George T. Calvert M.D[1]., Arun Singh M.D[2]., Noah Federman M.D.[3], Judith Sato M.D.[4], and J. Dominic Femino M.D.[1]
1. Department of Surgery, City of Hope, Duarte, CA
2. Division of Hematology/Oncology, UCLA, Los Angeles, CA
3. Division of Pediatric Oncology, UCLA, Los Angeles, CA
4. Department of Pediatric Oncology, City of Hope, Duarte, CA

Malignant Transformation of Dysplasia Epiphysealis Hemimelica (Trevor's Disease): The First Reported Case and Recommendations for Surveillance

Background: Dysplasia Epiphysealis Hemimelica (DEH), also known as Trevor's disease, is characterized by epiphyseal enlargement of bones which are histologically indistinguishable from osteochondromas. It is most commonly restricted to a single limb (lower > upper extremity) and one side of the involved limb (medial > lateral). Unlike multiple hereditary exostoses (MHE) and metachondromatosis, a genetic association has not been described and malignant transformation of DEH has not been reported.

Questions/Purposes: 1. Report the first case of DEH malignant transformation. 2. Propose a surveillance regimen for DEH based upon current recommendations for MHE.

Patients and Methods: Medical records, imaging, and pathology from multiple institutions over 10 years were reviewed. Literature review of the 154 reported DEH cases between 1926 and 2015 was performed. MHE literature was reviewed to ascertain current best practices for surveillance of maliganant transformation of multiple osteochondromas.

Results: A 17 year old, otherwise healthy male initially presented with a left ankle epiphyseal mass at age 9 months (Fig.1). Resection at 15 months demonstrated classic osteochondroma histology. The ankle mass recurred over the next year and he underwent repeat surgery with identical histologic findings. Left knee epiphyseal lesions were subsequently identified and knee symptoms worsened to point that surgical resections were performed at ages 7 and 8. Pathology again demonstrated osteochondromas. The patient subsequently developed osteochondromas at sites atypical for DEH including: an epiphyseal osteochondroma of the right index finger middle phalanx (age 11), contralateral lower extremity epiphyseal osteochondromas (age 14), and an extra-osseous chondroma of the right hand (age 16).

At 16 years 9 months he developed back pain with subsequent lower extremity weakness and numbness. Thoracic MRI revealed an epiphyseal osteochondroma of the left 8^{th} rib head at its junction with the vertebral body. There was a large destructive soft tissue mass extending from the osteochondroma causing spinal cord compression. Pathology obtained from emergent decompressive surgery demonstrated a high grade osteosarcoma. Staging studies identified pulmonary metastases at osteosarcoma presentation. Despite multiple lines of therapy, the patient died of metastatic osteosarcoma at age 18.

As this is the first report of DEH malignant transformation, no surveillance guidelines exist. Review of the MHE literature indicates that there is no consensus for surveillance. We note at least 4 atypical features of DEH in this case: involvement in more than 1 limb, aggressive local recurrence after excision, extraskeletal mass, and axial involvement. All have been previously reported in DEH, but we propose that the presence of any of these findings warrants closer surveillance. The axial location of the transformed lesion would have been difficult to identify with standard biplanar radiographs. Roach et al. reported spinal canal encroachment in 27% of MHE patients studied with MRI and advocated obtaining at least 1 whole spine MRI prior to skeletal maturity. Sonne-Holm et al. systematically reviewed malignant transformation of MHE and proposed biennial whole body MRI or bone scintigraphy (for those unable to have MRI) for all patients >16 years old or skeletally mature. Pedrini et al. emphasized the importance of serial clinical examinations, a skeletal survey at skeletal maturity, and a pelvis radiograph every 18 months after age 30. Table 1 summarizes these recommendations with proposed application to DEH.

Conclusions: We believe the orthopaedic community will benefit from this index report of DEH malignant transformation. We caution physicians treating DEH to maintain a heightened awareness for malignant degeneration when atypical findings are identified. A potential criticism of our study is that unlike MHE and metachondromatosis, there is no confirmatory genetic test for DEH. We note that the clinical presentation, imaging, and pathology were all most consistent with DEH as affirmed by numerous physicians at multiple institutions over more than a decade of treatment. Furthermore, this case illustrates the importance of clinical suspicion in cases of multiple osteochondromas regardless of the diagnosis (MHE, DEH, or metachondromatosis).

