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Solid Tumour Section

Short Communication

Bone: Vascular Tumors

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Abstract

Review on Vascular tumors of bones, with data on clinics, and the genes involved. Vascular tumors of bone spans a spectrum with on one side the overtly benign lesions consisting of the haemangiomas and on the other side the frankly malignant lesions consisting of the angiosarcomas. In between there are the intermediate locally aggressive epithelioid haemangiomas and the low grade malignant epithelioid hemangioendotheliomas. Recently translocations and specific mutations have been identified to aid the classification of many entities in the spectrum of vascular bone tumors.

Keywords

Haemangioma; Epithelioid haemangioma; Epithelioid haemangioendothelioma; Angiosarcoma; WWTR1; CAMTA1; YAP1; TFE3; FOS; LMNA; MBNL1; VIM; ZFP36; FOSB

Identity

Note

In the spectrum of vascular tumors, ranging from benign to frankly malignant, the benign vascular lesions of bone are relatively common and occur most frequently as an asymptomatic incidental finding in the skull or spine. Primary malignant vascular tumors of bone are rare. They represent less than 1% of primary malignant bone tumors reported by the Netherlands Committee on Bone Tumors and 0,5% of those registered at the Mayo Clinic. Clinically they are extremely aggressive and have a very poor prognosis. Survival rates are unknown.

Phylum

Bones:Vascular tumors

Classification

Over the years, the terminology and classification of vascular tumors of bone has been highly controversial and in literature a great variety of names has been proposed. Illustrating this are cases described in literature as haemangioendothelioma of bone, which probably represents epithelioid haemangioma. With the identification of different mutations and translocations, specific to the different vascular tumors, most of the controversy has been resolved.

The large variety of histological features of vascular tumors of bone suggests that it should be regarded as a spectrum with on one side the overtly benign lesions consisting of the haemangiomas and on the other side the frankly malignant lesions consisting of the angiosarcomas. In between there are the intermediate locally aggressive epithelioid haemangiomas and the low grade malignant epithelioid hemangioendotheliomas. Recently translocations and specific mutations have been identified to aid the classification of many entities in the spectrum of vascular bone tumors. For the haemangiomas VEGFR mutations have been

identified, and in epithelioid haemangioma fusion genes involving FOS and FOSB with different fusion partners have been identified. For epithelioid haemangioendothelioma WWTR1/CAMTA1-, and in a specific subset YAP/TFE3 fusions are identified and in angiosarcoma PTPRB, PLCG1, CIC, KDR, and FLT4 mutations and MYC amplifications have been found.

Schematic representation of histological spectrum of vascular tumors of bone.

Classification

Today, the most accepted classification of vascular tumors of bone is the 2013 WHO classification:

- Haemangioma and related lesions
- Epithelioid haemangioma
- Epithelioid haemangioendothelioma
- Angiosarcoma

Clinics and pathology

Disease

Haemangioma and related lesions

Note

Multiple lesions are defined as (haem)angiomatosis.

Phenotype / cell stem origin

Endothelial cell

Epidemiology

Haemangiomas are detected relatively common at autopsy with no clinical implications.

Clinics

In general asymptomatic.

Cytogenetics

No cytogenetic investigations reported.

Prognosis

Haemangiomas have a good prognosis and low recurrence rate.

When primary Angiosarcoma of bone exhibits more than 3 mitosis per 10 HPF with prominent nucleolus and fewer than five eosinophilic granulocytes per 10 HPF they will likely have a worse prognosis.

Disease

Epithelioid haemangioma

Epidemiology

Extremely rare.

Clinics

Pain localized to the involved anatomical site.

Cytogenetics

Fusions involving FOS with different fusion partners have been found (t(1;14)(q22;q24) FOS/LMNA; t(3;14)(q25;q24) FOS/MBNL1; t(10;14)(p13;q24) FOS/VIM). Atypical cases carry ZFP36-FOSB fusions (t(19;19)(q13;q13) ZFP36/FOSB).

Prognosis

Locally aggressive, can be multifocal, and can metastasize in very rare cases.

Disease

Epithelioid haemangioendothelioma

Epidemiology

Extremely rare

Clinics

Pain and swelling but sometimes asymptomatic.

Cytogenetics

WWTR1-CAMTA1 and YAP1-TFE3 fusions (t(1;3)(p36;q25) WWTR1/CAMTA1 and t(X;11)(p11;q22) YAP1/TFE3).

Prognosis

Involvement of two bones is associated with a worse prognosis regardless of the number of organs involved.

Disease

Angiosarcoma

Epidemiology

Extremely rare.

Clinics

In general, presents as a painful mass. Depending on the size and localization of the tumor, neurological deficit or other symptoms can occur.

Cytogenetics

No cytogenetic investigations of angiosarcoma in bone are reported.

Genes

PTPRB, PLCG1, CIC, KDR, and FLT4 mutations and MYC amplifications.

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