Original Article

Role of primary chemotherapy in management of large tumors of undescended testis: Our experience

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Abstract

Objective: This study aimed to share our experience with tumors of undescended testis (UDT) and to assess the impact of primary cisplatin-based chemotherapy on such tumors.

Materials and Methods: This study included the cases of tumor in UDT from February 2005 to December 2011. Evaluation of the cases was done with proper clinical examination and laboratory investigations along with tumor markers (alfa-feto protein, beta-human chorionic gonadotropin, lactate dehydrogenase) and contrast-enhanced computed tomography abdomen. Fine needle aspiration cytologywas done in all cases. Primary chemotherapy with three cycles of bleomycin, etoposide, and cisplatin regimen at three weekly intervals started in all cases. Response to treatment was seen after four weeks of the third cycle.

Results: Fourteen cases (12.5%) of germ cell tumor in UDT out of 112 cases of germ cell tumor of the testis were included. The age ranged from 16-60 years. Histological diagnosis was pure seminoma in all cases. After three cycles of BEP regime, complete response was seen in 11 cases and partial response in three cases where the residual tumor was excised along with retroperitoneal lymph node dissection RPLND. Of the 14 cases, 13 were in regular follow-up and one was lost to follow-up. All on follow-up were doing well without recurrence till now.

Conclusion: Surgical removal of the primary tumor in UDT with or without bulky metastasis is complicated. Primary chemotherapy with cisplatin-based regimen is a good option in such cases.

Key Words: BEP, cisplatin, undescended testis, primary chemotherapy

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INTRODUCTION

Undescended testis (UDT) is one of the most common congenital anomaly of the genitourinary system in young boys. UDT is found in approximately 3% of full-term male newborns.[1,2] Unilateral UDT is more common and bilateral UDT occurs in 1.6%-1.9% of boys.[3] Nearly 80% of UDT are clinically palpable and 20% are nonpalpable.[3]

UDT is a major risk factor for the development of testicular malignancy. About 7-10% of patients with testicular tumor have a history of cryptorchidism.[4] The relative risk of testicular cancer in patients with cryptorchidism is 3-14 times the normal.[5-7] Nearly 5-10% of patients with a history of UDT develop malignancy in the contralateral, normally descended gonad.[3] UDT (intra-abdominal) have five times more chance of malignant transformation than inguinal.[8] The risk of developing testicular malignancy is higher with bilateral than with unilateral UDT.[8] In men with unilateral cryptorchidism, the malignancy is usually on the affected side, although malignant degeneration is

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found on the normally descended side in about 20% of cases.[9] A study done by Pettersson *et al.*[10] in a cohort of 16,983 patients, showed that the risk of malignancy in UDT is almost double in boys not operated until after the age of 13 years. Factors favoring development of malignancy in UDT are:[11]

1. Abnormal germ cell morphology
2. Elevated temperature
3. Interference with blood supply
4. Endocrine dysfunction
5. Gonadal dysgenesis

Tumors in uncorrected UDT are now rare in the West, but in India, there are still patients with uncorrected UDT who go on to develop malignancy because of illiteracy, ignorance, and negligence.

The biological behavior and outcome of malignancy in undescended and descended testes appear the same, but the treatment of primary tumor may differ, especially when patients present with a large abdominal mass.

Induction chemotherapy followed by delayed excision of the primary, and excision of residual metastatic nodes appear to be a logical approach to large and bulky tumors in UDT with or without retroperitoneal disease.

AIM

The aim of this study is to share our experience with tumors of UDT and assess the impact of primary cisplatin-based chemotherapy alone on such tumors.

