

PAGET'S DISEASE
NEW PROGRESS AND FINDINGS

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I have written two rather extensive articles in this Journal in regard to Paget's disease. The etiology, pathology, microbiology, treatment, progress of the disease, etc., have been reviewed.

QUESTIONS AND ANSWERS

In this article I would like to answer a few of the questions that have been asked in regard to Paget's disease that are not properly answered.

As you know, Paget's disease is a disease of the bones. It is a chronic disorder and typically produces deformities and enlargement of the bones due to the excessive bone breakdown and also bone formation. It creates density of the bone and makes the bone rather fragile and tender. Clinically, this disease can create severe pain, followed by deformities and sometimes fractures. Almost every bone of the body can be involved. The major part of the involvement concentrates and localizes on the long bones; tibia, femur and pelvic bone, skull and spinal column. As a statistic, we are familiar with the frequency of the involvement of Paget's disease around the spine, pelvis and bones of the lower extremities, as well as the thigh and also lower leg. We find they may have one bone affected and others will demonstrate multiple bone involvement. In this area we should emphasize that when the skull is involved, showing Paget's disease, the patient may experience difficulties with vision and the nerves of the eyes are affected. Also, when the bones around the internal auditory meatus is involved as well as in the external auditory meatus, the tightness of the canal will also create nerve deafness and a loss of hearing results. This can involve both sides and both ears or can involve only one. It is said that Beethoven, the great musician, had Paget's disease which involved his skull and also his neural canal of hearing and he became deaf.

While the skull is showing the involvement of Paget's disease, the effect of that can also be observed on the facial bones and disturbances of the chewing mechanism may occur when the disease affects the teeth in the upper and lower jaws.

The answer as to what is the etiology of Paget's disease is as follows:

Recent studies of Paget's disease has suggested that a possible slow virus infection of the bone may be the cause. Also, other factors such as hereditary appears strong since Paget's disease has been seen in different members of a family. The hereditary factor may lead to susceptibility among family members. Isolation of this slow virus and exact nature has not been totally understood or explained. Research is still being done on this subject.

In regard to Paget's being in families, it is suggested that after the age of 40, it may be advisable for the siblings and children of a person with Paget's disease to have a standard alkaline phosphatase blood test done every two or three years. If it is elevated, further appropriate treatment should be carried out. If it is abnormal, further tests such as bone scanning and other tests in regard to the urine need to be initiated.

Paget's disease is most common among Caucasian people and also European descent. It has also been seen in African-Americans, Asian-Americans and even seen in people under 40 years of age. It is said that about 3 percent of the American population over 60 years of age have Paget's disease, whether they are diagnosed or not. Sometimes people with Paget's disease are not aware that they do have it unless it becomes painful. Most of the time this pain can be confused with plain arthritis or other disorders. The proper way to establish a Paget's diagnosis is by x-rays, bone scanning, testing the blood for alkaline phosphatase. Only when elevation of the alkaline phosphatase is observed can we start making a diagnosis. In regard to bone scan and why it should be done in Paget's disease, it is said that not only does it identify the involved bone, it may identify multiple bones and is a rather safe procedure to be carried out. The material given to the patient is radioactive but not enough to disturb the patient and create multiple complications.

We have explained that the pain can be mistaken for arthritis. What can differentiate this pain and also what is the relationship between arthritis and Paget's disease?

It is true that Paget's disease can cause arthritis by changing the long bones around the joints, such as the thigh and leg. Ankylosis, bowing, shortening and malalignment can

all be true in the case of Paget's disease, as well as arthritis but Pagetic bone may become rather enlarged and cause the joint surface to undergo excessive wear and tear. Arthritis is common among Paget's disease patients and many of the patients with Paget's disease complain of back pain, leg pain, knee pain and spinal arthritis. Differentiation of osteoarthritis, rheumatoid arthritis and Paget's disease should be carefully evaluated by the physician. We should also remember that osteoporosis is a condition of generalized loss of the bone mass, which can lead to fractures, as well as Paget's disease which can do the same. In the same patient, you can see osteoporosis as well as Paget's disease combined. Treatment of Paget's disease can also cure, or at least stop the growth of the osteoporosis. Therefore, these two diseases can be very much connected and related.

SYMPTOMS OF PAGET'S DISEASE

Now we will ask what are the symptoms of Paget's disease? The answer to this question is that pain may occur in any bone affected by the Paget's disease and pain is the number one symptom. It is often localized in adjacent joints, headaches, hearing loss and visual problems. Also, pressure on the vagus nerve by enlargement of the bone which can create pain again. Pain can start prior to deformities and can be many different forms of pain. There can be headaches, radicular pain, muscular pain, skeletal pain or osteoarthritic pain. The most frequent symptoms are the deformities of the bones such as increase in head size, bowing of the limb, or curvature of the spine has been seen in advanced cases. These deformities are usually due to enlargement and softening of the affected bone. Hip pain may occur when the pelvis and thigh bone are involved. Damage to the cartilage of joints adjacent to the affected bone may lead to arthritis. Pagetic bone is susceptible to fracture with moderate stress. Although Paget's disease is rarely a fatal disease, due to the transformation of the Pagetic bone to osteogenic sarcoma accounts for 1% of all Paget's disease involvement.

