/L (*Normal*)
- Left radical orchiectomy- 3.5cm classic seminoma, lymphovascular invasion (LVI) negative, tunica/epididymis negative, rete testis negative, spermatic cord margin negative, pT1b
- Staging CT Thorax- non specific 3mm pulmonary nodule
- Staging CT Abdomen/Pelvis- 1.2cm x 0.9cm x 0.8cm node in left para-aortic region, Figure 1A and B.
- Postoperative tumor markers- AFP 2 ng/mL HCG 1 IU/L LDH 225 microkat/L (*Normal*)

This patient has borderline findings placing him between a stage I and IIA presentation. He was referred for a multidisciplinary opinion from radiation oncology, medical oncology and uro-oncology.

Given the borderline findings, he underwent an early repeat CT at 3 months to determine if the node in the retroperitoneum was true disease or false positive.
His CT at 3 months showed shrinkage of the left para-aortic node, such that it now measures 7mm, thus rendering him Stage I.

Options: Active surveillance, Radiotherapy, Chemotherapy, Primary retroperitoneal lymph node dissection (RPLND)

The majority of the attendees at the meeting favoured a surveillance approach however primary RPLND in stage I seminoma is currently being evaluated in clinical trials [3]. It was felt that primary RPLND for stage I seminoma should not be considered standard of care at this point.

Issues raised

Issue #1: Re-imaging the borderline node

The challenge of surveillance in a case with borderline lymph nodes lies in the timing of the first scan and the risk of progressive disease. Most clinicians agree that an early 're-staging' CT scan is appropriate in borderline cases. There needs to be a balance between risk of recurrence, overtreatment, length of surveillance and exposure to radiation with number of scans. In this case, if one had actively treated him based on his initial CT scan representing a Stage II cancer, he would have been overtreated with unnecessary morbidity. Regarding repeat imaging, options to reduce radiation dose include low-dose CT scans, or MRI. The Princess Margaret group compared the effectiveness of a low dose with standard dose CT protocol which provided an acceptable quality of image in 99% and reduced the dose by 55% for stage 1 testis cancer surveillance [4]. This low dose protocol is now the standard at the Princess Margaret Cancer Centre. In this case, a low-dose CT was used as follow-up imaging. An issue that came up was whether a low dose CT is optimal in such borderline cases, and whether patients are better served with a repeat full-dose CT with intravenous contrast to aid in making the final staging decision. Most felt a standard dose CT with intravenous contrast was preferable. Abdominal MRI is an alternative and is the imaging modality of choice in the Swedish and Norwegian Testicular Cancer Group (SWENOTECA) and can be used by experienced radiologists [5,6]. The acknowledged unknowns at present are the cost, resource availability and access, as well as the true sensitivity and specificity in detecting retroperitoneal relapse in a timely way compared to the gold-standard CT scan. The TRial of Imaging and Schedule in Seminoma Testis (TRISST) is a trial from the UK comparing MRI and CT for surveillance in CS1 seminoma. The primary endpoint is to assess the proportion of patients relapsing with Stage 2C disease or greater. The study is no longer recruiting patients and had aimed for 660 patients. It is due to report this year [7].

Issue #2: Pathology review

It is well accepted that given the implications for management with significantly different morbidity profiles- that all testis cancer cases should be reviewed by an expert genitourinary pathologist [8-11]. Harari et al demonstrated that a second opinion pathology report from an expert centre resulted in a 31% discrepancy of histological subtype and the pathologic stage was altered in 23% of cases [12]. A similar rate of discrepancy was found in Ontario, using population level data. Our group observed that while only 10% of orchiectomy specimens underwent a second review, 40% of them had a meaningful change in parameters, although only a 5% change in histological subtype [13]. Similar central review of radiological imaging with standardised reporting would be welcomed.

Case 2

A 37-year-old man presented with a painless left testis mass and left flank/back pain.

