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TUMOR INDUCED OSTEOMALACIA : ASSOCIATED WITH GIANT CELL GRANULOMA ON THE GINGIVA

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Thr rickets or osteomalacia, that was induced by nonendocrine osseous or soft tissue tumor, is extremely rare disease and fourteen patients has been reported since 1947. The real nature of this disease is unknown, but postulated that unknown phosphaturic subtance which was elaborated from the tumor affect the renal tubule and produce hypophosphatemia and failure of calcification of osseous tissue. This case presented is that of 41 - year - old man who suffered from severe generalized aching pain, severe muscular dystrophy, and shortening of the stature 4 years prior hospitalization. The causal coexisting tumor is walnut sized peripheral giant cell granuloma on the upper gingiva. After surgical removal of the tumor, patient's biochemical findings of the serum and urine were returned to the normal limits 12 days later, and clinical symptoms were marked relieved at 6 weeks later. The dental radiograms which were obtained 4 months later revealed remarkable bone regeneration and newly formed alveolar lamina dura.

I. INTRODUCTION

The ricketes or osteomalacia is a group of disorders in which there is effective mineralization of the newly formed organic matrix of the skeleton, an its characteristic clinical symptoms are diffuse skeletal pain and tenderness, muscular weakness, and fractures of involved bones. 1).

There are a number of conditions that result in rickets or osteomalacia such as inadequate dietry intake of vitamine - D, intestinal malabsorption of vitamine - B, renal tubular defects which produce hypophosphatemia or acidosis, and chronic administration of anticonvulsants. 1).

The therapeutic approach of this disease is daily supplement of vitamin - D, renal tubular defects which produce hypophosphatemia or acidosis, and chronic administration of anticonvulsants.

The therapeutic approach of this disease is daily supplement of vitamin - D or inorganic calcium or phosphorus supplement was combined. But, in some peculiar cases, the surgical removal of the coexisting osseous or soft tissue tumor can produce systemic curable effect, 2 - 13 and they called tumor induced osteomalacia or rickets.

This case reported is one additional case of tumor induced osteomalacia. The causal coexisting tumor was peripheral giant cell granuloma on the upper gingiva, and there has been no report of such a tumor being found in the gingiva.

II. CASEREPORT

A 41 - year - old male patient was referred from the department of internal medicine in Kyung Hee medical center for evaluaton of tumor mass that occupied buccal side of right upper premolar and molar area on October, 1981. The patient showed severe emaciated state with 148cm tall and 35kg weight and completely confined to the bed.

He complained generalized aching pain, weight loss, and shortening of the stature that were iniciated with lower back pain and gradually severed from 4 years ago. He was finally unable to sit up in bed or to change his position without assistant and 18cm of height and 15kg of weight were diminished in these 4 years.

Physical examination disclosed generalized bony tenderness, muscle spasm, severe motion limitation of extremities, wasting of muscular mass particularly in the legs and arms, marked depression of the right thoracic cage, and little space between the lower rib and iliac crest (fig. 1).

Fig. 1. Photograph shows severe emaciated state and depression of thoracic cage.

Patient received clinical and radiographic examination for some times in other hospital, but no certain diagnosis was obtained, and nonspecific treatment was done except indomethacin 250mg/day for pain relief. Patient's familial history was nonspecific. The intraoral tumor mass was also initiated with gingival enlargement on the right upper premolar area about 4 years ago.

Mouth opening was limited to 2.5cm in height at incisal edge due to pain on the temporomandibular joint area and 2.5cm in height at incisal edge due to pain on the temporomandibular joint area and 2.5 cm by 3cm sized pedunculated reddish white tumor mass occupided on the buccal side of premolar and first molar area (Fig. 2). Generalized tooth mobility was observed and premolar regions are more severe.

Dental radiogram revealed complete loss of alveolar lamina dura, multiple bone destruction on the apical areas which were occlusal load bearing areaes (Fig. 3).

Skeletal radiograms revealed marked decrease of radiographic bone density in skull, cervical spine, hand, and pelvis. In chest P-A view, multiple rib fractures, scoliokyphosis, and vertebral collapse were seen. Fractures with aseptic necrosis of the bone in both hip joints were found and typical Looser's zone and thinned cortex were observed in femur shaft(Fig. 4).

The biochemical examination showed that the hemoglobin concentration, hematocrit, erythrocyte count, total leukocyte and differential count, serum protein, serum glucose, SGOT, SGPT, serum creatinine, chloride, and potassium values were all within

Fig. 2. The tumor mass occupied right upper gingiva.

