Oral pathology

MALIGNANT BONE TUMORS د.بشار

Osteosarcoma

Osteosarcoma is the most frequent primary bone malignancy, exclusive of hematopoietic malignancies. It usually occurs in patients between 10 to 25 years of age and is exceptionally rare in preschool children. Another peak age incidence occurs after 40, in association with other disorders.

Osteosarcomas of the jaws are uncommon and represent 6-8 % of all osteosarcomas. The tumors have been diagnosed in patients ranging from young children to the elderly, but they occur most often in the 3rd to 4th decade of life. The mean age for patients with osteosarcoma of the jaw is about 33 years, which is 10 to 15 years older than the mean age for osteosarcomas of the long bones. As is seen in extragnathic locations, a slight male predominance is noticed.

Predisposing Factors

Most osteosarcomas arise de novo; however, some arise within the context of the following:

1. Paget's disease.
2. Radiation exposure.
3. Chemotherapy.
4. Pre-existing benign bone lesions, e.g. fibrous dysplasia.
5. Foreign bodies, e.g. orthopedic implants.

Location

Most osteosarcomas in the long bone are located in the metaphyseal region particularly the lower end of the femur, upper end of the tibia, and the upper end of the humerus. A few cases arise in the diaphysis and even smaller number in the epiphysis. Less commonly, they are found in flat bones e.g. (craniofacial bones, pelvis, and scapula), spine and short bones.

Jaw Tumor

Clinical and Radiographic Features

The maxilla and mandible are equally affected. The mandibular tumors mostly arise in the posterior body and ramus. Maxillary lesions are discovered more commonly in the inferior portion (alveolar ridge, sinus floor, palate). Swelling and pain are the most common symptoms. Other features include loosening of the teeth, parasthesia, and nasal obstruction.

Radiographically: variable, from dense sclerosis to a mixed sclerotic and radiolucent lesion, to an entirely radiolucent. The border is mostly ill defined, making it difficult to determine the extent of the tumor. Occasionally, there is resorption of the roots of the teeth involved by the tumor. The classical sunburst, or sunray appearance is due to the osteophytic bone production on the surface of the lesion noted in about 25% of jaw osteosarcoma, mostly seen on an occlusal projection. Widening of the periodontal ligament may be seen as an early finding due to tumor infiltration along the PDL.

Gross and Histological Findings

The gross appearance of the cut surface of an osteosarcoma varies a great deal, depending on the relative amount of bone, cartilage and cellular stroma, and vessels. The range extends from bony hard to cystic, friable and hemorrhagic. The tumor may spread from the following pathways :

1. Spread along the marrow cavity.
2. Invade the cortex.
3. Elevate or invade the periosteum.
4. Extend into the soft tissue.
5. Metastasize through blood stream to distant sites, particularly to the lung.

Microscopic Findings

Osteosarcoma may destroy the pre-existing bone trabeculae or grow around them in an appositional fashion. The key feature for the diagnosis is the detection, somewhere in the tumor, of osteoid and calcified osteoid produced directly by the tumor cells, without interposition of cartilage. Osteoid is recognized by its eosinophilic-staining quality, its glassy appearance, irregular contours, and the fact that it is surrounded by a rim of osteoblasts. In addition to osteoid, the cells of the tumor may produce chondroid material and fibrous connective tissue. The tumor cells may vary from uniform round or spindle-shaped cells to highly pleomorphic cells with bizarre nuclear and cytoplasmic shapes.

Depending on the relative amounts of osteoid, cartilage, or collagen fibers produced by the tumor, many pathologists subclassify osteosarcomas into the following types:

1. osteoblastic.
2. chondroblastic.
3. fibroblastic.

These histopathologic subtypes do not have any prognostic significance. Other variants, may include, malignant fibrous histiocytoma-like, small cell, epitheloid, telangiectatic, and giant cell rich.

The chondroblastic type constitute the major portion of all osteosarcomas of the jaws.

Treatment and Prognosis

It is believed that osteosarcoma of the jaw is less aggressive than those occurring in the long bones. Most of these tumors are low grade and metastases are seen less frequently.

