Case Report

Embryonal Rhabdomyosarcoma of the Prostate: Clinico-Pathological Highlights with Review of Literature

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Abstract

Rhabdomyosarcoma (RMS) is the third most common extra-cranial sarcoma occurring in childhood, adolescents, and young adults (AYAs); and is rare in adults. Literature about RMS mainly considers RMS in AYAs, either with that in the children or adults, even though histological, molecular, and clinical characteristics of RMS in AYAs are significantly different from either of the two. Herein, we report a case of prostatic embryonal RMS, in a 17-year-old boy, along with the review of literature of prostatic RMS, with emphasis on AYAs. Our patient presented with clinical complaints of acute urinary retention, Grade IV prostatomegaly and, low serum prostate-specific-antigen (0.11ng/dl). The diagnosis was clinched by prostatic biopsy, which revealed diffuse 'small round blue cell' tumour admixed with larger rhabdomyoblasts, displaying positivity for desmin and myogenin, on immunohistochemistry. Clinicians should be mindful that RMS is found in all age groups ranging from childhood to adults; however, the clinical, histological, and molecular features are different. RMS in AYAs is often treated according to the guidelines provided for the paediatric age group. Treatment mostly comprises a multimodality approach, including surgery with/without chemo- and radiotherapy. Prognosis in AYAs is worse than in children but is better than in adults. Thus, early diagnosis gains utmost importance to provide comparatively more probability of rendering treatment and, hopefully, a better quality of life.

Keywords: *Embryonal; prostate; prostatic neoplasms; rhabdomyosarcoma, rhabdomyosarcoma; sarcoma*

Introduction

RMS is the most common sarcoma in children and adolescents, affecting the genitourinary tract in approximately 20% of cases.[1] Histologically, it has three subtypes: embryonal (ERMS), alveolar (ARMS), and pleomorphic (PRMS) subtypes. In children and AYAs, the most common histological variants are embryonal and alveolar subtypes. ERMS is more common in children and ARMS in AYAs.[2] ERMS occurs most commonly in the paratesticular soft tissue, head and neck, extremities, and genitourinary tract, in the decreasing order; and is the most common soft tissue sarcoma of the lower genitourinary-tract in the paediatric age group.[1,2]

Overall, ERMS forms 0.3%–1% of all prostatic malignancies.[3] ERMS exhibits bimodal age distribution, with a more significant peak in childhood (0–5 years); and more minor in adolescents.[2] RMS is not only rare in adults but also histologically different. In adults, pleomorphic and RMS-not-otherwise-specified (RMS-NOS) are the most common histotypes.[1,2] Given these differences, our manuscript aims to elucidate the biology, clinical characteristics, diagnosis, management, and late effects of treatment of RMS, with emphasis on AYAs.

Case History

A 17-year-old boy presented with complaints of acute urinary retention for the past 1 day. Digital rectal examination revealed left-sided grade-IV prostatomegaly predominantly obliterating rectal lumen, with ipsilateral external iliac lymphadenopathy. Serum prostate-specific-antigen was within the normal limit (0.11 ng/dL). Contrast-enhanced CT showed a large enhancing mass in the pelvis with non-visualisation of the prostate separately from the mass. The mass infiltrates the left lateral wall of the urinary bladder and reaches up to the pelvic sidewall on the left side. The left lower ureter is infiltrated by the lesion, causing left

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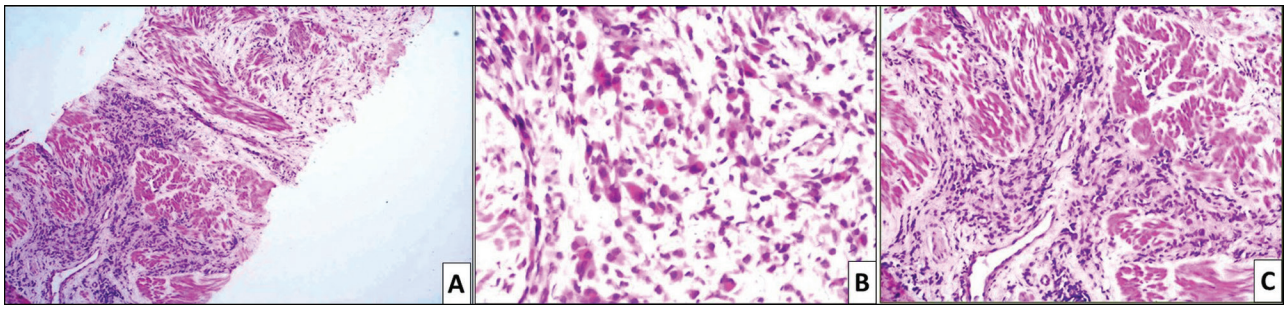

Figure 1: Haematoxylin and eosin-stained (H&E) sections shows a prostatic fibromuscular stromal tissue infiltrated by small round to spindle cells with scant to abundant eosinophilic cytoplasm (A x100; C x400). Higher magnification shows round, oval, or spindle shaped rhabdomyoblasts having abundant eosinophilic cytoplasm, large vesicular nuclei, prominent nucleoli, and frequent cross-striations (B x400)

