



CASE REPORT

Prostatic sarcoma of the Ewing family in a 33-year-old male – A case report and review of the literature



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Abstract Ewing sarcoma is the second most common primary bone tumor seen in children and adolescents, typically presenting between 10 and 20 years of age. Extrasosseous sarcomas of the Ewing family in adults are rare. We report a manifestation of this tumor entity in the periprostatic tissue of a 33-year-old male and discuss our treatment approach. Transrectal biopsy is a feasible and simple diagnostic tool for unclear pelvic masses. Multi-modal therapy and central registries are needed to gain knowledge of rare pelvic tumors like Ewing sarcoma.

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1. Introduction

Ewing sarcoma is the second most common primary bone tumor seen in children and adolescents. However, extrasosseous sarcomas of the Ewing family in adults are very rare. We report a manifestation of this uncommon tumor entity in the periprostatic tissue of a 33-year-old male.

2. Case presentation

A 33-year-old patient who had recently migrated from Afghanistan presented to the emergency department with symptoms of pelvic pain and urinary tract infection (dysuria, urgency, mild pyuria on dipstick) for several days. Patient's past medical history was unremarkable and without any recollection of exposure to toxic substances or genetic predisposition. Upon suspicion of a pelvic mass on transrectal ultrasound during initial assessment, magnetic resonance imaging (MRI) of the pelvis was performed. It revealed a 6.0 cm × 4.5 cm × 4.6 cm mostly solid pelvic mass showing signs of central necrosis located between bladder and rectum with suspected infiltration of the prostate and left internal obturator muscle (Fig. 1).

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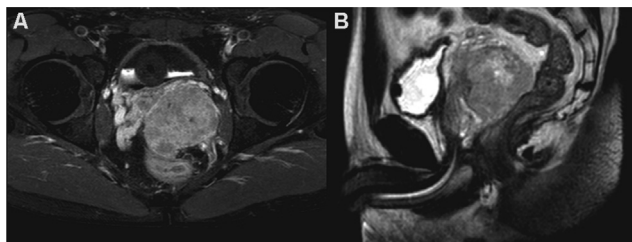


Figure 1 The 6.0 cm × 4.5 cm × 4.6 cm mostly solid pelvic mass on T1-weighted, contrast-enhanced (A) as well as T2-weighted MRI-study (B). It shows signs of central necrosis and displacement of bladder and rectum with suspected infiltration of the prostate and left internal obturator muscle; partly contrast-filled bladder with placed foley catheter.

In order to complete tumor-staging, additional cranial MRI, chest/abdominal computed tomography (CT), bone-scan as well as colonoscopy were performed. Besides unspecific enlargement of a cervical lymph node on the left hand side, no signs of metastatic disease were detected.

For further histological evaluation of the mass, ultrasound-guided transrectal biopsies were obtained. Upon pathological examination the tumor was preliminarily described as a “small, round and blue-cell-like tumor” of the periprostatic soft-tissue infiltrating the capsule of the prostate without further classification (Fig. 2).

Besides the Ewing’s sarcoma family of tumors, the initial differential diagnoses included desmoplastic round cell tumor and neuroendocrine carcinoma. Other possible differential diagnoses, such as neuroblastoma, rhabdomyosarcoma as well as non-Hodgkin’s lymphoma [1–3], were excluded by immunohistochemistry. With a symptomatic aggressive tumor and in order to get the complete histology, an initial surgical resection was chosen. Radical tumor resection with prostatovesiculectomy, extended regional lymph node dissection as well as resection of the pelvic floor were performed using an open retropubic approach. The bladder neck was then closed and a cystostomy-catheter was inserted for urine-diversion (Fig. 3).

