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## Paget's disease of bone in a Chinese patient: A case report and review of the literature

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Although it is fairly common in the Western countries, Paget's disease of bone is very rare in Chinese individuals. Through an extensive literature search, only 8 Chinese Paget's disease cases were found in the English language literature and all were reported in local medical journals of Asia that may not be accessible to international readers. To enhance the awareness of the rarity of Paget's disease in Chinese individuals to pathologists worldwide, we present a case of Paget's disease in a 54-year-old Chinese male. We also compare the clinical features of Paget's disease reported in Chinese patients to Paget's disease reported in the Western countries. No familial cases and no malignant transformation are found in the reported cases of Paget's disease in Chinese patients. In addition, more often skull involvement, higher frequency of monostotic cases, and symptomatic cases are observed in this limited number of Paget's disease cases reported in Chinese individuals. (**Oral Surg Oral Med Oral Pathol Oral Radiol Endod 2005;99:727-33**)

Paget's disease of bone was first described by Sir James Paget under the term "osteitis deformans" in 1877.<sup>1</sup> It is a chronic progressive monostotic or polyostotic disorder characterized by rapid bone resorption and deposition resulting in a "mosaic" pattern of lamellar bone with extensive local vascularity and fibrous tissue in marrow.<sup>2</sup> Most of the patients are asymptomatic.<sup>3-7</sup> For symptomatic individuals, bone pain, deformity, and fractures are the main presenting features.<sup>8</sup> The enlarged and deformed bones may compress surrounding nerves and vessels that cause neurological symptoms.<sup>8</sup> Jaw bones are involved in about 17% of patients of Paget's disease and radiographically it shows the characteristic "cotton-wool"-like radiopacity.<sup>9,10</sup> Other radiographic and dental findings in Paget's disease include well-circumscribed radiolucency, loss of lamina dura, pulpal

radiopacity, root resorption, and hypercementosis.<sup>10,11</sup> Therapeutic agents for Paget's disease include calcitonin, bisphosphonate, and mithramycin.<sup>10</sup> Bisphosphonate appears to gradually become the primary treatment for symptomatic Paget's disease patients. A recent clinical trial suggested that second and third generation bisphosphonate, such as pamidronate and alendronate, were more effective than calcitonin and etidronate, the first generation bisphosphonate.<sup>12</sup>

The pathogenesis of Paget's disease is still not totally clear, although both slow virus infection such as measles virus, canine distemper virus and respiratory syncytial virus, and genetic factors have been suggested to play a role.<sup>13-16</sup> Conflicting research findings led to the long-time debate on whether slow virus was involved in Paget's disease of bone.<sup>17-22</sup> Recent findings suggested that the contradictory results were probably due to sensitivity of the technique used.<sup>23</sup> To date, 7 genetic loci have also been identified to be associated with development of Paget's disease.<sup>16</sup> Malignant transformation is the most serious complication for Paget's disease and osteosarcoma is the most common malignancy arising in Paget's disease.<sup>24-26</sup> A common genetic mechanism between Paget's disease and osteosarcoma has also been discovered in chromosome 18.<sup>27,28</sup>

The incidence of this disease varies widely among different ethnic groups and geographic areas throughout the world.<sup>29</sup> Most cases were reported in the populations of European descent.<sup>29,30</sup> It occurs commonly in England, North America, Australia, New Zealand, France, and Germany, with highest incidence in England (3%-4% in individuals over age 50),<sup>31</sup> although recent studies revealed a decline in the prevalence in these countries.<sup>32-35</sup> The prevalence of Paget's

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Fig 1. Clinical photograph showing facial deformities of the patient, including enlargement of the skull; broadened forehead; swelling in the maxilla, the mandibular ramus, and the mandibular angle; and deviation of the mandible.

disease in the United States was also reported to be approximately 3% in white individuals older than 55 years old.<sup>31</sup> Interestingly, Paget's disease is very rare in Africa and Asia, and rarely occurs in Chinese.<sup>31,36</sup> An extensive literature search reveals only 8 Chinese cases of Paget's disease in the English literature<sup>37-41</sup> and all were reported in local medical journals in Asia that might not be accessible to international readers. To increase the awareness of the rarity of Paget's disease in Chinese individuals, we present a case of Paget's disease in a 54-year-old Chinese male in Taiwan. We also review and compare the clinical features of Paget's disease reported in Chinese patients to the clinical features of Paget's disease reported in the Western

countries to evaluate the similarities and differences between these 2 groups of patients.