- Medical History- Nil
- Social History- Married, 2 children (no desire for more)
- Left radical orchiectomy- Mixed germ cell tumor (90% embryonal 10% choriocarcinoma), LVI positive, rete testis positive, spermatic cord positive, pT3
- Staging CT Thorax- normal
- Staging CT Abdomen/Pelvis- 4.5cm x 2.9cm node in left para-aortic region, Figure 2.
- Post operative tumor markers- AFP 76 ng/mL HCG 2713 IU/L LDH 225 microkat/L
- Discussed at multidisciplinary rounds and was referred to medical oncology.
- The patient received chemotherapy BEP x3.
- Post chemotherapy markers normalized- AFP 2 ng/mL HCG 3 IU/L LDH 225 microkat/L
- CT Abdomen/Pelvis 4 weeks following completion of chemotherapy- left para-aortic mass had shrunk from 4.5cm to 1.2cm in short-axis dimension.

Options- Surveillance, salvage chemotherapy, radiotherapy, post-chemotherapy RPLND

The majority of attendees at this stage favored a surveillance approach with a short interval repeat CT, while some advocated immediate post-chemotherapy RPLND (pcRPLND).
The patient underwent an initial period of surveillance. Repeat CT scan at 3 months showed the mass to now measure 9mm with normal markers. He was maintained on surveillance and 10 years later the mass remained 8mm with normal markers.

Issues raised

Issue#1: Measurement of nodal masses

The measurement of nodal masses can be an area for confusion. The current EAU guidelines specify that the node be measured 'in greatest dimension' where as some recommend decision making based on maximum axial diameter or short axis diameter [10,14,15]. Even this terminology is confusing. Lymph nodes are usually larger in the cranio-caudal dimension (best visualized on a coronal view of the CT). The "long-axis" can be pictured as a line measuring the greatest length in the cranio-caudal fashion. The "short-axis" is perpendicular to the long-axis. This would be the largest dimension measured in the axial view on the CT scan. For large masses it is not of consequence but for small or borderline masses it can change management. Literature supporting surveillance of <1cm masses was based on maximum short-axis dimension. Howard et al, demonstrated that craniocaudal diameter was an independent predictor of relapse for NSGCT [15]. Accuracy and standardisation of reporting are of paramount importance.

Issue#2: Repeat CT in good responders

Given the good response to chemotherapy in this case resulting in a node that is just over 1cm in short-axis dimension, the group felt that an initial period of surveillance is reasonable. It was acknowledged that in many health systems with fixed operating room resource, such as Canada, there are challenges with surgical waiting lists and thus an initial period of surveillance often occurs anyway. Although a repeat CT in 'good responders' was favoured by many as opposed to proceeding to post chemotherapy RPLND, there is a lack of data to support this practice.

Issue #3: Surveillance of post-chemotherapy masses ≤1cm

The initial dilemma in this case centred around the mass being just over 1cm as described. However, once repeat imaging showed the mass to be ≤1cm, there was uniform agreement on surveillance. However, such agreement is not true world-wide.

Two series from the Journal of Clinical Oncology in 2011 provide the most compelling data in support of surveillance of patients who achieve a complete response following chemotherapy (defined as normalization of markers and a residual mass ≤1cm). They reported relapse free rates of 94% at 5 years and 92% at 15 years respectively [16,17]. At Princess Margaret, surveillance is the preferred option for patients with a complete response. Our data of 191 men demonstrates a 8.4% relapse on surveillance [18].

The concern with a mass >1cm is that at surgical resection these masses will harbor teratoma in up to 45% and viable cancer in 10% [19]. Post-chemotherapy RPLND is a morbid procedure- associated with a complication rate of up to 40%- including significant morbidity such as chylous ascites, ejaculatory failure, vascular injuries, bowel obstruction, ventral hernia and concomitant procedures such as nephrectomy, adrenalectomy, bowel and vascular resection [20,21]. Thus, there is merit in potentially avoiding PC-RPLND if it could be done safely.