Course of postoperative recovery was unremarkable. The intraoperative setting suggested at least an R1-situation, even though surgical margins were later reported as tumor-free (R0) by pathology. After further molecular profiling by a reference pathologist (Prof. Leuschner, Kiel, Germany)

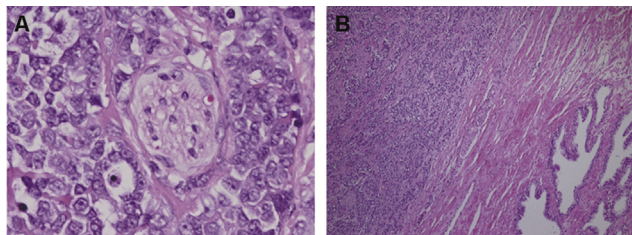


Figure 2 Upon pathological examination the transrectal biopsy was preliminarily described as a small-blue-round-cell tumor and later classified as a Ewing-like tumor of the periprostatic tissue. (A) Nerve fibre infiltration of the tumor (400×); (B) Tumor formation with close proximity to the prostatic tissue (40×).

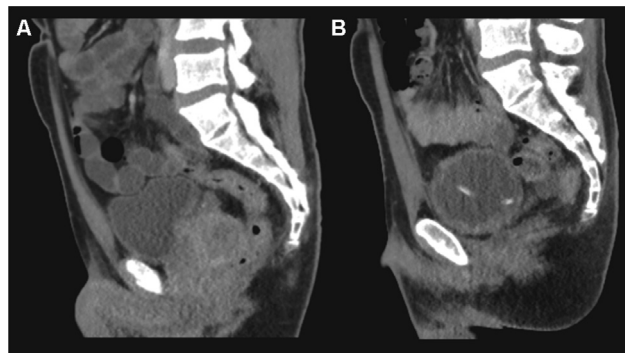


Figure 3 Contrast enhanced staging CT-scan of the pelvis (A) and re-staging 2 months after surgery and first cycle of adjuvant chemotherapy (B): no signs of residual disease or recurrence of the Ewing-like tumor. Urine-diversion via cystostomy-catheter after closure of the bladderneck.

the tumor was shown to hold genetic alterations of the *EWSR1*-gene consistent with the tumor of the Ewing sarcoma family, even though cytokeratin positivity as expressed by this tumor is a rather uncommon histopathological feature only found in a minority of cases in this entity [4,5]. Due to the aggressive nature of this disease and given the likely presence of residual disease an intensive regime of adjuvant chemotherapy was initiated shortly after surgery. It consisted of six courses of VIDE (vincristine, ifosfamide, doxorubicin, etoposide) applied 3-weekly. Most recent restaging 12 months after surgery and after completion of the VIDE-regime showed no signs of residual disease or recurrence. Currently further chemotherapy is being administered with an alternating VAI- (vincristine, actinomycin, ifosfamide) and VAC-regime (vincristine, actinomycin, cyclophosphamide). Continuous remission provided, a second surgery for definitive orthotopic or cutaneous continent urinary diversion is intended upon completion of adjuvant therapy.

3. Discussion

Ewing sarcoma is a rare malignant disease in which cancer cells are found in the bone or in soft tissue. Approximately 25% of patients with Ewing sarcoma have metastatic disease at the time of diagnosis. Ewing sarcoma occurs most frequently in teenagers and young adults, with a male/female ratio of 1.6:1 [6]. In patients aged 10–19 years, the incidence is between nine and 10 cases per million people, the incidence for all ages is even more rare with one case per million people in the United States. The polymorphism (*EGR2*-gene on 10q21.3) associated with the increased risk is found at a much higher frequency in whites than in blacks or Asians, possibly explaining the epidemiology of the relative infrequency of Ewing sarcoma in the latter populations [7].

For extraosseous primary tumors, the most common primary sites of disease include the following: trunk (32%), extremity (26%), head and neck (18%), retroperitoneum (16%), other sites (9%). The Surveillance, Epidemiology, and End Results (SEER) database was used to compare patients younger than 40 years with Ewing sarcoma who presented

with skeletal and extraosseous primary sites. Patients with extraosseous Ewing sarcoma were mostly older (mean age of 20 years), white and presented axial primary sites [8]. Extraosseous Ewing sarcoma in adults represent an extremely rare tumor entity with no more than a few hundred reported cases of various forms of presentation in terms of localization and stages of disease [9–11]. Overall no definitive causation of this tumor entity has yet been identified [12].

