Report of a Primary Testicular Embryonal Rhabdomyosarcoma

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Primary testicular rhabdomyosarcoma is a rare pediatric genitourinary tumor with few cases reported in the literature. The clinical presentation is identical to that of other common testicular neoplasms. Diagnosis entails careful microscopic examination and immunohistochemical analysis to rule out other primary testicular malignancies. Treatment consists of radical orchiectomy and adjuvant chemotherapy with possible retroperitoneal lymph node dissection. This multimodal approach is required to improve survival outcomes and reduce disease recurrence. We present the case of a primary testicular embryonal rhabdomyosarcoma in a 19-year-old male who presented with a rapidly, enlarging, painless testicular mass. He was treated with radical orchiectomy and adjuvant chemotherapy. Once found with metastatic disease, he then received salvage chemotherapy and radiotherapy without success. [*P R Health Sci J 2022;41(4):250-253*]

Key words: Pediatric cancer, Testicular cancer, Rhabdomyosarcoma

Rhabdomyosarcomas (RMSs) are the most common pediatric soft tissue sarcoma. Yet, primary RMS of the testis is rarely encountered, accounting for 1-2% of all pediatric intratesticular malignancies (1-4). We report the case of a primary testicular rhabdomyosarcoma (PTRMS) in a 19-year-old male.

Case Report

A 19-year-old male presented with an enlarging, painless, right scrotal mass since 10 months prior. Past medical history and systems review were unremarkable. Physical examination identified a fixed, poorly defined, non-transilluminating, right scrotal mass. Ultrasound revealed a 10-cm testicular mass with solid appearance. Abdominopelvic CT scan showed an enhancing, right testicular mass (8x6.7cm) without retroperitoneal adenopathy, bony lesions, or infiltrated lung bases. Chest X-ray was negative for metastatic lung lesions. B-HCG, LDH, and AFP tumor markers were within normal limits.

The patient underwent a right radical orchiectomy with partial scrotectomy. The surgical specimen contained a soft tissue mass (9.8 x 8.9 x 5.9cm) with focal necrosis and hemorrhage that completely replaced normal testicular parenchyma. No epididymal tissue was identified. Grossly, tumor extension was limited to the testis without invasion into the spermatic cord, tunica vaginalis, or scrotal skin. Microscopy revealed extensive lymphovascular invasion and rhabdomyoblastic differentiation with scattered necrosis and anaplasia. Immunohistochemistry revealed positive expression of desmin, muscle actin, myogenin, and ASMA; but, none for CD30, CD34, EMA, keratins, AE1/AE3, OCT4, PLAP, S100, and SMA. The diagnosis of intratesticular embryonal rhabdomyosarcoma was corroborated by a national pathology reference laboratory.

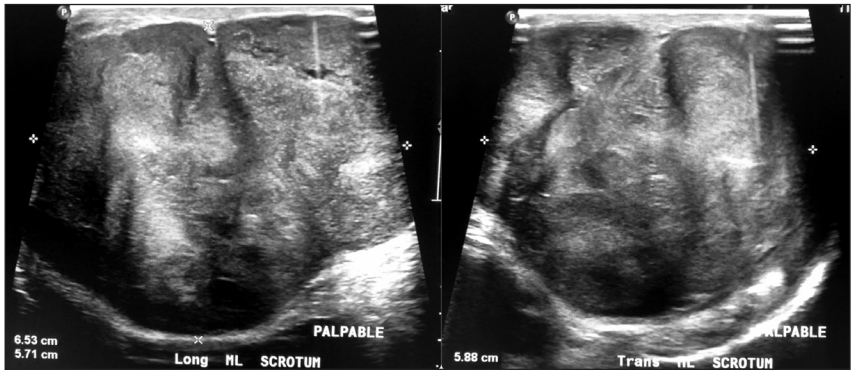

Figure 1. Testicular Ultrasound. Imaging of the right testicle demonstrates total replacement of normal testicular parenchyma by a solid, inhomogeneous mass.