Issue #4: Extent of post-chemotherapy surgery

If patients are to undergo a pc-RPLND for small masses, the extent of a surgical resection is continually debated. Cho et al., summarized the Indiana experience with modified retroperitoneal template pcRPLND and observed a 7% relapse rate, but all relapses were outside of what a full bilateral RPLND would have covered. They argued in favour of modified template for select patients with small volume, unilateral disease [22]. Carver et al, suggest that up to 32% of patients will relapse outside the boundaries of a modified unilateral template pc-RPLND for NSGCT [23] and as a result they advocate for all patients to undergo a full bilateral template. Debate remains regarding the definitions of the modified templates used in the Carver study and it is refuted that a modified template is safe in unilateral masses <5cm [24,25]. It was the feeling of the group that most centres in North America perform bilateral pcRPLND and this remains the reference standard. There was complete agreement that pcRPLND must be performed by experienced surgeons at experienced sites.

Case 3

A 36-year-old man presented with a painless left testis mass.

- Medical History- Nil
- Pre-operative Tumor markers- AFP 1.2 ng/mL HCG 1.1 IU/L LDH 180 microkat/L (*Normal*)
- Left radical orchiectomy- 3.5cm classic seminoma, LVI negative, tunica/epididymis negative, rete testis negative, spermatic cord margin negative, pT1b
- Staging CT Thorax- normal
- Staging CT Abdomen/Pelvis- 3.7cm node in left para-aortic region, Figure 3A and B.
- Post operative tumor markers- AFP 1.1 ng/mL HCG 1.2 IU/L LDH 175 microkat/L (*Normal*)
- This patient has Stage 2B disease.

Options- Chemotherapy (BEPx3), Radiotherapy, primary RPLND

Patient received radiotherapy (25Gy in a dog-leg pattern to the retroperitoneal and pelvic nodes) and remains disease free 4 years later.

Issues raised

Issue #1: Shared and multidisciplinary decision making in the stage IIB seminoma

The dilemma in this patient is which treatment option is optimal. There needs to be a shared decision-making process with a well-informed patient. Most of the decision focuses on the risk of relapse and the treatment related morbidity given the long-term outcome is excellent with both approaches [26].

The Princess Margaret approach to Stage 2 seminoma has been to favour radiation treatment. Chung et al demonstrated between 89- 91% relapse free rate with radiation treatment alone [27,28] for the overall cohort. However, in observing that enlarging tumor size and number of nodes were associated with a higher risk of relapse, the risk of relapse for the IIB sub-group is 10.3% [28] and this is what should be quoted to this particular patient. Patterson et al improved the relapse free rate to 96% with the addition of a single cycle of carboplatin which is used in the UK [29]. The use of neoadjuvant chemotherapy may also reduce the extent of the radiotherapy field [30]. However, the addition of chemotherapy either before or after radiation therapy is not standard of care and is not reflected in any guidelines to date.

Standard chemotherapy in this case would be bleomycin, etoposide and cisplatin for 3 cycles. Relapse rate after chemotherapy for IIB seminoma is 8% [31].The toxicity related to chemotherapy needs to be weighed against that of radiotherapy and the long term consequences of second malignancy risk [32]. There is a concern regarding the increased secondary malignancy risk following treatment- this risk pertains equally to both chemotherapy and radiotherapy [33,34]. The PLATINUM study group has highlighted

several of the key long-term toxicities of chemotherapy with over 40% reporting >1 adverse health outcome [35].

If this patient were to have had stage IIC disease – there was agreement that chemotherapy remains the standard of care [36].