MATERIALS AND METHODS

This study included 14 cases of tumor in UDT from February 2005 to December 2011, who attended Department of Urology. Evaluation of the cases with history and careful clinical examination was done. Laboratory investigations included routine hematocrit, coagulation profile, renal function tests, liver function tests, and tumor markers serum alfa-feto protein (s-AFP), serum beta-human chorionic gonadotropin (s-β-HCG), and serum lactate dehydrogenase (s-LDH). Imaging studies included chest X-ray, ultrasound of whole abdomen, and contrast-enhanced computed tomography scan (CECT) abdomen. Fine needle aspiration cytology was done in all cases for histological diagnosis. Primary chemotherapy with three cycles of the bleomycin, etoposide, and cisplatin (BEP) regimen at three weekly intervals was started in all cases.

Dose:

1. Bleomycin-30 units/m^2 BSAon days 1, 8, and 15
2. Etoposide-100 mg/m^2 BSA on days 1-5
3. Cisplatin-20 mg/m^2 BSA on days 1-5.

Response to the treatment was observed four weeks after completion of third cycle with clinical examinations, tumor markers (AFP, β-HCG, and LDH), chest X-ray, and CECT abdomen. Complete response is considered if there is no positive findings in clinical examination, normal tumor markers, and normal CT findings (disappearance of primary tumor and residual fibrous tissue of size <3 cm). Patients were followed up at three-monthly intervals with clinical examinations, tumor markers, chest X-ray and CECT abdomen for first two years. In the next year, patients were followed up at three-monthly intervals with clinical examinations, tumor markers, chest X-ray, and six-monthly CECT abdomen. Later, patients were followed up with six-monthly clinical examinations, tumor markers, chest X-ray, and annually one CECT abdomen.

RESULTS

In our study, 14 cases (12.5%) of germ cell tumor in UDT out of a total 112 cases of germ cell tumor of testis were included. The age ranged from 16-60 years (mean: 34.7). We had 11 cases of tumor in unilateral UDT and three cases of bilateral UDT (with tumor in one UDT). Nine patients presented with pain and mass, three with only pain, and two with only mass in UDT. Of the 14 cases of tumor in UDT, 6 were located in the right inguinal region, four were in the left inguinal region, and four cases were totally intra-abdominal. In two cases, surface ulceration of the tumor was present. The size of the tumor ranged from 7-18 cm (mean: 12.5 cm). The levels of AFP and β-HCG were within normal limit, but s-LDH was raised in seven cases (1.5-10 times the normal). Histological diagnosis was pure seminoma in all cases. Out of 14 cases, 11 were in stage II-C, 1 in stage III-B, and 1 in stage II-B [Table 1].

After three cycles of the BEP regimen, complete response was seen in 11 cases and partial response in 3 cases (decrease in size of primary tumor to 4-6 cm and residual mass >3 cm) where we excised the residual tumor along with RPLND [Figures 1 and 2]. All cases tolerated the chemotherapy, except one case where we contemplated dyselectrolytemia, which was managed conservatively and five cases had minor complications such as nausea, vomiting, and headache. Of 14 cases, 13 were on regular follow-up and one was lost to follow-up after four months. Two

Table 1: Clinical stages of the cases

Clinical staging	No. cases (total: 14)
I-B	
T-4/N-0/M-0/S-0	1
II-B	
T-4/N-2/M-0/S-0	1
II-C	
T-4/N-3/M-0/S-0	5
T-4/N-3/M-0/S-1	6
III-B	
T-4/N-3/M-0/S-2	1

patients are on regular follow-up for >5 years and another seven patients for >2.5 years, and the remaining four are on follow-up for <2 years. Median follow-up of 34.3 months (range: 4-63 months) [Figure 3]. All patients on follow-up were doing well without recurrence till now.

DISCUSSION

Undescended testis is the most common congenital genitourinary abnormality in males and is associated with malignancy and infertility.[12] Nearly 7-10% patients with testicular tumor have a history of UDT.[4] In the present study, 12.5% cases of germ cell tumors of the testis had tumor in UDT.