#### CASE REPORT

A 54-year-old Chinese male presented to our Department of Oral and Maxillofacial Surgery seeking cosmetic surgery for his facial appearance. The patient stated that he initially noted the facial enlargement as early as the age of 16. There were no other family members having the same condition as he. He also complained of blurred vision of the left eye for about 2 months. High pressure in his left eye was diagnosed by an ophthalmologist. Extraoral examination revealed facial deformities including marked enlargement of the skull; broadened forehead; swelling in maxilla, mandibular ramus, and



Fig 2. Panoramic radiograph showing radiopacities in a “cotton-wool” pattern in both the maxilla and the mandible. Severe alveolar bone resorption around the residual teeth was also noted.

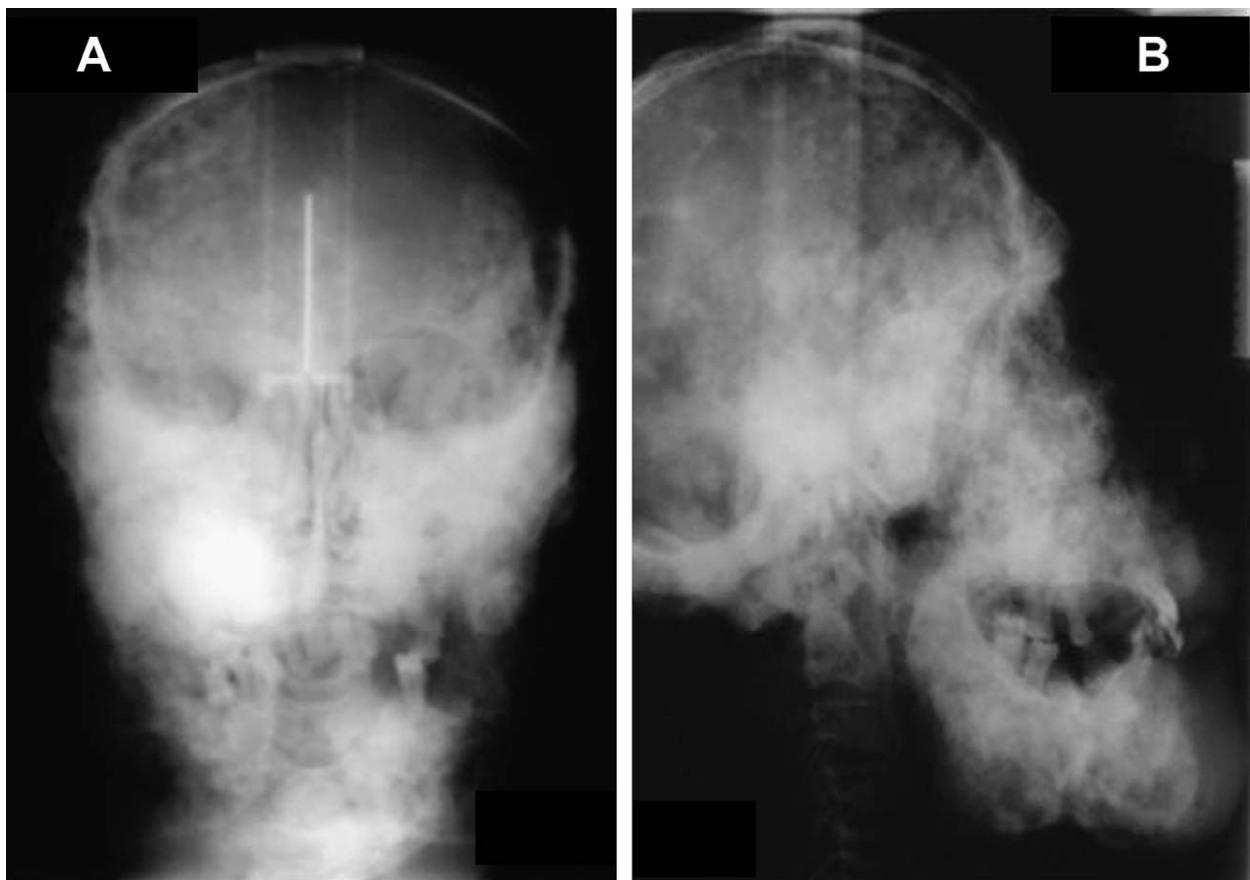


Fig 3. Cephalometric radiographs showing radiopacities in a “cotton-wool” appearance in the entire skull and the mandible. **A**, Postero-anterior view. **B**, Lateral view.