Issue #2: Primary RPLND for seminoma

The alternate strategy discussed was a primary RPLND. There are two ongoing phase 2 trials for primary RPLND in patients with clinical stage 2A/B seminoma assessing progression free survival without adjuvant treatment: the German PRIMETEST trial and the U.S. based SEMS trial [3,37]. The group felt a primary RPLND could be offered within a trial setting. Interim results from the PRIMETEST trial were presented at GU ASCO in 2019 and observed 11 patients who underwent RPLND. Three of these patients (22%) received one cycle of carboplatin prior to RPLND. With a mean follow-up of 18 months, they had a 36% recurrence rate [37]. Acknowledging this recurrence rate, the group felt that while primary RPLND could be offered within a trial setting that we best await final results from PRIMETEST and SEMS before considering this as a standard of care recommendation.
If RPLND is to be chosen, internationally debate persists regarding whether RPLND should be robotic or open. The early reports of primary robotic RPLND are encouraging. It appears a safe and feasible procedure and the reported ejaculation rates with a nerve sparing approach exceed 90% [38,39]. Debate also remains regarding the extent of RPLND - a full bilateral template reduces the risk of recurrence however is associated with greater morbidity and operative time [21,24,40,41].

A patient centred approach is important in these cases where the individual has more than one viable option available to them.

Case 4

A 37-year-old man presented with a painless right testis mass.

- Medical History- Nil
- Social History- Not currently employed; otherwise unremarkable
- Pre-operative Tumor markers- AFP 1.4 ng/mL HCG 1IU/L LDH 165 microkat/L (*Normal*)
- Right radical orchiectomy- 2cm classic seminoma, LVI negative, tunica/epididymis negative, rete testis negative, spermatic cord margin negative, pT1a
- Staging CT Thorax- normal
- Staging CT Abdomen/Pelvis- 1.8cm node in inter aortocaval region, Figure 4.
- Post operative tumor markers- AFP 1.1 ng/mL HCG 1 IU/L LDH 180 microkat/L (*Normal*)
- This patient has Stage 2A disease.

Options- Chemotherapy (BEPx 3), Radiotherapy, primary RPLND, Surveillance

This patient was unfortunately incarcerated in jail and refused appointments – he only re-presented 3 months later with a CT showing a stable 1.8cm node in inter aortocaval region.

Treatment options remained the same as before, but the group was in favour of active surveillance given the complete stability of the node over 3 months. The drawback of this approach is that an abdominal CT scan using conventional size criterion for lymph node enlargement will miss a significant percentage (false-positive rates of 22-44%) of patients with retroperitoneal metastases [42].

The challenge here also pertains to patient compliance. Ernst et al, demonstrated patient compliance varies on surveillance protocols with 78% being compliant with clinic visits and 64% with CT scans across 7 different Canadian centres [43]. Paffenholz et al recently demonstrated that non-guideline direct care results in worse relapse free survival rates [44]. In a patient in which compliance to surveillance may be an issue- consideration and discussion needs to be given to upfront treatment. Despite this- this patient ultimately underwent a period of surveillance given his non-compliance with appointments- as his disease remained stable on imaging he continue on surveillance as opposed to adjuvant treatment and remained disease free at end of follow-up.

We do not advocate a surveillance approach to Stage 2 disease however this patient enforced a surveillance protocol due to his non-compliance. We recommend repeat imaging in advance of intervention to get an up to date overview of the disease state.

Conclusions

This selection of clinical cases provides an insight into the complexity of the management of local and regional testis cancer. Overarching themes include the importance of a multi-disciplinary approach to testis cancer, willingness to involve a high-volume experienced centre, and given that the oncological outcomes are excellent, a reminder that clinical decisions need to prioritize selecting a strategy with the least treatment related morbidity when safe. Testis cancer patients are usually young fit men and their needs to be an individualised patient centred approach to their care to fit with their long term life goals and expectations.