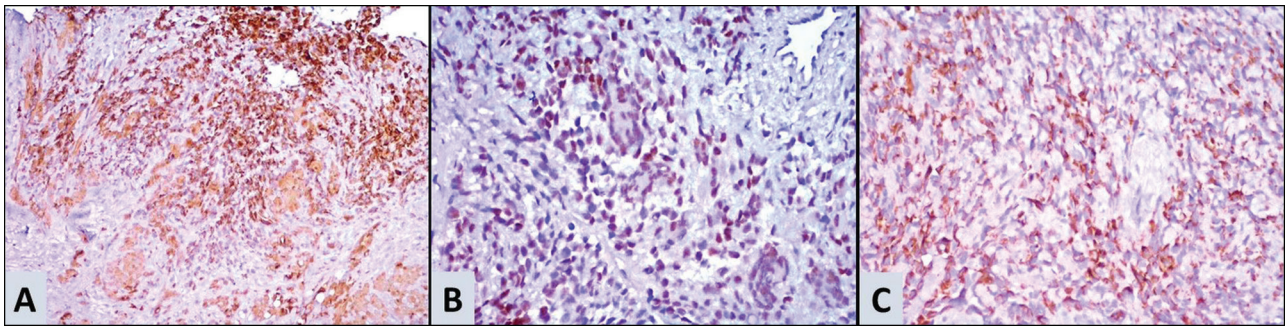

Figure 2: A-Immunohistochemistry (IHC) demonstrating cytoplasmic Desmin immunopositivity. B-Myogenin immunopositive cells on IHC. C-Shows tumour cells immunopositive for Vimentin IHC

moderate hydroureteronephrosis with infiltration of the left psoas muscle. Anteriorly the mass is eroding the pubic symphysis and posteriorly infiltrating into the rectum. Large lymph nodal mass is also seen in the pelvis with multiple retroperitoneal lymphadenopathies. Multiple lytic bony metastases with metastatic deposits along bilateral pleura, a paravertebral region with epidural extension.

Prostatic biopsy was performed, which revealed a small round cell tumour disposed of in sheets, with an intermixed population of larger rhabdomyoblasts displaying large eccentric nuclei, prominent nucleoli and moderate-to-abundant dense eosinophilic cytoplasm. Small round cell population exhibited round nuclei, fine chromatin, inconspicuous nucleoli, and scant cytoplasm [Figure 1A–C]. On immunohistochemistry, tumour cells were Desmin and Myogenin and Vimentin positive [Figure 2A–C]. With these immunohistopathological features, diagnosis of embryonal rhabdomyosarcoma (RMS) was rendered. Before commencement of treatment, the patient developed lower abdominal distension, pain, and complaint of not passing stool for two days. The patient underwent diversion colostomy and was transferred to the medical oncology department for chemotherapy and further management.

Discussion

Sarcomas are rare in the prostate and form 0.3%–1.0% of all prostatic tumours, of which 30% are ERMS.[4] Prostatic RMS are predominantly found in children. In them, it is the main prostatic neoplasm. In AYAs, only six cases have been reported to date, summarised in Table 1. Prostatic RMS usually presents with obstructive urinary symptoms and/or haematuria, incontinence, pelvic pain, and intestinal obstipation.[1,5-9]

Most RMS occur sporadically, but syndromic associations are also known, for example, Li–Fraumeni syndrome, neurofibromatosis type-1, Costello syndrome, Noonan syndrome, hereditary retinoblastoma; most frequent being Li–Fraumeni syndrome.[3-5] Studies in animal models have shown chemical, physical, and biological factors responsible for RMS, which have established a link between RMS and other diseases, like muscular dystrophy.[4-6] Nearly all ERMS display loss of heterozygosity in region 11p15.5, which includes genes for IGF2, H19, and CDKN1C.[2-4] Characteristic chromosomal translocations are identified in 70%–80% of ARMS, namely t(2;13)(q35;q14) and t(1;13)(p36;q14); causing expression of chimeric transcription factors PAX3-FKHR(PAX3-FOXO1) or PAX7-FKHR(PAX7-FOXO1), respectively.[5-8] Fusion gene status may be pivotal in ARMS risk stratification, owing to significantly different clinical behaviour and molecular characteristics of ARMS with/without a fusion gene.[6-9] Other molecular alterations detected in both ARMS and ERMS include alterations in p53, Rb1, CDKN2A, MYCN, RAS, MET and ALK genes.[1-3] PRMS is more common in adults, with scant literature available regarding its biological pathways.[2]

Table 1: Summary of case reports of Prostatic RMS in adolescents and young adult male