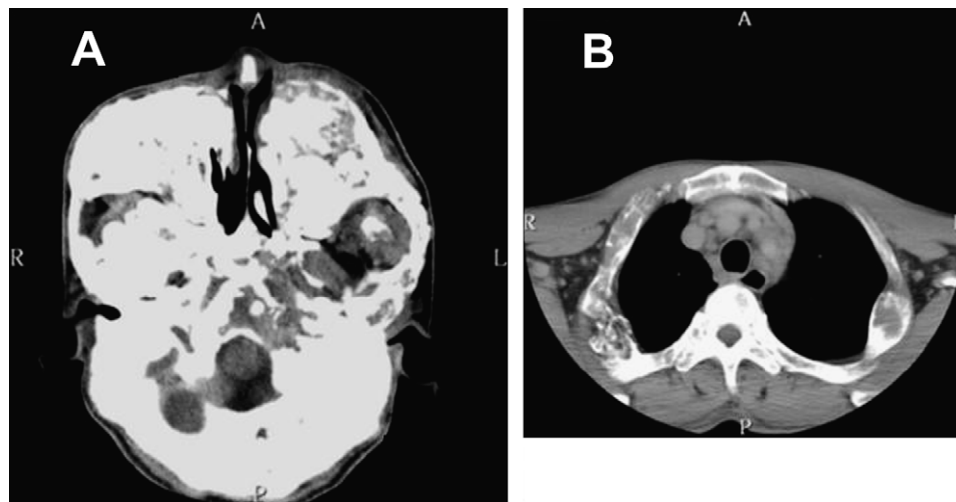


Fig 4. Computed tomography scan demonstrating involvement of the skull (A), the cervical vertebrae, and the first ribs (B).

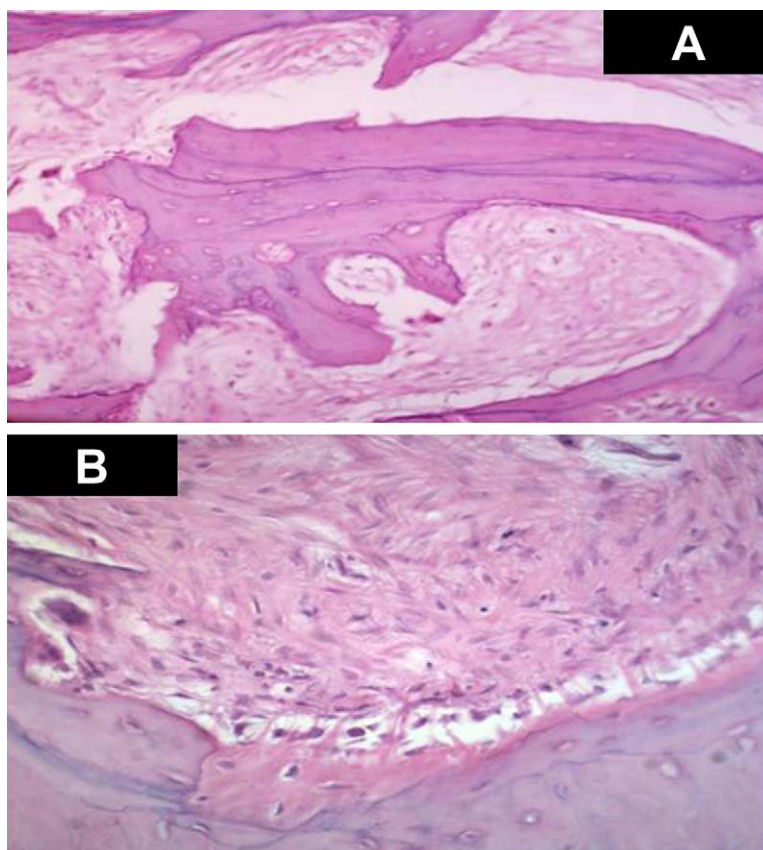


Fig 5. Histology of the decalcified surgical specimens showing irregular, thickened trabeculae with cement lines in a “mosaic” pattern (A) (hematoxylin & eosin stain, original magnification  $\times 100$ ), and increasing osteoclast and osteoblast activities in the same trabeculae (B) (hematoxylin & eosin stain, original magnification  $\times 100$ ).