In the presented case we had a 33-year-old Asian male patient with no known exogenic noxae and no known disposition to genetic diseases in the family.

With tumors of the Ewing family general guidelines include neoadjuvant chemotherapy with vincristine, doxorubicin and cyclophosphamide, alternating with ifosfamide and etoposide [13]. Furthermore neoadjuvant radiotherapy for improved surgical resection as well as adjuvant irradiation with positive surgical margins are viable options in this disease [14]. Definitive radiotherapy is generally considered in those cases deemed unsuitable for surgery, even though the assumed superiority of resection for local control remains a suspect of ongoing studies [15]. In our case a solely adjuvant course of regime with initial surgical resection was chosen mostly due to the uncommon initial histopathological presentation of the tumor and therefore an overall inconclusive classification upon pre-operative needle-biopsy. As rapid proliferation and high-aggressiveness had to be expected prompt surgical extirpation was chosen as primary course of care in order to provide definitive classification and potentially enable targeted systemic treatment of the tumor depending on its entity (e.g., monoclonal antibody therapy in non-Hodgkin's lymphoma [16]).

Existing data suggests similar outcome of adult extraosseous Ewing sarcoma compared to that of bone-confined disease in terms of response to multi-modality treatment and the prognostic factors influencing treatment success [17,18]. As for the field of urology, individual cases of extraosseous Ewing sarcomas have also been reported in the urinary bladder, kidneys, adrenal glands and even the penis [19–22]. To our knowledge only nine other cases of (peri-)prostatic Ewing sarcoma are known worldwide being first described in 2003 [23–31]. Outcome in these patients was overall very poor with reported survival between as little as 2 [24] up to 12 months [30]. These survival rates are significantly inferior compared to outcome in the largest available prospective, randomized collection of patients studied today on children or adolescents with extraosseous Ewing sarcomas: 130 of 2792 patients (under 21 years of age) registered on three Intergroup Rhabdomyosarcoma Study clinical trials (IRS-I, -II, and -III) from 1972 to 1991 had an extraosseous Ewing sarcoma. Eight-two percent of the patients achieved a complete response with 10-year-overall survival being as high as 62%, 61%, and 77% on IRS-I, IRS-II, or IRS-III multi-modal therapeutic protocols, respectively. The therapeutical strategy included mixed groups with adjuvant and neoadjuvant protocols, and no subgroup analyses are available [18]. With the lack of larger randomized control trials and the vast majority of studies focusing on osseous Ewing sarcomas in children, choosing the right course of treatment was challenging in this setting. Retrospectively, a neoadjuvant approach would

have most likely been the treatment of choice based on current evidence. Also adjuvant radiotherapy after suspicion of positive surgical margins could have been considered. With the patient being in full remission 1 year after diagnosis and a reported average survival of less than 12 months in comparable cases treated with neoadjuvant chemotherapy, our adjuvant approach might be regarded at least non-inferior. Further follow-up could give vital additional information on the optimal treatment sequence in this rare tumor entity. In general transrectal or perineal biopsy seems to be a feasible procedure for the initial diagnosis of unclear pelvic masses. Given the fact that sarcoma is a very rare entity, central registries of rare pelvic tumors would be helpful, in order to get an evidence based, standardized therapy.

4. Conclusion

Sarcomas are a rare but clinically relevant differential diagnosis in pelvic masses of the young adult. Histological confirmation and definitive classification is paramount for optimal treatment, which should include a multimodal approach in an interdisciplinary team. Initial surgery followed by adjuvant chemotherapy might be an alternative approach to neoadjuvant treatment.

Conflicts of interest

The authors declare no conflicts of interest.

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