Diaphyseal medullary stenosis with malignant fibrous histiocytoma (DMS-MFH)

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Identity

Alias: Bone dysplasia with medullary fibrosarcoma; Bone dysplasia with malignant fibrous histiocytoma; Hereditary bone dysplasia with malignant change

Note: DMS-MFH is an hereditary bone dysplasia / cancer syndrome.

Inheritance: Autosomal dominant; rare hereditary cancer syndrome with only four families identified worldwide; etiology unknown.

Clinics

Note
Radiologic evidence of bone dysplasia not evident in childhood; X-ray findings become apparent during adolescence.

Phenotype and clinics
Main features include:
- Bone dysplasia (100%)
- Cortical growth abnormalities: diaphyseal medullary stenosis with overlying endosteal cortical thickening and scalloping, metaphyseal striations, scattered sclerotic areas symmetrically affecting the long bones; bilateral mandibular radiolucent and sclerotic lesions
- Bone infarctions
- Pathologic fractures: subsequent poor healing or non-union
- Progressive wasting or bowing of the lower extremities
- Bone pain
- Pre-senile cataracts (25%)

Photograph A: Lateral X-ray view of the left tibia and fibula of an 18 year old male with DMS-MFH and MFH. Note the extensive diaphyseal cortical thickening, areas of resultant medullary stenosis, endosteal irregularities, overall permeative pattern in the medullary cavity, and metaphyseal striations.
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- Bone malignant fibrous histiocytoma (MFH) (35%)
  Diagnosis: X-ray skeletal findings are unique; however, there may be some radiologic overlap with other diaphyseal dysplasias including Camurati-Engelman and Kenny-Caffey diseases and radiation osteitis; no hematologic or urinary markers of disease have been identified; 201Thallium chloride radionucleotide scans may offer discrimination between areas of increased metabolic bone activity found in DMS-MFH patients and malignant change.

**Neoplastic risk**

Thirteen cases of osseous MFH; thirty-five per cent of DMS-MFH patients develop MFH; the age distribution has been from the second to fifth decades; no sex predilection; in its sporadic form, MFH represents approximately 6% of all bone cancers and is the most frequently occurring adult soft-tissue sarcoma.

**Treatment**

No known treatment for the dysplasia; the tumors are highly aggressive - treated with surgical ablation and the same chemotherapeutic regimens as osteosarcoma; it is believed that preoperative chemotherapy improves surgical outcome.

**Evolution**

The disease becomes radiologically apparent only in adolescence; however, retrospectively, clinical signs and symptoms may be evident in childhood; these include unexplained bone pain and pathologic fractures; in some, crippling pain and weakness of the lower extremities ensues following the sixth decade; malignancy occurs most frequently between the second to fifth decades and is particularly aggressive; only two long-term survivors, greater than five years, are known; pre-senile cataracts have been noted as early as in the third decade.

**Other findings**

**Note**

Collagen fibrils from the endosteal surface of bones appear frayed and unravel (unpublished results); chemical crosslink analysis of bone biopsy samples reveal altered hydroxylysylpyridinolin (HP) / lysylpyridinoline (LP) ratios (unpublished results).

**Genes involved and proteins**

**Note**

The gene has been mapped by linkage analysis to a 3 cM region on chromosome 9p21-22; all families used in the study generated positive LOD scores in this region and all affecteds had similar phenotypic findings consistent with the syndrome being genetically homogeneous; a number of genes in the region,
including p15 and p16, have been excluded as the DMS-MFH gene by DNA sequencing analysis; under the hypothesis that hereditary and sporadic MFH tumors are genetically identical, the DMS-MFH tumor-suppressor gene region has been further narrowed to 1.5 cM using loss of heterozygosity analysis; the continued search for the common minimally deleted region in MFH tumors should provide the most powerful method for gene identification.

References


This article should be referenced as such: