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Research article

Tumor thrombus in the large veins draining primary pelvic osteosarcoma on cross sectional imaging

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ABSTRACT

Purpose: To evaluate the frequency of tumor thrombus in the large veins draining primary pelvic osteosarcoma on early cross-sectional imaging studies and its effect on patient survival.

Materials and methods: Our retrospective study included all patients with primary pelvic osteosarcoma treated at our facility between January 2000 and May 2014, who were ≤ 45 years of age, and had adequate imaging studies and clinical follow up. Four radiologists evaluated for tumor in the large draining veins on initial CT, MRI and PET/CTs. A consensus evaluation by the four radiologists together with findings on operative reports, pathology reports or follow-up imaging was used as the reference standard.

Results: Thirty-nine patients with primary pelvic osteosarcoma met final inclusion criteria. Tumor thrombus was identified in the large draining veins in 10 of the 22 (45%) patients who underwent tumor resection and 10 of the 17 (59%) who did not. In the 22 patients who underwent tumor resection, tumor thrombus was significantly associated with worse overall survival ($p = 0.03$).

Conclusions: Tumor thrombus in the large draining veins is identified in a significant proportion of initial imaging studies in patients with pelvic osteosarcoma, and is associated with worse overall survival in patients who undergo tumor resection.

1. Introduction

Tumor thrombus in the draining veins has been identified as a poor prognostic factor in various types of malignancies including osteosarcoma, renal cell carcinoma, hepatocellular carcinoma, colorectal carcinoma and gastric carcinoma [1–5]. Tumor thrombus in the large veins that drain primary and metastatic osteosarcomas has not been studied in detail; the existing information is available from few case reports and case series [6–9]. Benezech et al [1] reported peri-tumoral vascular invasion in 29% of surgically resected pediatric osteosarcomas after neo-adjuvant chemotherapy at pathologic examination. Kawai et al [10] reported intravascular extension into the large vessels in 23% of patients who underwent surgical resection for pelvic osteosarcoma. To our knowledge, no prior study has described the frequency of tumor thrombus in the large veins draining primary osteosarcoma on imaging studies and its effect on patient survival of patients. In our experience, a lack of familiarity with tumor thrombus in the veins draining the osteosarcoma and the small caliber of the draining veins in extremity osteosarcomas may lead to the under-recognition of this finding on imaging studies.

The primary purpose of this retrospective study was to evaluate the frequency of tumor thrombus in the large extra-tumoral veins draining primary pelvic osteosarcoma on imaging studies obtained within 6–12 months of initial diagnosis and prior to definitive surgery in patients who underwent surgical resection. The pelvic location was chosen over other sites as the draining veins are larger and comparison with

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contralateral veins is possible on most imaging studies acquired for pelvic osteosarcoma. The secondary purpose of the study was to determine the effect of tumor thrombus within the large draining veins on the overall survival of patients.

2. Materials and methods

2.1. Patients

The institutional review board approval, including a waiver of informed consent for the retrospective review was obtained. The institutional tumor registry was searched for all patients with pelvic osteosarcoma who had been diagnosed between January 2000 and May 2014. Our institution started using digital imaging with Picture Archiving and Communication System in 2000.

2.2. Inclusion and exclusion criteria

All patients with pelvic osteosarcoma who had at least one pelvic CT or MRI study of reasonable quality within six months of diagnosis; had at least two sets of imaging studies (at least one contrast enhanced CT or MRI) on institutional PACS (including outside facility imaging studies); and adequate clinical follow up (at least 3 years for living patients and follow up until death for patients who died) were included. All patients with incomplete imaging studies, osteosarcoma secondary to prior radiation therapy to the pelvis, age at diagnosis greater than 45 years, alternative final diagnosis and alternative location of tumor, primary tumors centered on the sacrum with isolated sacral involvement, and inadequate clinical follow up were excluded. Patients with primary tumors centered on the sacrum and isolated sacral involvement can drain into veins on both sides of midline. Hence, comparison with normal contralateral veins may not be possible and unless these sacral tumors showed asymmetric involvement of one sided ilium, they were excluded from this study. Of the 132 patients with pelvic osteosarcoma, 44 met the initial inclusion/exclusion criteria and were selected for image analysis.