Treatment is by excision with safe margin, i.e. complete surgical removal ± chemotherapy, the prognosis remains serious, with 30-50% survival rates.

Other variants include:

Peripheral "juxtracortical" osteosarcoma:

These tumors grow outward from the surface, and do not involve the medullary bone, this type my include:

Parosteal type: is a lobulated nodule attached to the cortex by a short stalk. There is no elevation of the periosteum and no peripheral periosteal reaction.

Periosteal type: is sessile lesion that arises within the cortex and elevates the overlying periosteum, which provokes the production of peripheral periosteal reaction.

The prognosis of periosteol is poorer than paraosteol type

Cartilage Forming Tumors

Chondroma

Chondromas are benign tumors composed of mature hyaline cartilage. It is one of the common bone tumors and is located most often in the short tubular bones of the hand and

feet. A diagnosis of chondroma in the jaw, facial bones, and the base of the skull should be viewed with great skepticism, because many of these are actually low-grade chondrosarcoma.

Clinically:

Usually arise in the 3rd to 4th decade of life. Mostly seen in the condyle or anterior maxilla of adult patient. They are painless slow growing lesions.

Radiographically:

chondroma appears radiolucent with central radio-opacity.

Histologically

Chondroma appears as a circumscribed mass of mature hyaline cartilage, with well formed lacunae containing small chondrocytes with pale cytoplasm and small round nuclei.

Treatment and Prognosis

It is wise to consider any lesion diagnosed as chondroma of the jaw to represent a potential chondrosarcoma and treated with radical resection.

Chondrosarcoma

Is a malignant tumor characterized by the formation of cartilage, but not bone, by the tumor cells. Chondrosarcoma comprises about 10% of all primary tumors of the skeleton but are considered to involve the jaws very rarely. Only 1-3 % of all chondrosarcomas arise in the head and neck area.

Clinical and Radiographic Features

It is a disease of adulthood with peak prevalence in the 5^{th} to 7^{th} decade of life. Although chondrosarcoma arise over a wide age range, the majority of affected patients are over 50 years of age.

When occurring in the head and neck, chondrosarcoma mostly arise in the maxilla, body of mandible, ramus, nasal septum, and paranasal sinuses.

A painless mass is the most common presenting sign. This may be associated with separation or loosening of teeth. In contrast to osteosarcoma, pain is an unusual complaint. Maxillary tumors may cause nasal obstruction, congestion, epistaxis, photophobia, or visual loss.

Radiographically

The tumor shows a radiolucent process with poorly defined borders. The radiolucent area usually contains a variable amount of radio-opaque masses, which is caused by calcification or ossification of cartilage matrix.

Histopathology

The tumor is composed of cartilage showing varying degrees of maturation and cellularity. In most cases, typical lacunae formation within chondroid matrix is visible.

Chondrosarcoma may be divided into 3 grades of malignancy, which correlates well with the rate of tumor growth and prognosis,

e.g. grade I, closely resemble chondroma, which is composed of chondroid matrix and chondroblast, that show only subtle variation from the appearance of normal cartilage. The tumor should be considered malignant when large-plump chondroblasts and binucleated chondrocytes are present.

Grade II, present with greater number of cells with moderately sized nuclei and increased cellularity.

Grade III is highly cellular, with spindle cells proliferation. Mitoses may be prominent.

Treatment and Prognosis

Treatment is by resection. Prognosis is related to size and location. 5-years survival rate varies from 43%-95%

MARROW TUMORS

Ewing's Sarcoma/Primitive Neuroectodermal Tumor

This tumor has been traditionally regarded as an undifferentiated type of bone sarcoma of children, now it has been linked with the peripheral or primitive neuroectodermal tumor "PNET", and the term Ewing's sarcoma /PNET "ES/PNET" is currently used. The tumor cells demonstrate a reciprocal translocation between chromosomes 11 and 22.

Clinical Features

ES/PNET of bone is usually seen in patients between the age of 5 and 20 years, with only a minority of the cases presenting in infancy or adulthood. The peak incidence is in the second decade of life, with approximately 80% of patients being younger than 20 years of age at time of diagnosis. The vast majority of affected patients are white, with blacks almost never developing this tumor. The long bones, pelvis, and ribs are affected most frequently, but almost any bone can be affected.