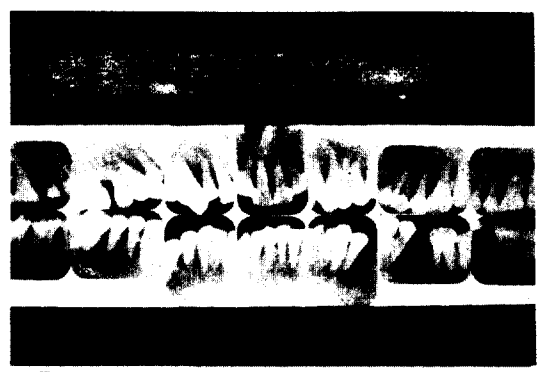

Fig. 3. Full mouth periapical radiograph shows multiple bone destruction and complete loss of alveolar lamina dura.

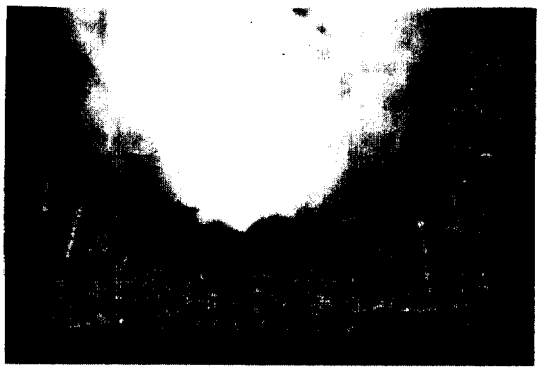

Fig. 4. Pelvic radiograph. Note the aseptic necrosis of femoral heads and Looser's zone

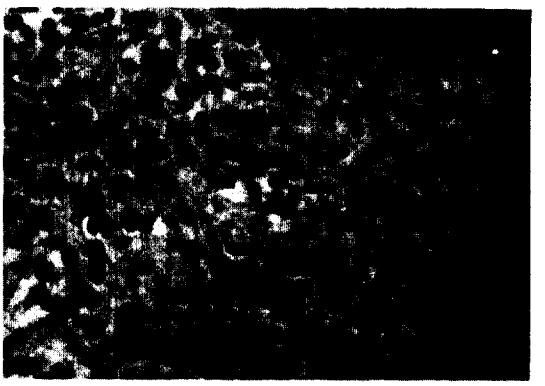

Fig. 5. photomicrograph of gingival tumor demonstrating giant cells in the lesion.

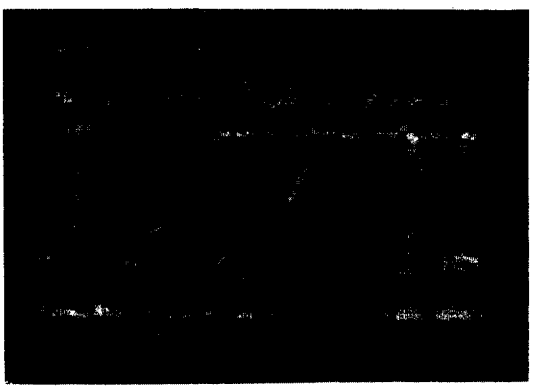

Fig. 6. Polarizing microscopic finding of iliac crest shows lamellated structures of increased osteoid seam.

normal limits. Other biochemical findings showed hypophosphatemia with a serum phosphorus concentration of 1.5mg percent associnated with a normal se-

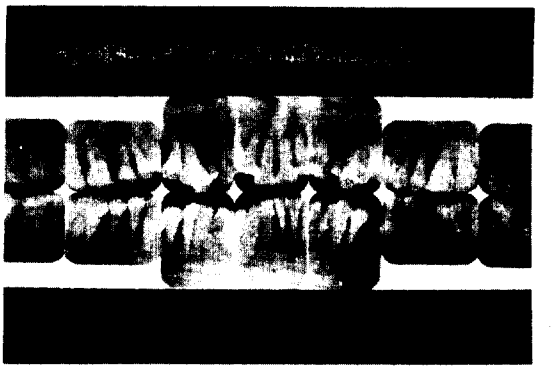

Fig. 7. Periapical radiograph at 4 months after tumor resection. Note the newly formed alveolar lamina dura and new bone formation.

rum calcium concentration of 4.6mEg/liter. The serum alkaline phosphatas level was found to be elevated with 73.7 K-A unit.

The urinary excretion of phosphorus was elevated with 494mg/ 24hours and the tubular resorption of phosphorus was 73 percent.

The pathologic finding of the intraoral tumor mass was typical giant cell granuloma(fig. 5). And the patient was discharged because of this privite problems.