Level of Evidence: Prognostic Level IV

Figure 1. (A) Radiographs of the left lower extremity at age12 demonstrating predominantly lateral joint involvement and extensive recurrence post-resection. (B) Foot radiographs at age 16 reveal hindfoot autofusion as the patient neared skeletal maturity (C) Right index finger radiograph at age 16 demonstrating an upper extremity osteochondroma (D) Right calcaneus radiograph at age 16 demonstrating a large contralateral limb osteochondroma (E) CT of T7/T8 at age 16 demonstrating a left rib head osteochondroma with associated soft tissue mass (F) Spine MRI detailing the spinal cord compression caused by the soft tissue mass.

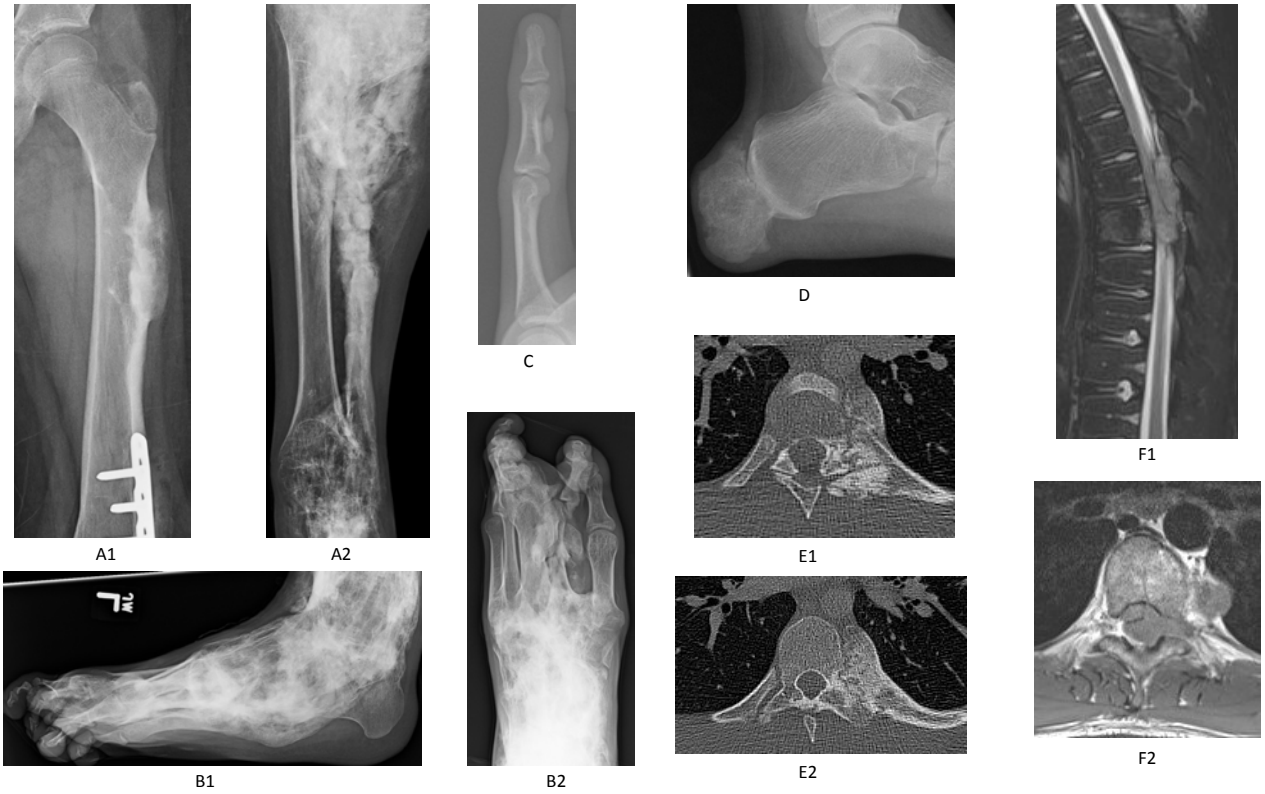

Table 1. Proposed surveillance regimen to assess for spinal canal compromise and malignant degeneration among DHE patients.

Examination	Risk Group	Timing
History & Physical	All	Annual
Skeletal Survey[1]	Low	At Skeletal Maturity
Whole Spine MRI[2]	High*	Prior to skeletal maturity
Whole Spine CT[2] (if unable to undergo MRI)	High*	Prior to skeletal maturity
Whole Body MRI[3]	High*	At skeletal maturity and biennial thereafter if concerning lesions identified
Whole Body Bone Scan[3] (if unable to undergo MRI)	High*	At skeletal maturity and biennial thereafter if concerning lesions identified

*High risk group is defined by involvement of more than one limb, axial involvement, recurrence after resection, or extraosseous lesion(s).

References

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