References

1. Canadian Cancer Statistics. A 2018 special report on cancer incidence by stage. www.cancer.ca
2. Znaor A, Lortet-Tieulent J, Jemal A, et al. International variations and trends in testicular cancer incidence and mortality. Eur Urol. 2014 Jun;65(6):1095-106.
3. https://clinicaltrials.gov/ct2/show/NCT02537548
4. O'Malley ME, Chung P, Haider M, et al. Comparison of low dose with standard dose abdominal/pelvic multidetector CT in patients with stage 1 testicular cancer under surveillance. Eur Radiol. 2010 Jul;20(7):1624-30.
5. Tandstad T, Dahl O, Cohn-Cedermark G, et al. Risk-adapted treatment in clinical stage I nonseminomatous germ cell testicular cancer: the SWENOTECA management program. J Clin Oncol. 2009 May 1;27(13):2122-8.
6. Honecker F, Aparicio J, Berney D, et al. ESMO Consensus Conference on testicular germ cell cancer: diagnosis, treatment and follow-up. Ann Oncol. 2018 Aug 1;29(8):1658-1686.
7. Cafferty FH, Gabe R, Huddart RA, et al. UK management practices in stage I seminoma and the Medical Research Council Trial of Imaging and Schedule in Seminoma Testis managed with surveillance. Clin Oncol (R Coll Radiol). 2012 Feb;24(1):25-9.
8. Wood L, Kollmannsberger C, Jewett M, et al. Canadian consensus guidelines for the management of testicular germ cell cancer. Can Urol Assoc J. 2010 Apr;4(2):e19-38.
9. Stephenson A, Eggener SE, Bass EB, et al. Diagnosis and Treatment of Early Stage Testicular Cancer: AUA Guideline. J Urol. 2019 May 6:101097JU0000000000000318
10. Albers P, Albrecht W, Algaba F, et al. Guidelines on Testicular Cancer: 2015 Update. Eur Urol. 2015 Dec;68(6):1054-68.
11. Purshouse K, Watson RA, Church DN, et al. Value of Supraregional Multidisciplinary Review for the Contemporary Management of Testicular Tumors. Clin Genitourin Cancer. 2017 Feb;15(1):152-156. 27.
12. Harari SE, Sassoon DJ, Priemer DS, et al. Testicular cancer: The usage of central review for pathology diagnosis of orchiectomy specimens. Urol Oncol. 2017 Oct;35(10):605.e9-605.e16
13. Nason GJ, Sweet J, Landoni L, et al. Discrepancy in pathology reports upon second review of radical orchiectomy specimens for testicular germ cell tumors. Can Urol Assoc J. 2020 Jun 16.
14. Hilton S, Herr HW, Teitcher JB, et al. CT detection of retroperitoneal lymph node metastases in patients with clinical stage I testicularnonseminomatous germ cell cancer: assessment of size and distribution crite ria. AJR Am J Roentgenol. 1997 Aug;169(2):521-5.
15. Howard SA, Gray KP, O'Donnell EK, et al. Craniocaudal retroperitoneal node length as a risk factor for relapse from clinical stage I testicular germ cell tumor. AJR Am J Roentgenol. 2014 Oct;203(4):W415-20.
16. Kollmannsberger C, Daneshmand S, So A, et al.Management of disseminated nonseminomatous germ cell tumors with risk-based chemotherapy followed by response-guided postchemotherapy surgery. J Clin Oncol. 2010 Feb 1;28(4):537-42.