He received four cycles of adjuvant chemotherapy with vincristine, adriamycin, and cyclophosphamide. Nuclear

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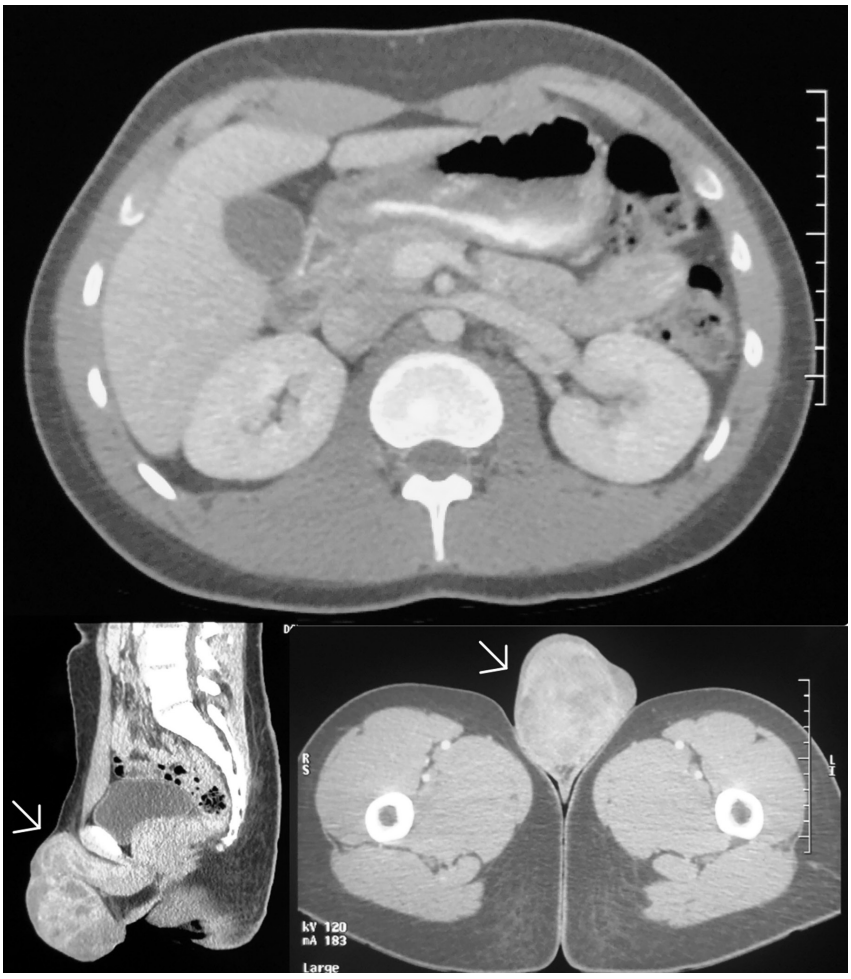

Figure 2. Preoperative radiological workup. Abdominopelvic CT scan with IV contrast shows the presence of an enhancing, 8 cm x 6.7 cm mass in the right testicle, as indicated by the white arrows. No evidence of retroperitoneal adenopathy is identified.

imaging at one and six months follow up was found without evidence of metastatic disease. However, he developed diffuse pulmonary metastatic disease by one year follow up. He was treated with a second round of chemotherapy and chest radiotherapy, but eventually succumbed to his disease within four months of this new finding.

Discussion

RMSs account for about 5% of all pediatric malignancies and half of childhood soft tissue sarcomas (1-5). Genitourinary RMSs arise from mesenchymal elements of the urinary bladder or paratesticular tissues, including the spermatic cord, epididymis, or testicular envelopes (1-3,5). Paratesticular RMSs represent 4-7% of primary RMSs and nearly 17% of all pediatric intrascrotal malignancies (6). However, testicular RMSs are much rarer and represent 1-2% of all intratesticular pediatric malignancies (3,4).

PTRMSs present with a clinical history indistinguishable to that of other testicular neoplasms. Classic tumoral markers are usually negative and imaging often fails to discern the site of origin. RMSs, associated with an aggressive clinical course, often present with lymphatic and/or hematogenous spread at the time of diagnosis (2-5,7).

