

A brief note on giant cell tumor of bone

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Editorial

I decided to write brief paper about bone tumors with the high incidence of this lesion but it's so diffused subject and explanation is so difficult. Thus, I reviewed sequentially some of important bone tumor as a reminder for physician and surgeon to distinguish tumor symptoms and diagnosis in less time. On the other hand, According to dispersal nature of bone tumor, I have written a brief paper about bony giant cell tumor because of the importance of this tumor, its natural history and tendency to recurrence and metastasize.

Giant cell tumor of bone.

Epidemiology

Giant cell tumor of bone (GCTB) first described by Cooper and Travers in 1818.¹ Their local aggressiveness explained by Later Nelaton and malignant features showed by Virchow.^{2,3}

Mayo Clinic reported GCTB included approximately 5% of bone primary tumors. Over all age range of this was reported between 20 to 40 years old and this is more common in female population. Some authors revealed that more than half of GCTB present in the 3rd and 4th decades of life.^{1,4}

Clinical features

The most common symptoms in patients are pain which is progressive. These symptoms usually raise with activity at the beginning but became permanent with time passes. It may be worse at night as other bone tumors. Generally it is not intense pain unless pathological fracture has happened. Different papers showed this catastrophic phenomenon rate as 10% to 30% of cases.^{3,5}

GCTB is the most challenging benign bone tumors. On the other hand, the natural history of this bony tumor may be different from local bony lesion to local metastasis, even malignant transformation which is rare. Symptoms are highly variable and may range from asymptomatic in some patients, joint pain in tumor near the joint and even pathologic fracture. In long-term follow up swelling or palpable mass may be seen after tumor has been grown up.^{3,4}

Location

This tumor is located more commonly the distal femur, the proximal tibia and the distal radius, respectively which the last ones are more aggressive type of tumor. Other location is the proximal humerus. On the other hand, this lesion involved skeletally mature bone close to the joint space in young adults. This lesion includes most common benign tumor which involves sacrum but other part of spine involvement is rare. GCTB classified as a locally aggressive lesion that originates within the epiphyses of long bones, but they often spread to the metaphysis. Even some authors confirmed that

only in 1.2% of GCTs we find no epiphyseal involvement but the metaphysis or diaphysis is involved.^{6,7}

This tumor is an eccentric lytic, progressive lesion which some time has potentially malignant transformation (less than 5%) and tendency to destruct the bone, local recurrence or even metastasize. In metastatic cases, pulmonary involvement was reported nearly 3% of cases. Usually it's a solitary tumor but approximately 1% to 2% of this may be exists in another location (present as multicentric). This form may be more clinically aggressive and tend to involve the small bones of the hands and feet.^{3,6,7}

Metastasis in gctb

An interesting point is that pulmonary metastases don't always progress, in some cases regression may be seen and even this tumor may be asymptomatic for many. Therefore, the exact history of these pulmonary metastases is unpredictable. Another point is that pulmonary metastasis could be exist at the time of initial surgery or in some patients, may be undetected for 10 years or longer.^{2,4} overall, GCTB pulmonary metastases present approximately 3-5 years after the initial diagnosis. This point should be considered in physicians mind to diagnosis of recurrence as soon as possible. This metastasis may be present as clusters of this tumors located within the lung. Generally the mortality rate of this tumor in patients with pulmonary metastases is nearly 15%. Patients with aggressive radiographic features recurrence caused suspicion to pulmonary metastases.^{6,8}

Radiology

Radiographic features mostly are diagnostic. As you know, the location of this lesion is the epiphyses of long bones but this is not fixed rule, because in some rare cases in immature patients, it originates in the metaphysis of bone. The zone of transition in this lytic tumor may be poorly specified. Although these lesions usually are benign, the lesion expands or destroys bony architecture.⁹

The subchondral bone often is not involved so extension to joint space is rare. Thus, the surgeon should be so careful to avoid

destruction through the subchondral bone into the intraarticular space which causes joint involvement.^{4,9}

Differential diagnosis

The differential diagnosis includes other giant cell bone lesion such as simple bone cyst, ABC, osteoid osteoma, osteoblastoma, osteosarcoma, chondroblastoma and brown tumor in hyperparathyroidism. Therefore, we should rule out hyperparathyroidism at least by lab test in this situation.^{1,10}

Pathology

Histopathology of the lesion showed many multinucleated giant cells in a field of mononuclear stromal cells which are diagnostic to the nuclei of the giant cells tumors and could rule out other lesions which concluded giant cells in microscopic view. Also foamy macrophages or reactive bone formation could be seen in this view. Proliferation of mononuclear cells and giant cells fulfilled the bone marrow space and only a few residual bone trabeculae can be seen among the tumor cells.^{4,11}

Local recurrence

Recurrence rates with new treatment method documented from 5% to 15%, but by old treatment and delayed diagnosis this rate was catastrophic and in some cases was more than 50%. In this successfulness, we should consider different agents such as modern diagnostic method for on-time and exact diagnosis, Betterment in surgical technique such as curettage for enough pulls out of tumor cell by cortical window and also use of a new tools such as power burr to extend this window to appropriate size as helpful effects. Bone involvement as a recurrence will be seen expanding lytic lesion on the plain radiograph. Ossification or mass which is seen on MRI reveal soft tissue involvement. Thus, for better diagnosis of soft tissue complications physicians should consider this modality in mind.^{9,12}

Treatment

GCTB should be considered as a clinical-radiologic-pathologic subject which better perception histopathology and radiologic method could be effective in an appropriate treatment. This treatment needs the collection of experts in orthopedic surgery, pathology, oncology and also radiology.

Treatment of GCTB may be variable from drug therapy, Radiation therapy, Embolisation and laser photoablation, Chemical adjuvant therapy and finally surgical treatment. We should be careful that the aim of our treatment is eradication of the tumor cell, preservation of limb function and avoiding of local recurrence and also distant metastasis.

Although there is no world-wide agreement toward the ideal treatment of this lesion but some authors believed that treatment of choice is aggressive, extended curettage then argon beam coagulation is done which is associated with few complications. Generally, Surgical resection is the standard treatment of GCTB is wide resection.^{1,6,7,12}

Drug

Some papers showed that that topical or systemic use of bisphosphonates (pamidronate or zoledronate) could be an appropriate adjuvant therapy in GCTB treatment. These agents select giant cells which is similar to osteoclast and caused apoptosis.¹³ Denosumab which is a RANKL-specific inhibitor is an effective agent in this treatment.¹⁴

Follow up

An important note in these patients is long-term follow-up because of accurate diagnosis of recurrences and metastases. Most authors believed that they occur within 3 years but papers showed that these metastases can be seen more than 10 years later. We should follow up patients by Chest radiographs and chest CT scan as a baseline method at the beginning.^{3,6}

Conclusion

In conclusion, although the GCTB usually is a benign condition and may be regret and could be asymptomatic, it should be taken into account in rare cases this lytic lesion may transform to malignant tumor even metastasizes to other part of body out of the bone such as lung which may be hard work to treat this transformation. Thus the surgeon should keep in mind this tumor and when he/she is suspicious, additional survey should be done to diagnose as soon as possible.

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None.

Conflicts of interest

None.

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