Jaw involvement is uncommon, with only 1% to 2% occurring in the gnathic or craniofacial bones. Pain, with swelling, is the most common symptom. It is usually

intermittent and varies from dull to severe. Fever, leukocytosis, and an elevated ESR also may be present and this may cause an erroneous diagnosis of osteomyelitis.

The tumor commonly penetrates the cortex, resulting in a soft tissue mass, overlying the affected area of bone. Jaw involvement is more common in the mandible, parasthesia and loosening of teeth are common findings.

Radiographically, there is irregular lytic bone destruction with ill-defined margins. Cortical destruction or expansion may or may not be present.

Histopathologic Features

Microscopically, the tumors consist of sold sheets of cells divided into irregular masses by fibrous strands. The cells are small and uniform. The cell outlines are indistinct, resulting in a "syncytial appearance". The nuclei are round, with frequent indentations, small nucleoli, and variable mitotic activity. There is a well developed vascular network; large areas of hemorrhage and necrosis are commonly present. Some contain foci or may be composed mostly of larger cells, these are designated as Large cell "atypical" Ewing's sarcoma.

About 75% of cases contain glycogen granules in the cytoplasm of the tumor cells. This help in the diagnosis, to differentiate it from other round cell tumors.

The diagnosis may be very difficult, and should be differentiated from other primitive "small cell tumors" involving bone and soft tissues in young patients particularly, lymphoblastic lymphoma, desmoplastic small cell tumor. And embryonal/alveolar rhabdomyosarcoma.

The immunohistochemical and molecular genetic features are very useful for differentiation.

Spread and Metastases

To lung and pleura, other bones particularly the skull, CNS, and rarely to the lymph nodes.

Treatment

The treatment in the past consisted of surgical excision, and radiation therapy resulting in a 5 year survival rate of less than 10%. The combination of high dose radiotherapy and multidrug chemotherapy has dramatically changed the picture and the 5 year survival to 75%.

Malignant Lymphoma

Malignant lymphoma can involve the skeletal system primarily or as a manifestation of systemic disease.

1) Large Cell Lymphoma

Primary of bone is more common in adults than children, 60% of cases occurring in patients over the age of 30 years.

Grossly, most cases involve the diaphysis or metaphysis of long bones or the vertebrae producing patchy cortical and medullary destruction. Lymphoma of bone may cause vague pain or discomfort, which might be mistaken for a toothache. The patient may complain of parasthesia, particularly with the mandibular region.

Radiographically, ill-defined or ragged radiolucency, although in the early stages, may be non-existent.

Gradually the process causes bone expansion, and eventually perforation of the cortical plate producing a soft tissue lesion.

Microscopically

The tumor is composed of sheets of large cells with pleomorphic nuclei, some are indented, multilobulated, or horse-shoe shaped. They usually have prominent nucleoli. The cytoplasmic outlines are well defined. These are distinguishing features from Ewing's sarcoma cells, which are smaller, with fine nucleoli, the cytoplasmic borders are indistinct, with less amount of cytoplasm.

Treatment

According to the stage, and includes radiation and chemotherapy.

2) Burkitt's Lymphoma

Is a malignancy of B-lymphocyte origin that represents an undifferentiated lymphoma and it seems to have a predilection to jaws. This type of lymphoma was originally described in young children from Africa and was termed the African Burkitt's lymphoma or endemic Burkitt's lymphoma. This tumor is thought to be related pathogenetically to Epstein-Bar virus (EBV), because more than 90% of the tumor cells, particularly in the African type, show expression of EBV nuclear Ag. and the affected patients have a high titer to EBV.

Tumors with a similar histomorphology, commonly referred to as sporadic or American Burkitt's lymphoma have been observed in other countries where the neoplasm is usually first detected as an abdominal mass.

Clinical and Radiographical Features

50-70% of the cases presented with jaw mass. The malignancy usually affects children (peak prevalence 7 years of age). The posterior segments of the jaws are more commonly affected maxilla more than the mandible. The American type tends to affect patients over a greater age range, with the abdominal region typically affected, although the jaw has been reported to be affected.