RMSs arise from primary mesenchymal cells committed to varying degrees of skeletal muscle differentiation (1,2). Yet, the etiology of PTRMSs is not as clear as that of paratesticular RMSs. Some argue that PTRMSs result from the overgrowth of the sarcomatous component of a primary germ cell tumor (3,4,7). Rhabdomyoblastic differentiation of undifferentiated mesenchyme in testicular tissues or displacement of embryonal muscle tissues during early development may also explain the etiology of PTRMSs. Neoplastic involvement of paratesticular tissues could also suggest testicular extension of a primary paratesticular sarcoma (3).

The most common histologic variant is the embryonal RMS, which accounts for 59% of all childhood RMSs and 80% of genitourinary RMSs. Alveolar RMSs, the second most common, are more prevalent in adolescents and grant an unfavorable prognosis (1,2). Rhabdomyoblasts, characteristic of skeletal muscle differentiation, can be identified on light microscopy as small, elongated, pleomorphic tumor cells with central hyperchromatic nuclei, eosinophilic cytoplasms, and poorly defined myofilaments or cross striations. Both variants share the same tumor cell morphology, but differ in that alveolar RMS resembles pulmonary alveoli (1,2).

Immunohistochemistry and cytogenetic studies provide additional evidence supportive of rhabdomyoblastic differentiation to help narrow differential diagnoses. Expression of muscle-actin, myosin, desmin, myoglobin, Z-band protein, and myogenic-differentiation-1 is highly sensitive and specific for skeletal muscle differentiation. Over 99% of RMSs express polyclonal desmin. Muscle-actin, myogenin, and myoglobin are expressed in 95%, 95%, and 78% of tumors, respectively (1,3-5,8,9). Notably, myogenin expression is greater in less differentiated tumor cells, more prevalent in alveolar RMSs, and associated with poorer outcomes (1). Neoplasms of other lineages can be excluded with negative expression of their characteristic tumor markers. For example, testicular germ cell tumors, which often have a mixed sarcomatous component, can be excluded with negative immunohistochemistry for