angle; and deviation of the mandible (Fig 1). Intraoral examination revealed multiple missing teeth and heavy calculus deposition on the remaining teeth. Panoramic radiography revealed a “cotton wool” appearance in both

maxilla and mandible, and severe alveolar bone loss among the remaining teeth (Fig 2). Cephalometric radiography also demonstrated the “cotton wool” appearance in the skull and jaws (Fig 3). Computer tomographic (CT) scan showed bony

**Table I.** Clinical information on Paget’s disease of bone occurring in Chinese patients

Case	Authors and publishing year	Country	Age/Sex	Site(s)	Symptoms and signs	Treatment	Follow-up
1	Khoo, 1955 <sup>37</sup>	Malaysia	57/Male	3rd lumbar vertebral body	No	No	Stabilized, 10 months later
2	Sirikulchayanonta et al, 1991 <sup>38</sup>	Thailand	44/Female	Skull, clavicle, lumbar, and sacrum	Bone pain	Calcitonin	Not available
3	Yip et al, 1996 <sup>39</sup>	Hong Kong	91/Male	Skull, jaw, and tibia	Enlarged skull, broad forehead, wide jaw, and bowed tibia; deafness	No (due to old age of the patient)	Not available
4	Hsu et al, 1998 <sup>40</sup>	Singapore	78/Female	Skull and pelvis	No	Not stated	Not available
5	Hsu et al, 1998 <sup>40</sup>	Singapore	61/Male	Pelvis	Bone pain	Not stated	Not available
6	Hsu et al, 1998 <sup>40</sup>	Singapore	53/Female	Tibia	Bowed tibia	No (patient refused)	Not available
7	Hsu et al, 1998 <sup>40</sup>	Singapore	80/Male	Pelvis, hip, vertebral body, and sacrum	Bone pain and pelvic bone expansion; deafness	Yes, but detailed information was not given	Not available
8	Wang et al, 1999 <sup>41</sup>	Taiwan	66/Female	Tibia	Bone pain	Oral sodium cloronate	Stabilized, 16 months later
9	Wang et al, present study	Taiwan	54/Male	Skull, jaw, ribs, and spine	Enlarged skull, broad forehead, and wide jaw; blurred vision	Surgical treatment for cosmetic purpose	Pathologic fracture of ribs, 6 months later

**Table II.** Comparison between Paget’s disease of bone occurring in Chinese individuals (9 reported cases) in 5 Asian countries and Paget’s disease of bone occurring in Western countries

	Paget’s disease in China	Paget’s disease in Western countries
Sites of involvement	Spine and sacrum (44%), skull (44%), pelvis (33%), tibia (33%), jaw (22%), clavicle (11%), rib (11%), femur (11%)	Pelvis and sacrum (58.3%), spine (36.6%), femur (31.6%), tibia (20%), skull (19%), jaw (17%), <sup>9</sup> rib (4.3%), clavicle (3.8%) <sup>42</sup>
Age	44 to 91, average 64.9	Older than 40 <sup>9</sup>
Gender predilection (Male to Female)	5 to 4	1 to 1, <sup>42</sup> 3 to 1 <sup>4</sup>
Monostotic	44% (4/9)	17%, <sup>6</sup> 17%-31% <sup>7</sup>
Asymptomatic cases	22% (2/9)	67%, <sup>3</sup> 80%, <sup>7</sup> 95% <sup>4,5</sup>
Symptoms and signs in symptomatic patients	Bone pain (33%), deformity (33%), neurological symptoms (33%)	Bone pain, deformity, neurological symptoms
Treatment	Calcitonin, sodium cloronate, surgery	Bisphosphonates, calcitonin, surgery
Familial case reported	No	Yes, <sup>43-45</sup> 14% of the patients <sup>6</sup>
Malignant transformation	No	Yes <sup>24,46</sup>

involvement of the entire skull, cervical vertebrae, and bilateral first ribs (Fig 4). Laboratory tests revealed a markedly elevated serum alkaline phosphatase level (714 IU/L; normal range: 32-92) with otherwise normal liver enzyme levels. The serum calcium was 4.6 mg% (normal range: 4.0-5.5) and the phosphorus level was 3.2 mg/dL (normal range: 2.5-4.6). Due to a previous history of an allergic reaction to medically used radioisotopes, technetium scintigram was not performed. Urine hydroxyproline test was not evaluated. Based on the clinical, radiographic, and laboratory findings, a diagnosis of polyostotic Paget’s disease was rendered and was explained to the patient.