The tumor may produce facial swelling and proptosis, pain, tenderness, and parasthesia, with marked tooth mobility.

Radiographically, radiolucent destruction of the bone with ragged ill-defined margins.

Histopathology

Undifferentiated small, non-cleaved B-lymphocytes. The lesion is composed of sheets of tumor cells that exhibit round nuclei with minimal cytoplasm, prominent nucleoli, and prominent mitoses.

The classic starry sky pattern associated with the lesion is caused by the presenc of histiocytes within the tumor tissue, which appear less intensely deeply stained malignant lymphocytes.

Treatment and Prognosis

The tumor is aggressive; death will result in 4-6 months if not treated. Treatment by intensive chemotherapy.

3) Angiocentric T-cell lymphoma

Is a rare condition that characterized clinically by aggressive destruction of the midline structures of the palate and nasal fossa. For many decades the nature of this disease has been controversial, this reflects the variety of terms by which this tumpr has been called (e.g. Midline lethal granuloma, Midline malignant reticulosis, etc.).

Based on modern diagnostic cytogenic, immunologic, and molecular methods, this lesion has been classified as T-cell lymphoma. The tumor should be differentiated from other that lead to destruction of the palate e.g. Wegener's granulomatosis, Tertiary syphilis.

Clinical Features

The condition mostly affects adults, which presents initially as nasal stuffiness or epistaxis, pain may be present. Swelling of the soft palate may precede the formation of a deep, necrotic, ulceration that ends with palatal destruction, which typically creates oro-antral fistula.

Histopathology

Mixed infiltrates of inflammatory cells, arrange around blood vessels "angiocentric". The lesion destroys tissues, with necrosis. Large angular lymphocytes with an atypical appearance are usually present. Immunohistochemical evaluation of this infiltrates often shows a monoclonal T-lymphocyte proliferation.

Treatment

Untreated tumor will lead to death, which follow progressive and highly destructive malignancy.

Localized condition is treated by radiation. Disseminated condition is treated by chemotherapy.

Multiple Myeloma and Plasmacytoma (MM)

MM. is a relatively uncommon malignancy of plasma cell origin within bone. MM. accounts for nearly 50% of all malignancies that involve the bone. The malignant plasma cells that compose this tumor are monoclonal, which arise from a single malignant precursor that has spread throughout the body. Because the neoplasm develops from a

single cell, all the daughter cells have the same genetic makeup and produce the same proteins.

The proteins are the immunoglobulin components, which the plasma cell would normally produce. The effects of tumors results due to abnormal proliferation of the cells and the uncontrolled production of their protein product.

Clinical and Radiographic Features

MM. is a disease of adults, the median age at diagnosis is 60-70 years, and rarely diagnosed before the age of 40. Bone pain, pathologic fractures, fatigue, fever, infection, and bleeding tendency due to abnormal platelet function.

Radiologically

Multiple well-defined, punched out radiolucencies, or ragged radiolucencies may be seen in MM. These may affect the skull, although any bone can be affected. The jaws may be involved in 30% of cases.

Histopathology

Show diffuse, monotonous sheets of neoplastic, variably differentiated, plasmacytoid cells that invade and replace the normal host tissue, with frequent mitoses. Amyloid deposits may be seen in association with neoplastic cells, which appear as a homogenous, eosinophilic acellular material.

Diagnosis

1. Skeletal X-ray ► Radiolucency.
2. Histopathology ► Neoplastic plasma cells.
3. Bone-marrow examination ► at least 10% atypical plasma cells of marrow population.

4. Bence-Jones proteins in urine (30-50%).
5. serum protein electrophoresis ► Myeloma protein (M band), massive overproduction of one abnormal protein “immunoglobulin” by the neoplastic clone of cells.

Treatment

Chemotherapy – with poor prognosis, 5 year survival rate is 25% only.

Plasmacytoma

Is a unifocal, monoclonal, neoplastic proliferation of plasma cells that usually arises within bone, although extramedullary type is present.