2.3. Imaging studies and analysis

One radiologist (SY) reviewed the patients' charts, including clinical notes, pathology reports, radiology reports and imaging studies (CT/MRI/PET-CTs) and recorded data on patients' demographics, primary tumor size on the initial study, metastasis at presentation, histologic subtype, extent of tumor thrombus in the large draining veins on initial imaging studies, findings from operative reports, pathology reports, follow up imaging, surgical resection status of the primary tumor, local recurrence and timing, and metastatic disease sites on the last available imaging studies and clinical notes until December 2016. For each patient, this radiologist selected 2–4 relevant initial imaging studies (a total of 108 studies) obtained at least one month apart for further review by three other radiologists (BA, AM and US) and consensus evaluation. The first studies included MR or CT imaging of the pelvis or both within six months of diagnosis; of these, contrast enhanced studies were available for 42 patients and only non-enhanced CTs were available for two patients. The last imaging study was a contrast enhanced MRI or CT before surgery in patients who underwent surgical resection and after the initial chemotherapy in patients who did not. At least one contrast enhanced study within the first year of diagnosis was available for all patients.

On initial contrast enhanced CT and T1 weighted MRIs, the radiologists evaluated for filling defects within the large draining veins (inferior vena cava (IVC); common, external, and internal iliac veins; and common femoral vein) and compared them with contralateral veins. Detection of tumor in the distal veins, particularly internal iliac vein is difficult and comparison with the contralateral veins is very helpful. On T2 weighted MR images, the radiologists evaluated for absence of flow void within the draining vein and compared with the flow voids on the contralateral side. On PET/CT increased FDG uptake corresponding to the course of the vein and on non-contrast CT / follow up imaging (including CT portion of the PET-CT) mineralization, i.e., osteoid matrix along the course of the vein were evaluated. A dilated tubular structure filled with material that showed imaging characteristics similar to primary tumor and connecting the primary tumor and the large draining veins was considered a tumor thrombus on any imaging modality. The imaging findings by consensus evaluation by all four radiologists, including the presence and location of the tumor in the draining vein, were correlated with the operative report, pathology findings and follow-up imaging. The consensus evaluation by four radiologists together with confirmation of the findings by operative report, pathology findings or follow-up imaging was used as the reference standard for the study.

2.4. Statistical methods

Summary statistics of tumor thrombus in the large draining veins and other patient characteristics were provided using frequencies and percentages. Age and tumor size were summarized using mean, standard deviation, and range. Cox proportional hazard model was used to assess the effects of patient characteristics on overall survival and time-to-local recurrence, where events were defined as death of any cause and local recurrence, respectively. Survival curves were estimated using Kaplan-Meier method and compared using log-rank test. Fisher's exact test was used to determine the association between metastatic disease at presentation and tumor histologic subtype with tumor thrombus. All tests were two-sided and p-values of 0.05 or less were considered statistically significant. Statistical analysis was carried out using SAS version 9.4 (SAS Institute, Cary, NC) and Spotfire S + version 8.2 (TIBCO, Palo Alto, CA).

3. Results

3.1. Patient cohort

The study identified 132 patients with pelvic osteosarcoma of which 88 were excluded as detailed in Fig. 1. Incomplete imaging studies i.e., unavailability of at least one pelvic CT or MRI of reasonable quality within six months from diagnosis and at least two sets of imaging studies (of which at least one included contrast enhanced CT or MRI) on institutional PACS, was the primary reason for patient exclusion (49% of excluded patients). Forty-four patients met the study criteria and were initially included in the study for consensus evaluation of tumor thrombus in the large draining vein on imaging studies by the radiologists.

Tumor thrombus in the large draining veins was identified in 25 of 44 (57%) patients by consensus scoring by all four radiologists. The presence of tumor in the draining veins was confirmed by findings from operative reports, pathology reports, or both (n = 7) or follow-up imaging (n = 13) in 20 of the 25 patients with tumor thrombus on imaging (Figs. 2 and 3). Four patients who did not undergo surgical resection died early in the course of their disease before undergoing surgery, and therefore they did not have operative or pathology reports and did not have follow up imaging studies for confirmation of tumor in vein. In addition, no operative or pathology reports were available for one patient who underwent surgery at an outside facility. These 5 patients with tumor thrombus in large draining veins on imaging per final consensus score who lacked confirmation by either operative findings or pathology reports or follow up imaging were excluded from the subsequent statistical analysis. Thirty-nine patients formed the cohort for statistical analysis.