The patient insisted on having only the cosmetic surgery and refused to receive any other therapeutic management for

the treatment of Paget’s disease. Consequently, the patient was treated with surgery of facial bone trimming under general anesthesia. The bony specimens were sent to department of oral pathology for histological examination. Microscopic examination of the decalcified surgical specimens revealed thickened irregular bony trabeculae with prominent basophilic reversal lines in a “mosaic pattern” (Fig 5, A). The marrow spaces were replaced by fibrovascular tissue. Numerous osteoclasts and osteoblasts were found surrounding the irregular bony trabeculae, indicating increased osteoclast and osteoblast activities (Fig 5, B). These microscopic findings were also consistent with Paget’s disease of bones. The patient recovered uneventfully from surgery but a pathological fracture of the first ribs was found 6 months later. The patient

failed to show up for the subsequent appointment and was lost for follow-up since then.

## DISCUSSION

Although it is a relatively common disease in Western countries, the incidence of Paget's disease of bone in the Chinese population is reported very low in epidemiological studies.<sup>3,30,31</sup> To the best of our knowledge, there were only 9 Chinese cases of Paget's disease (including ours) reported in the English literature; 1 each from Malaysia,<sup>37</sup> Thailand,<sup>38</sup> and Hong Kong (cases 1-3)<sup>39</sup>; 2 from Taiwan (cases 8 and 9)<sup>40</sup>; and 4 from Singapore (cases 4-7)<sup>41</sup> (Table I). Because all these cases were reported in the local medical journals of these 5 Asian countries and pathologists worldwide may not be aware of the rarity of Paget's disease in Chinese individuals, the main purpose of this report is to present this rare case in a journal that is accessible to international readers to increase the awareness.

The clinical features of the reported Chinese Paget's disease patients are also summarized and compared to the clinical features of Paget's disease reported in Western countries (Table II).<sup>3-7,24,42-46</sup> The age, gender predilection, symptoms, and treatment in these 9 Chinese cases show similarities to the cases reported in Western countries. The sites of involvement in Chinese Paget's disease patients are also similar to the sites reported in Western countries. However, while the pelvis, spine, and femur are the most frequent affecting sites found in most Western studies,<sup>7,42,47</sup> the skull appears to be one of the most common sites in Chinese patients and is affected more often than the pelvis and femur. Monostotic cases account for almost half of the Chinese Paget's disease patients (cases 1, 5, 6, and 8 in Table I), which is slightly higher than the reported percentages of monostotic cases (17%-31%) in most of the studies in Western countries.<sup>6,7</sup> Most of the Chinese patients are symptomatic, in contrast to the cases reported in Western countries where the majority of the patients are asymptomatic (Table II). Perhaps the symptoms in these patients also play a role in the discovery of these rare cases. All Chinese cases of Paget's disease are sporadic and familial cases have not been reported. Malignant transformation has not been found in Chinese patients to date.

Like the etiology of Paget's disease of bone, the reason for the distinctive distribution of Paget's disease in different ethnic groups and geographic regions is still unclear. Paget's disease is extremely rare in the Chinese population and only 9 cases have been reported in the English literature. We do not have explanations for this phenomenon but speculate that genetic variation in different ethnic groups and/or other environmental

factors may contribute to this observed fact. Investigation on the 7 genetic loci associated with Paget's disease<sup>16</sup> in Chinese patients and the Chinese population perhaps can cast a light on this interesting issue.

## CONCLUSION

We report a rare case of Paget's disease of bone occurring in a 54-year-old Chinese male and compare the clinical features of Paget's disease occurring in Chinese patients to Paget's disease reported in Western countries. No familial cases and no malignant transformation are found in these 9 reported cases of Paget's disease in Chinese individuals. In addition, more often skull involvement and higher frequency of monostotic cases and symptomatic cases are observed in this limited number of Paget's disease cases reported in Chinese patients.

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