17. Ehrlich Y, Brames MJ, Beck SD, et al. Long-term follow-up of Cisplatin combination chemotherapy in patients with disseminated nonseminomatous germ cell tumors: is a postchemotherapy retroperitoneal lymph node dissection needed after complete remission? J Clin Oncol. 2010 Feb 1;28(4):531-6.
18. Nason GJ, Jewett MAS, Bostrom PJ, et al. Long-term surveillance of patients with complete response following chemotherapy for metastatic nonseminomatous germ cell tumor (NSGCT) European Urology Focus.
19. Albers P, Weissbach L, Krege S, et al Prediction of necrosis after chemotherapy of advanced germ cell tumors: results of a prospective multicenter trial of the German Testicular Cancer Study Group. J Urol. 2004 May;171(5):1835-8.
20. Baniel J, Foster RS, Rowland RG, et al. Complications of post-chemotherapy retroperitoneal lymph node dissection. J Urol. 1995 Mar;153(3 Pt 2):976-80.
21. Heidenreich A, Pfister D, Witthuhn R, et al. Postchemotherapy retroperitoneal lymph node dissection in advanced testicular cancer: radical or modified template resection. Eur Urol. 2009 Jan;55(1):217-24.
22. Cho JS, Kaimakliotis HZ, Cary C, et al. Modified retroperitoneal lymph node dissection for post-chemotherapy residual tumour: a long-term update. BJU Int. 2017 Jul;120(1):104-108.
23. Carver BS, Shayegan B, Eggener S, et al Incidence of metastatic nonseminomatous germ cell tumor outside the boundaries of a modified postchemotherapy retroperitoneal lymph node dissection. J Clin Oncol. 2007 Oct 1;25(28):4365-9.
24. Beck SD, Foster RS, Bihrle R, et al Is full bilateral retroperitoneal lymph node dissection always necessary for postchemotherapy residual tumor? Cancer. 2007 Sep15;110(6):1235-40.
25. Hiester A, Nini A, Fingerhut A, et al. Preservation of Ejaculatory Function After Postchemotherapy Retroperitoneal Lymph Node Dissection (PC-RPLND) in Patients With Testicular Cancer: Template vs. Bilateral Resection. Front Surg. 2019 Jan 17;5:80.
26. Kollmannsberger C, Tyldesley S, Moore C, et al. Evolution in management of testicular seminoma: population-based outcomes with selective utilization of active therapies. Ann Oncol. 2011;22(4):808-814.
27. Chung PW, Warde PR, Panzarella T, et al. Appropriate radiation volume for stage IIA/B testicular seminoma. Int J Radiat Oncol Biol Phys. 2003 Jul 1;56(3):746-8.
1. 28 . Chung PW, Gospodarowicz MK, Panzarella T, et al. Stage II testicular seminoma: patterns of recurrence and outcome of treatment. Eur Urol. 2004 Jun;45(6):754-59; discussion 759-60.
28. Patterson H, Norman AR, Mitra SS, et al. Combination carboplatin and radiotherapy in the management of stage II testicular seminoma: comparison with radiotherapy treatment alone. Radiother Oncol. 2001 Apr;59(1):5-11.
29. Horwich A, Dearnaley DP, Sohaib A, et al. Neoadjuvant carboplatin before radiotherapy in stage IIA and IIB seminoma. Ann Oncol. 2013 Aug;24(8):2104-7.
30. Giannatempo P, Greco T, Mariani L, et al. Radiotherapy or chemotherapy for clinical stage IIA and IIB seminoma: a systematic review and meta-analysis of patient outcomes. Ann Oncol. 2015 Apr;26(4):657-68.