Clinical and Radiographic Features

Affects adult males with average age at diagnosis of 55 years. Most of the lesions are central within a bone. The spine is the most common site.

The presenting features are pain and swelling although some cases are asymptomatic.

X-Ray ► well defined unilocular radiolucency.

Histopathology

The same as MM.

Differentiation from MM.

All the findings mentioned in the diagnosis of MM. are negative in Plasmacytoma.

Treatment

Radiation or surgery, It may evolve to MM. in 30 to 50% of cases.

Langerhans Cell Histiocytosis

The old term Histiocytosis-X was introduced to describe a spectrum of disorders which characterized by proliferation of histiocyte-like cells, that are accompanied by varying numbers of eosinophils, lymphocytes, plasma cells, and multinucleated giant cells. The neoplastic cells are the Langerhns cell, which are dendritic mononuclear cells normally found in the epidermis, mucosa, lymph nodes, and bone marrow.

Clinical and Radiographic Findings

1. Monostotic or polyostotic epsinophilic granuloma of bone without visceral involvement.
2. Chronic disseminated histiocytosis- disease involving bone, skin, and viscera ► Hand-scűler-christian disease.
3. Acute disseminated histiocytosis, prominent cutaneous, visceral, and bone marrow involvement ► Letterer-Siwe disease.

The lesion may affect any bone, but skull, ribs, vertebrae, and mandible are mostly affected.

50% of patients are under the age of 10 years.the jaws are affected in 10-20% of all cases, with dull pain and tenderness.

Radiographically, punched out radiolucent lesions.

- Mandibular bone involvement ► posterior region, ► destruction of alveolar bone ► scooped appearance.
- bone destruction and loosening of teeth ► floating in air appearance.

Histopathology

Diffuse infiltration of large pale-staining mononuclear cells that resemble histiocytes. The cells have indistinct cytoplasmic borders with rounded or indented vesicular nuclei. Varying numbers of eosinophils are seen.

Treatment

Maxillary and mandibular lesions ► curettage.

Metastatic Tumors to the Jaw

Metastatic carcinoma is the most common form of cancer involving bone. Studies show that 2/3 of breast carcinoma. 1/2 of prostate carcinoma, 1/3 of kidney and lung cancer ► bone spread.

Jaw bone metastasis is mainly from breast, lung, kidney, thyroid, prostate ► by hematogenous route.

Clinical Findings

Elderly individuals are mostly affected. The mandible may be involved in about 10% of metastatic extra oral carcinoma. Maxillary metastasis is uncommon.

Clinically, the patient may report pain, lump, loosening of teeth, and parasthesia, or the patient may be completely asymptomatic. The jaw lesion may be the 1st indication of the existence of an occult primary tumor.

Radiographic Features

May be lytic, resembling a cyst, sometimes causing widening of periodontal ligament. Others may stimulate new bone formation ► radiopaque or mixed lesion e.g. prostate and breast carcinoma.

Histopathological Features

The microscopic appearance of metastatic carcinoma in bone varies. In some instances, the metastatic tumor is well differentiated and closely resembles a carcinoma of a specific site, such as the kidney, colon, or thyroid. In such instances, the pathologist can say with reasonable certainty that a given metastatic tumor comes from a specific primary site . More often, however, metastatic carcinomas are poorly differentiated and histopathologic study of the metastatic deposit gives little clue as to the primary site of the tumor. Poorly differentiated metastatic carcinoma may be difficult to differentiate from anaplastic small cell sarcomas, malignant lymphomas, and malignant melanoma . Immunohistochemical reactions are usually necessary in such cases to establish the diagnosis. Although the diagnosis of metastatic carcinoma can usually be determined by microscopic examination, the final diagnosis depends mostly on a careful medical history and complete physical examination with appropriate laboratory studies.

Treatment and Prognosis

The prognosis for metastatic carcinoma of the jaws is poor because. by definition, osseous metastasis automatically places the patient in Stage IV disease, Although a solitary metastatic focus may be treated by excision or radiation therapy, jaw involvement almost always is associated with widely disseminated disease, Five-year survival after detection of metastatic carcinoma Involving the jaws is exceedingly rare, and most patients do not survive more than 1 year.