SUCCESSFULLY MANAGED CASE OF RHABDOMYOSARCOMA OF BLADDER AND PROSTATE WITH POOR RESPONSE TO INTENSIVE CHEMOTHERAPY AND OBSTRUCTIVE UROPATHY

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Abstract. Rhabdomyosarcoma (RMS) is the commonest soft tissue sarcoma in children. Of these bladder-prostate (BP-RMS) is one of the most common primary sites. Treatment of these has recently revolved predominantly around chemotherapy with adjunct radiotherapy. Surgical excision is reserved for non responding cases. We present the case of a 2 year old boy with BP-RMS who had a turbulent course during treatment, complicated by obstructive uropathy, recurrent urinary tract infections with febrile neutropenia episodes and non response to chemotherapy and radiation. Obstructive uropathy and deranged renal functions secondary to pelvic tumors especially BP-RMS should be aggressively managed especially since these tumors are highly chemo-sensitive and it is imperative to start cytotoxic, nephrotoxic agents as soon as possible. Recurrent UTI is frequent problem associated with external urinary drainages especially in presence of febrile neutropenia and in malignant cases; exteriorisation of the ureters is an excellent option to tide over the treatment period.

Key words: Rhabdomyosarcoma, Obstructive Uropathy, Chemotherapy, Radiotherapy

Introduction

Rhabdomyosarcoma (RMS) is the commonest soft tissue sarcoma in children. Of these bladder-prostate (BP) RMS is one of the most common primary sites. The role of aggressive surgery has taken a back seat over the recent years and intensive chemotherapy and radiation has become the primary treatment modality for managing these tumors especially as they provide an opportunity for bladder preservation. Surgery carries a high risk of urinary incontinence and denervation of the neurovascular bundles leading to erectile dysfunction and complications are frequently reported following radical surgery. Complication following radical surgery include, wound infection, abscess formation, fistula, malnutrition, hydronephrosis and bowel obstruction.

Treatment of BP-RMS can follow a torrential course at times, both due to the mass and the intensive chemotherapy. Management of these complications can be tricky and may require multi-modality measures. Obstructive uropathy and deranged renal functions secondary to pelvic tumors especially BP-RMS should be aggressively managed especially since these tumors are highly chemo-sensitive and it is imperative to start cytotoxic, nephrotoxic agents as soon as possible. Chemotherapy for BP-RMS achieves good overall survival and event-free survival rates but it can be difficult to determine whether a residual mass that remains after chemotherapy and radiotherapy represents tumour or not. The pathological interpretation of RMS treated with radiotherapy is extremely difficult. Therefore, a residual mass can subject patients to more local therapy than is necessary, whereas in other cases, a prolonged delay in local treatment can result in death. Surgical excision may be the only choice in such cases.

Case Report

A two year old male child presented with complaints of decreased appetite and weight loss for last two months and altered sensorium for last 1 day. Blood investigation revealed
a markedly deranged renal function test and imaging revealed a large lesion occupying the bladder and prostate. The boy underwent cystoscopy which revealed a large mass occupying almost entire bladder, obscuring both the ureteric orifices. A biopsy was taken from the mass and bilateral percutaneous nephrostomies were inserted under fluoroscopy guidance. The biopsy reported the mass to be RMS, embryonal variety. Metastatic workup was negative. The renal function returned to normal in a few days and the child was started on intensive chemotherapy according to International Rhabdomyosarcoma Study Group regime IV (Vincristine, Actinomycin D, Cyclophosphamide) protocol. In a few weeks, the child started developing recurrent episodes of febrile neutropenia and urinary tract infections (UTI). The repeat scan revealed resolution of the hydronephrosis, however the mass persisted to be of the same size. The child underwent a repeat endoscopy to attempt a retrograde insertion of double J (DJ) stents and getting rid of external nephrostomy tubes. However the ureteric orifices were still not accessible and hence only the tubes were changed. The chemotherapy was escalated to Ifosfamide, Cisplatin and Etoposide (ICE). In an attempt to reduce the UTIs, the tubes were frequently changed. However the UTIs persisted. The child also received Intensive Pelvic Radiotherapy (39.6Gy in 22 fractions over 39 days). In view of the persistent multidrug resistant urinary infections, it was decided to get the child rid of the external draining tubes. The tumor showed no signs of shrinking and the child was not fit for any major surgical interventions due to the cytotoxic chemotherapy confounded by recurrent infections and episodes of febrile neutropenia. Hence the baby underwent bilateral end low ureterostomies and the nephrostomy tubes were removed. The episodes of infections ceased and the child continued to receive a total of six episodes of ICE chemotherapy. A Positron Emission Tomography (PET) scan was executed to assess the response. The mass persisted to be the same size however it showed no signs of FluoroDeoxyGlucose (FDG) uptake. Considering poor response to chemotherapy and radiation, it was decided to excise the tumor. The child underwent radical cystoprostatectomy (Fig. 1 & Fig. 2). Intra-operatively, the bladder and prostate were densely adherent to surrounding structures (post radiation fibrosis). The left common iliac was injured and repaired during the dissection. The post-operative period was uneventful. The entire mass, although persisting in size, showed no viable cells on histopathology. One year following the surgery, the child is recurrence free and passing urine through the end ureterostomies. He is planned for an orthotopic neobladder reconstruction after a minimum two years of recurrence free survival.