31. Garcia-del-Muro X, Maroto P, Gumà J, et al. Chemotherapy as an alternative to radiotherapy in the treatment of stage IIA and IIB testicular seminoma: a Spanish Germ Cell Cancer Group Study. J Clin Oncol. 2008 Nov 20;26(33):5416-21.
32. Fung C, Fossa SD, Milano MT, et al. Solid tumors after chemotherapy or surgery for testicular nonseminoma: a population-based study. J Clin Oncol. 2013 Oct 20;31(30):3807-14.
33. van den Belt-Dusebout AW, de Wit R, Gietema JA, et al Treatment specific risks of second malignancies and cardiovascular disease in 5-year survivors of testicular cancer. J Clin Oncol. 2007 Oct 1;25(28):4370-8.
34. Fung C, Sesso HD, Williams AM, et al. Multi-Institutional Assessment of Adverse Health Outcomes Among North American Testicular Cancer Survivors After Modern Cisplatin-Based Chemotherapy. J Clin Oncol. 2017 Apr 10;35(11):1211-1222.
35. Detti B, Livi L, Scoccianti S, et al Management of Stage II testicular seminoma over a period of 40 years. Urol Oncol. 2009 Sep-Oct;27(5):534-8.
36. Lusch A, Gerbaulet L, Winter C, et al. Primary retroperitoneal lymph node dissection (RPLND) in stage IIA/B seminoma patients without adjuvant treatment: a phase II trial (PRIMETEST) Journal of Urology. 2017;197(4):e1044–e1045.
37. Cheney SM, Andrews PE, Leibovich BC, et al Robot-assisted retroperitoneal lymph node dissection: technique and initial case series of 18 patients. BJU Int. 2015 Jan;115(1):114-20.
38. Pearce SM, Golan S, Gorin MA, et al Safety and Early Oncologic Effectiveness of Primary Robotic Retroperitoneal Lymph Node Dissection for Nonseminomatous Germ Cell Testicular Cancer. Eur Urol. 2017 Mar;71(3):476-482.
39. Steiner H, Peschel R, Bartsch G. Retroperitoneal lymph node dissection after chemotherapy for germ cell tumours: is a fullbilateral template always necessary? BJU Int. 2008 Aug;102(3):310-4.
40. Ehrlich Y, Yossepowitch O, Kedar D, et al. Distribution of nodal metastases after chemotherapy in nonseminomatous testis cancer: a possible indication for limited dissection. BJU Int. 2006 Jun;97(6):1221-4
41. Fernandez EB, Moul JW, Foley JP, et al. Retroperitoneal imaging with third and fourth generation computed axial tomography in clinical stage I nonseminomatous germ cell tumors. Urology. 1994 Oct;44(4):548-52.
42. Ernst DS, Brasher P, Venner PM, et al Compliance and outcome of patients with stage 1 non-seminomatous germ cell tumors (NSGCT) managed with surveillance programs in seven Canadian centres. Can J Urol. 2005 Apr;12(2):2575-80.
43. Paffenholz P, Heidegger IM, Kuhr K, et al. Non-Guideline-concordant Treatment of Testicular Cancer Is Associated With Reduced Relapse-free Survival. Clin Genitourin Cancer. 2017 Sep 6. pii: S1558-7673(17)30273-2.

Figures and Tables

Fig. 1. Case 1: Stage 1/2A seminoma. Computed tomography demonstrating 1 cm node in left para-aortic region.

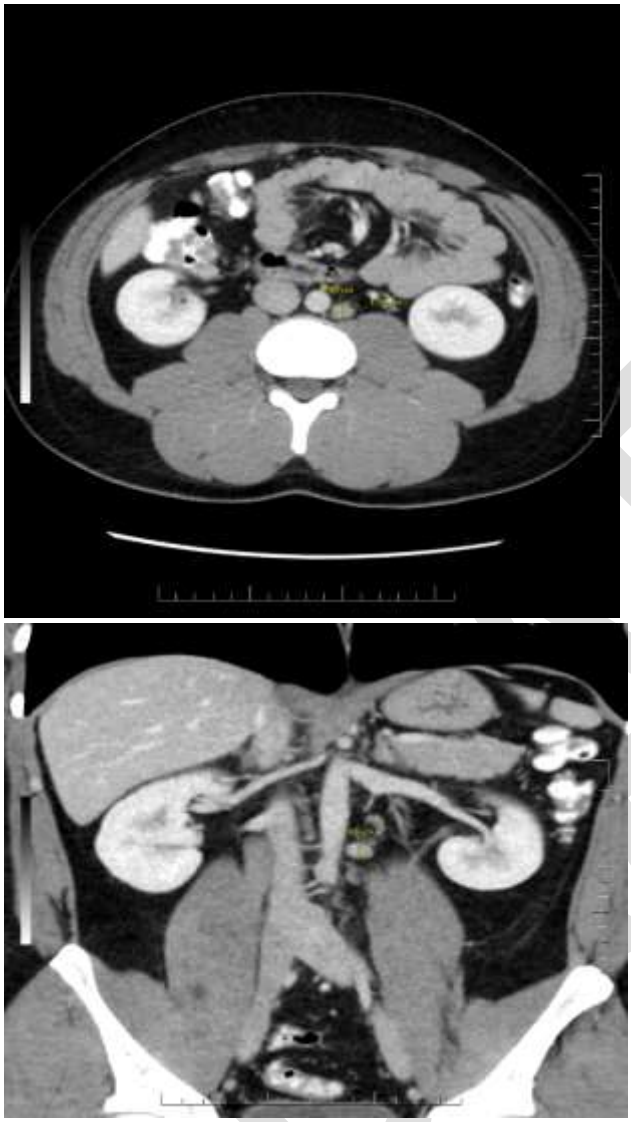


Fig. 2. Case 2: Stage 2B non-seminoma. Computed tomography demonstrating 4.5 cm left para-aortic lymph node.