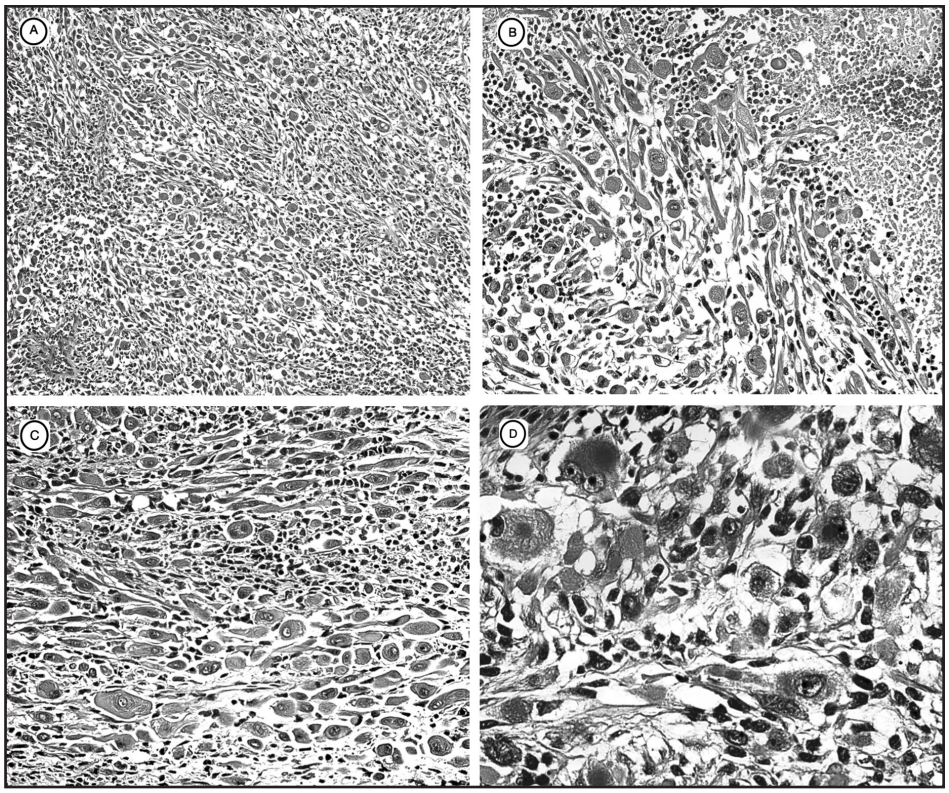

Figure 3. Microscopic examination of orchiectomy specimen consistent with an embryonal rhabdomyosarcoma. (A) reveals the presence of large, atypical cells intermixed with round, spindle cells in a loose myxoid stroma (H&E, 10x). (B) and (C) show large, atypical cells intermixed with round, spindle cells with hyperchromatic nuclei and scant eosinophilic cytoplasm. Tumoral necrosis is also present (H&E; 20x). (D) demonstrates the presence of large atypical cells with variable degrees of skeletal muscle differentiation in a loose myxoid stroma. Many rhabdomyoblasts can be identified and characteristically contain large, eccentric, vesicular nuclei with prominent nucleoli and deeply eosinophilic, granular cytoplasm (H&E; 40x).

OCT4 and alkaline phosphatase (3). Furthermore, embryonal RMSs consistently show a loss of heterozygosity in the 11p15 region, which codes for IGF2, H19, and CDKN1C. Parental imprinting of this region results in IGF2 overexpression and unopposed tumor growth (1,2). More typically of alveolar RMS are chromosomal translocations, like t(2;13)(q35;q14)), and their resulting fusion proteins, such as PAX-FKHR(PAX-FOXO1) (1,2,8).

Treatment of PTRMSs combines surgical resection with possible retroperitoneal lymph node dissection (LPND), chemotherapy, and radiation (2,4,6,10-13). Radical inguinal orchiectomy with high dissection, ligation of cord structures, and negative tumor margins is the best primary treatment measure. Adjuvant chemotherapy, usually with vincristine, actinomycin, and cyclophosphamide, improves overall survival outcomes and limits disease progression (4-6,10). Because up to 40% of cases present with early retroperitoneal lymphadenopathy, management requires accurate disease staging (2,6,10-13). Some argue that surgical staging with RPLND results in improved detection of true retroperitoneal disease and lower disease recurrence when compared to radiological staging. Yet, there is no established consensus regarding the use of staging or therapeutic RPLND due its potential complications and morbidity (2,6,10-13). RPLND was not performed in our patient because imaging showed no evidence of lymphadenopathy. Nonetheless, RPLND aids in guiding adjuvant treatment and disease-debulking of positive nodes after chemotherapy. Lastly, radiotherapy is reserved for patients with unresectable masses, high tumor burden after surgery, disease recurrence, or unfavorable histology (4,6,10-13).

RMSs carry an overall poor prognosis, influenced by patient age, tumor histology, location, size, resectability, and metastasis (2,4,6). Overall survival of PTRMSs at one and five years is 68% and 30%, respectively. At three years after diagnosis, only 27% of patients are reportedly disease free (11,14). Thus, future studies are needed to expand our current understanding of this disease entity and the better assess the efficacy of available treatment modalities improve patient outcomes.

Resumen

Rabdmiosarcomas primario testicular es una malignidad poco común en la población pediátrica, con pocos casos reportados en la literatura médica. La presentación clínica es idéntica a aquella de los tumores testiculares más comunes. El diagnóstico conlleva un minucioso análisis microscópico e imunohistoquímico para así poder diferenciarlo de otros tumores testiculares. El tratamiento consiste en orquiectomía radical con quimioterapia auxiliar y possible disección de nódulos retroperitoneales. Presentamos el caso de un rabdomiosarcoma embryonal primario de testículo en un varón de 19 años. El paciente presentó con una masa testicular indolora que creció en tamaño rápidamente. Se trató con orquiectomía radical y quimioterapia auxiliar. Luego se trato con quimoterapia y radioterapia de rescate al presentar con enfermedad metastatica pulmonar.

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