In a study by Husseiny *et al.*,[13] the most common clinical finding was pain with mass (69%) followed by pain. In the present study, most common presentation was pain with swelling in 64% cases. Histologically, seminoma is most common in UDT with an incidence of 50-80%.[14] Coupland *et al.*[15] found that tumors in UDT are more commonly associated with seminoma. In our study, all 14 cases were seminoma. Seminoma in UDT is associated with increase in LDH in about 44% cases.[13] In our study, LDH was increased in seven cases (50%).

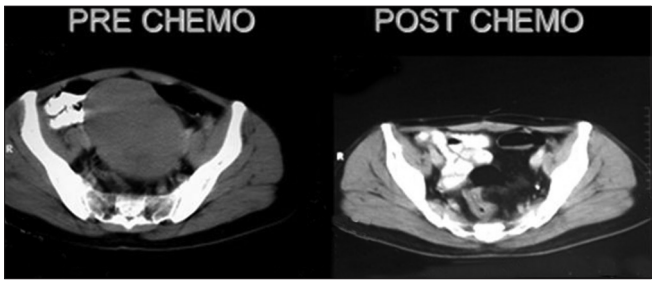

Figure 1: Pre- and post chemotherapy CT showing complete resolution of tumor

Figure 2: Picture showing complete resolution of tumor in UDT after three cycles of BEP chemotherapy

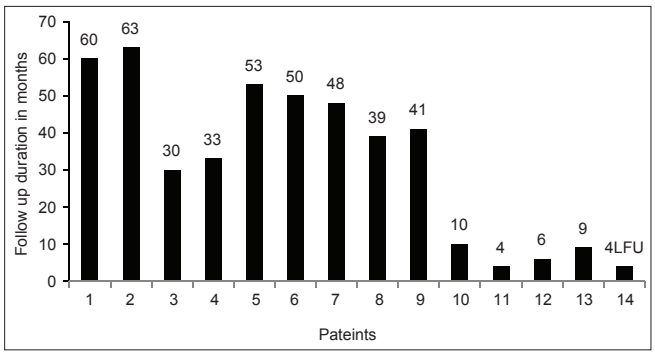

Figure 3: Histogram showing follow-up following primary chemotherapy

Patients with UDT presented with advanced stage as compared to normally descended testis.[16,17] Chivlers *et al.*[18] found 75% stage I disease in the normally descended testis as compared to 38% in UDT. In our series, only one case presented in stage I. Stages I and IIb tumors in UDT as per protocol should be managed either by radiotherapy or retroperitoneal node dissection. Kulkarni *et al.*[16] managed stages I and IIb either by radiotherapy or retroperitoneal node dissection, giving three- and five-year survival of 11/11 (100%) and 7/7 (100%), respectively. In our study, stage I and IIb cases were given induction chemotherapy and were recurrence free after four months (stage I case) and 39 months (stage IIb case) of follow-up. In the study by Kulkarni *et al.*,[16] patients in stages IIc and III received induction chemotherapy (VAB-6) first and showed complete response (CR) in four (45%) and partial response (PR) in five (55%). In our study, patients in stages IIc and IIIB received induction chemotherapy (BEP-3) alone and nine cases (64%) had complete response and three cases (21.4%) had partial response.

In our study, the high overall tumor response rate confirms that these tumors in UDT responds well to chemotherapy alone, and induction chemotherapy is a good option for the management for low as well as advanced stage of UDT tumors. Therefore, we can avoid technically challenging surgical intervention in such a situation and preserve them only for selected cases.

CONCLUSION

Surgical removal of the primary tumor in an UDT with or without bulky metastasis is technically challenging. It further delays induction of chemotherapy by at least three weeks. Primary chemotherapy with combination regimen (BEP) may be offered in such cases. Three cycles of standard cisplatin-based chemotherapy are sufficient to achieve optimal response in such situations. Although our series is small, it sheds light on the role of primary chemotherapy alone in tumors in UDT. A large series and long follow-up will ascertain the efficacy of primary chemotherapy in bulky tumors in UDT.

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