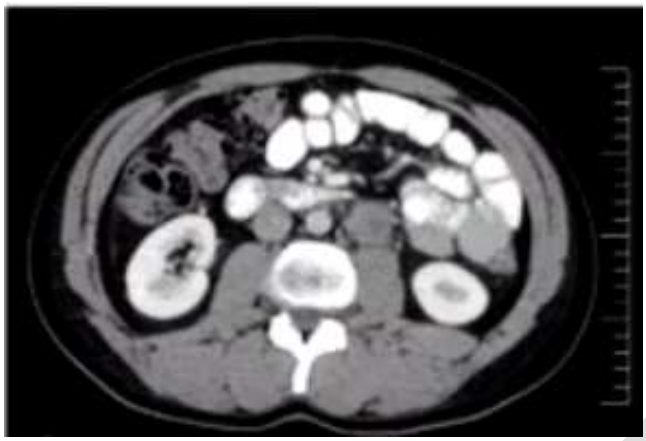
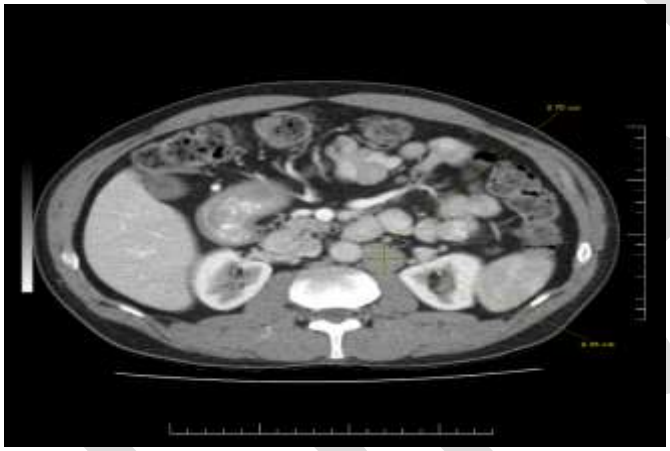


Fig. 3. Case 3: Stage 2 B seminoma. Computed tomography demonstrating 3.7 cm node in left para-aortic region.



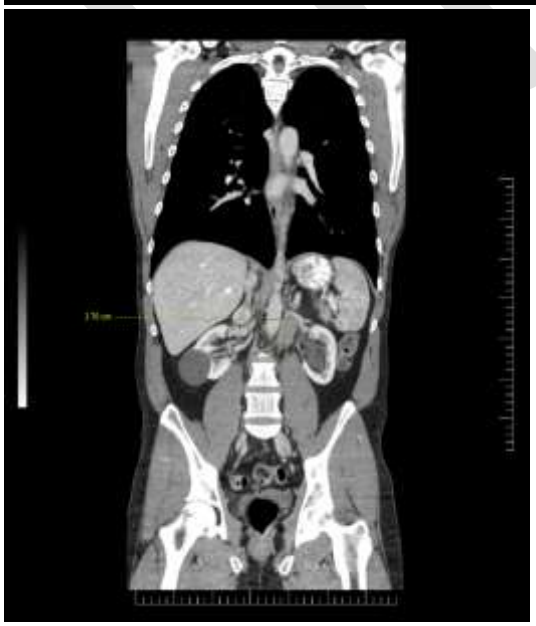


Fig. 4. Case 4: Stage 2A seminoma. Computed tomography demonstrating 1.8 cm inter-aortocaval node.