As we have recognized the diagnosis of Paget's disease being first by the elevation of alkaline phosphatase, we should also emphasize that the alkaline phosphatase is a chemical enzyme produced by bone cells and is over produced by Pagetic bone. Therefore, the blood level of alkaline phosphatase is a reflection of the extent of the disease and it's degree of activity. Repeated measurement of alkaline phosphatase from time to time can be used to determine if the condition is stable or not. It is especially helpful in finding and recognizing the patient's response to the treatment with a variety of anti-Pagetic medication.

Another question that needs to be answered is the connection between Paget's disease and heart disease. Mainly it has been emphasized that this usually does not occur due to the fact that the blood produces more bone, the circulation becomes more rapid and the heart works harder. Enlargement of ventricles of the heart can be seen. The majority of heart disease is due to arteriosclerosis, hardening of the arteries and the arteries of the heart can be more susceptible in the Paget's patient than a normal heart. There has been no known connection of the Paget's disease with diabetes mellitus. Nevertheless, the recommendation comes that both medications such as Insulin and Calcitonin should not be mixed together.

Paget's disease can create kidney dysfunction and kidney stones are somewhat more common and has been seen.

Other complications which may follow Paget's disease is in the nervous system such as compression of the spine. In case the Paget's hits the spine compression of the auditory meatus. In case the Paget's involves the skull and bone optic nerve pathology with pressure on the optic canal.

The question of whether sarcoma is related to Paget's disease, it has been mentioned that this is a rare occurrence that development of a malignant tumor, called a sarcoma is related. When there is a sudden onset of severe pain or motion abnormalities and worsening of the condition of the patient, multiple pathological fractures, sarcoma should be suspected and be treated. It is not known that sarcoma was the cause of the main Paget's disease.

The question as to whether Paget's disease has relationship with Calcium intake and vitamin D intake has not been clear. Nevertheless, the elevation of the Calcium and decrease of Calcium intake has not had anything to do with the production or treatment of the Paget's disease. In the patient who has kidney dysfunction or kidney stones, it is proper that the physician be notified of the course of the disease and the intake of Calcium or vitamin D.

Exercise is recommended as a treatment for Paget's disease to prevent further evidence of ankylosis but the exercise should not to be to the degree of creating a fracture.

Prognosis of the patient with Paget's disease varies greatly from the patient being completely stable to a patient who has gone into rapid progression. The symptoms in general progress slowly in affected bones but there is usually no spread to previously normal bone. The outlook is generally good, particularly if treatment is started early the condition can be controlled, as well as the pain being lessened.

TREATMENT OF PAGET'S DISEASE

Treatment of Paget's disease consists of treatment by an expert endocrinologist, a physician who recognizes hormonal and metabolism disorders. Consultation with a neurosurgeon, neurologist, orthopedic surgeon and otolarangologists at times are advisable. These physicians treat the patient with two types of medications which are FDA approved. They are Calcitonin, which is a synthetic salmon calcitonin (Calcimar, Miacalcin, or Osteocalcin) and sometimes synthetic human calcitonin which is referred to as Cibacalcin. This medication is always given by injection, although recently the medication has been advised by inhalation, as well as other newly investigated methods. The second medication is Bisphosphonates and is a new class of drugs known as bisphosphonates, which inhibits abnormal bone cell activity. Among this group Etidronate disodium, which is Didronel, is given to the patient by tablet. It is recommended to be taken on an empty stomach and at least 30 minutes before eating. No other medication or antacid should be given for two hours before or after this medication. Treatment with this medication should not exceed more than six months but repeat courses have been done. There are a group of medications called Pamidronate disodium or Aredia. This can be given intravenously. It has recently been approved by the FDA. It can have prolonged effects after a short course of treatment.

Other types of medication sometimes used for treatment of Paget's disease are Plicamycin (Mithracin) and gallium nitrate (Ganite). They are intravenous drugs approved for the treatment of high blood calcium levels in cancer patients. They have both been used in research studies for Paget's disease but are not specifically approved by the FDA for the treatment of Paget's disease.

Correction of Paget's deformities by surgery is not usually recommended. Nevertheless, when pressure on the nerves is involved, a neurosurgical approach by decompression of the cochlear nerve or optic nerve intracranially has been approached.

Treatment of Pagetic bone fracture by fixation or surgery also may need to be done as the case develops. Total joint replacement of the hips and knees should be reserved for the most severe cases of arthritis and Paget's disease when other methods of treatment fail. The procedure of osteotomy for surgical cutting and realignment of Pagetic bone and deformity may help weight bearing joints, especially the knee. Medical therapy prior to the surgery should be carried out to decrease the bleeding and other complications which usually follows on the Pagetic patient.

It should be emphasized that the Paget's Disease Foundation can provide the patient and doctor with further information for educational purposes of professional assistance in education or public education. Their research is also available at several different centers in the world.

A new medication, namely Fosamax, has been approved by the FDA for the treatment of Paget's disease of the bone in October of 1995 and is recommended to be given 40 mg. once daily for 6 months. Fosamax must be taken at least one-half hour before the first food or beverage. Waiting longer than 30 minutes will usually improve the absorption of Fosamax. Waiting less than 30 minutes or taking Fosamax with food, beverage, or other medication will lessen the effect of the Fosamax. It is recommended to be taken with a full glass of water and the patient should also avoid lying down for at least 30 minutes thereafter.

CONCLUSION:

The administration of Calcimar, Myacalcin, Osteocalcin and Cibacalcin are by injection, while administration of the Fosamax and Didronel is oral. Administration of the Pamidronate disodium or Aredia is by intravenous injection and drip. For further information in regard to the dosage of Calcitonin and Didronel, I will refer you to an article which has appeared in two issues of this Journal in the bibliography.