Authors	Age/ Sex	Histological subtype	Molecular/ cytogenetic alterations	Treatment	Clinical course	Outcome
Treetipsatit et al. 2009, Pediatric and Developmental Pathology.	28/M	Mixed embryonal and alveolar RMS	Both components expressed the PAX3-FKHR fusion gene.	Initial resection with chemoradiation and Radiotherapy.	Locally aggressive and multiple tumor metastases in the right obturator muscle, pancreas, intra-abdominal lymph nodes, and peripancreatic lymph nodes.	Died 9 months after diagnosis.
Niimi et al. 2010, International Journal of Clinical Oncology.	20yr	ERMS	KIT-positive tumor. Based on this finding this is the first report of post radiation sarcoma.	CT	Local disease with enlarged Prostate.	Good response to chemotherapy, further course unknown.
Latz et al. 2013, International Journal of Urology.	23yr	Spindle cell RMS	Not performed	Initial radiochemotherapy followed by radical Cytoprostatectomy.	Locally aggressive and disseminated disease.	Patient died 14 months after diagnosis.
Emir et al. 2016, The Turkish Journal of Pediatrics.	10yr	ARMS	Unknown	Initial CT, followed by tumour resection and CT; RT also given.	Unknown	Good response; patient followed up for 51 months; alive.
Schildhaus et al. 2016, Diagnostic pathology.	25 yr	Spindle cell ERMS	No PAX3-FOXO1A fusion and for translocation t(11;22) (q24;q12) were detected.	CT	Locally aggressive and bilateral pulmonary metastases.	Patient died 17 months after diagnosis.
Konno et al. 2019, Urologia Internationalis.	32yr	ERMS	Unknown	CT	Enlarged prostate with lung and internal iliac lymph node metastases.	Cured disease with no recurrence for 49 months after termination of maintenance chemotherapy that lasted for 24 months.
Present case	17yr	ERMS	Unknown	CT	Grade-IV prostatomegaly obliterating rectal lumen, with ipsilateral external iliac lymphadenopathy; developed intestinal obstipation later.	Lost to follow-up.

RMS: Rhabdomyosarcoma; ERMS: embryonal rhabdomyosarcoma; CT: Chemotherapy; RT: Radiotherapy

Diagnosis is made by prostatic biopsy. Histological differential diagnoses include prostatic lymphoma, small cell carcinoma, stromal tumours of uncertain malignant potential; leiomyosarcoma, inflammatory myofibroblastic tumours, malignant peripheral nerve sheath tumours; and rarely rectal gastrointestinal stromal tumours.[7-10] Diagnosis can be deciphered by correlation with age, clinical, immunohistochemical, cytogenetic and molecular findings.[5-8]

Radiological and nuclear scans are helpful in determining location, disease extent and metastases, which help in tailoring treatment and evaluating a patient's prognosis.[2,3] Paediatric RMS are staged using guidelines by various international collaborative groups, popular being Children Oncology Group (COG) protocols. Unlike paediatric RMS, no specific guidelines are available for adults.[4-7] Most clinical trials have been performed on children for whom prognostic characteristics are thus, described. The prognosis is worse in AYAs and adults compared to children.[5,6] A study reported a 5-year survival rate of 61% in children, while only 27% in adults.[8-10] Factors like unfavourable anatomic distribution, unusual histologies, lymph-node involvement, advanced disease, distant metastases, and no

standardised treatment protocols for adults are implicated in the above difference.[10]

Treatment includes a multimodality approach comprising chemotherapy with/without surgical resection and/or radiotherapy.[7-10] Consensus recommendations for the treatment of RMS are available for children but not adults. AYAs are, however, treated according to the guidelines provided for children. Paediatric cases respond to the treatment better than adults.[3-7] Survival rates for both the AYAs and adults with RMS are significantly worse than the children and need to be improved further. A study reported more applicability of ifosfamide-based chemotherapy in adolescents and adults<50 years of age due to its improved tolerance, asserting pharmacological and pharmacodynamic factors.[2-5]

Late effects of treatment occur in RMS survivors, infertility being the most important.[7,8] AYAs must be pre-informed about it and should also be provided with opportunities like sperm/ova preservation. Other effects include hematologic/peripheral neuro-toxicity, cardiomyopathy, head and neck anomalies, musculoskeletal growth delay, and bowel obstruction which may lead to decreased physical activity, exercise tolerance, cosmetic, speech, and occupational concerns; impacting the life of AYAs significantly.[4-7]

Conclusion

Prognosis in AYAs is worse than in children, but is better than the adults, highlighting the role of early diagnosis and prompt complete treatment, to proffer patients, with more probability of longer and better-quality life. Hence, we, through our manuscript, want to convey that firstly, RMS should be considered in the differential diagnoses to render an early diagnosis and avoid delay in patient management. Secondly, much has to be done to improve the prognosis and life quality of AYAs with RMS by increasing understanding of the biology of RMS found in adults and standardising the treatment for AYAs and adults. Moreover, AYAs should be enrolled in clinical trials to enlighten about their treatment and survival characteristics. Finally, late effects post-treatment have a significant impact on the lives of AYA survivors. Thus, long-term surveillance, early intervention, and other measures should be taken to improve their life.

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Conflicts of interest

There are no conflicts of interest.

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