Discussion

RMS is a highly malignant mesenchymal tumor representing 15–20% of malignancies of childhood and is the most common childhood soft-tissue sarcoma. BP-RMS makes up about one-fourth of all RMS. Histologically, 90% of BP-RMS are of the embryonal type. This type is considered a favourable type for prognosis. In our case too, the biopsy revealed an embryonal type but responded poorly to chemotherapy and radiation.

At the time of presentation, the tumors are usually more than 5 cm in size. The tumors usually present as obstructive uropathy, hematuria or suprapubic mass. Clinically, there is...
a similar presentation whether the tumor is of bladder or prostate origin. The obstructive uropathy needs to be aggressively managed for preservation of renal function especially for the initiation of nephrotoxic chemotherapeutic agents essential for treatment of such tumors. Meir et al. investigated the children with malignant pelvic tumors presenting with obstructive uropathies. BP RMS was the commonest of all these tumors. The study included 9 boys and 8 girls with the mean age and median follow-up of 5.7 years and 2.5 years, respectively. Twelve children underwent diversion by nephrostomy tubes and 3 by DJ stents; 2 patients underwent resection of the tumors with ureteroureterostomy. Complications after the insertion of the stents included febrile UTI or pyelonephritis in 4 of the children with DJ stents. In the nephrostomy group, febrile UTI developed in 3 and the tube fell out in 1, and was blocked in another. However none of the studies in the literature describes ureterostomy as a treatment modality for these recurrent UTI episodes. We firmly believe that in cases where DJ insertion is not possible and external drainage is causing recurrent problems, exteriorisation of the lower ends of the ureters is a viable option; especially if a cysto-prostatectomy is contemplated in the future.

Almost 80% of patients with BP-RMS show a complete response to chemotherapy with adjunct radiation while 20% achieve only partial or no response. Five-year failure-free survival is however similar for participants achieving complete response (80%) and partial or no response (78%). Almost 50% of the patients who undergo surgery following poor response reveal a viable tumor tissue.\textsuperscript{[10]} Tumors, which had no viable mass following chemoradiation, had a significantly higher 5 year survival rates (81%); compared to those who had viable tumor persisting following completion of chemotherapy and radiation (53%). Among the later group, the survival rates are better if the margins are histologically negative.\textsuperscript{[11]} In our case we hope for a favourable outcome as the entire specimen was free of any viable cells. Another dilemma arises when even following intensive chemotherapy, the mass persists. The only way to definitely state that the entire mass is non-viable is possible after excision and histo-pathological examination of the entire specimen. Approximately 7-12% patients who demonstrate completely radiological response may still harbour viable tumor cells.\textsuperscript{[11]} While in patients in whom there is no response is poor, 50% of cases still have viable cells. In our case the post-chemotherapy imaging revealed no decrease in the size of the mass of the tumor. Cystoscopic biopsies could not have established whether the entire tumor is free of viable cells or not. Hence, it was decided to proceed with a radical excision instead. We believe that it may be unwise to leave a tumor mass behind considering it to be completely necrotic and dead. Complete excision is the only way to prove that.

Conclusion
Obstructive uropathy and deranged renal functions secondary to pelvic tumors especially BP-RMS should be aggressively managed especially since these tumors are highly chemosensitive and it is imperative to start these nephrotoxic, cytotoxic agents as soon as possible. Recurrent UTI is frequent problem associated with external urinary drainages especially in presence of febrile neutropenia and in malignant cases; exteriorisation of the ureters is an excellent option to tide over the treatment period. Aggressive surgical treatment of poorly responding masses gives excellent local control and the prognosis is better if the entire specimen is devoid of viable cells.

References
Successfully managed case of rhabdomyosarcoma of bladder and prostrate with poor response to intensive chemotherapy and obstructive uropathy