The patient was readmitted at November, 1981. Biochemical findings at that time, normocalcemia(5.0 mEg/liter), hypophosphatemia(2.2mg percent), increased alkaline phosphatase(109.2 K-A unit), and hyperphosphaturia(595mg/ 24hours) were characteristics.

Hyperparathyroidism was ruled out because of normal parathyroid hormone level with 297 picogram /ml. Stool fat(1.37gm/day) and intestinal calcium absor ption level (80 percent) were within normal limits.

The pathologic findings of iliac crest showed typical osteomalacia with marked increase of osteoid seam which surrounded the calcified bone(Fig. 6).

A presumptive diagnosis of acquired adult onset hypophosphatemic osteomalacia was made, and the administration of 0.2-0.4mg of dehydroxytachysterol and 4.0-6.0gm of sodium phosphate per day was started. But, patient's clinical symptoms and bioche-

mical findings were not relieved and the tubular resorption of phosphorus was progressively decreased until 58 percent.

At that time, we considered the causal relationship between intraoral tumor mass and osteomalacia, and the final diagnosis of tumor induced osteomalacia was made.

In view of the diagnosis, the tumor mass was removed surgically, and vitamin-D and phosphorus supplements are discontinued.

Postoperative biochemical findings were dramatically recovered.

Tubular resorption of phosphorus of the first postoperative day was 79 percent, 92 percent at second day, and 93 percent at third day, and serum phosphorus level was increased to 3.0mg percent at third day. One week after removal of the tumor, patient complained dizziness and nausea which were regarded as transient hypercalcemic sign, and it was relieved by water infusion. Biochemical findings at 12 days after removal of the tumor were all within normal limits with serum calcium concentration of 4.7 mEg/liter, serum phosphorus level of 4.3mg percent, alkaline phosphatase level of 53.8 K-A unit, and tubular resorption of phosphorus of 87 percent. Patient was recovered from all suffering clinical symptom at postoperative sixth week, and discharged.

The patient was followed up at 4 months after tumor resection. At that time, the patient can use crutch, and dental radiograms revealed marked bone regeneration and newly formed alveolar lamina dura (Fig. 7).

III. DISCUSSION

Including our patient, fifteen patient with osteomalacia and rickets associated with osseous and soft tissue tumors have been reported since McCance had reported spontaneous recovery from hypophosphatemic rickets in young woman in 1947.

Of these fifteen patients, eleven were adults with osteomalacia, and four were children with rickets. Ten were male and five, female. The duration of symptoms ranged from five months to four years with an average of 2.5 years.

Pathological examination revealed seven bone and eight soft tissue tumors. In these case, different types of tumor cells were found 5 giant cell lesion. 3 mesenchymal tumor, 3 sclerosing hemangioma, and each one case of cavernous hemangioma, hemangiopericytoma, and primary bone tumor. Two tumors were malignant.

Such tumors were found in the osseous tissues of the hip, knee, toe, ankle, and mandible and in the soft tissues of the thigh, ribs, groin, and pharynx.

And in our case, the tumor arised from gingiva.

The characteristic clinical symptoms were prolonged back pain, generalized severe bone and muscle pain, and fractures of the involved bones. And common biochemical findings were normocalcemia, hypophosphatemia, increased serum alkaline phosphatase, and hyperphosphaturia. The main mebtabolic disturbance was extremely low tubular resortption of phosphorus, and hypophosphatemia and failure of bone mineralization were followed.

And myopathy may be a function of an inadequacy of substrate for phosphate dependent contractile system of muscle.

It seems clear that these tumors have an etiological role in the pathogenesis of the clinical syndrome, since their resection can cause its remission.

However the mechanism by which the tumors act remains obscure.

Salassa and his associates and Pollack and his associates described that the peptide hormone like substance which was elaborated from tumors increase the renal clearance of phosphorus. Then Evans, Olefsxy, and Linvovitz and their associates described the tumors may be elaborate vitamin-D antagonist.

In our case, the main disorder was extremely low tubular resorption of phosphorus and it was immediately corrected after tumor resection. This phenomenon aupport the hypothesis that unknown phosphatu-

ric substance which was elaborated from tumor affect to renal tubule directly.

In the treatment of tumor induced osteomalacia, various modalities of therapy including administration of vitamin-D and phosphates produce inconsistant clinical responses. Some patients responded to those drugs but pathologic abnormalities with hypercalcemia followed in some case. In our patient, vitamin-D and phosphate supplement was given, but we could not observe improvement in biochemical findings or symptom relief.

And postoperative healing process was uneventful in spite of discontinuance of these drug.

One should be aware of the presence of coexisting osseous or soft tissue tumor in acquired vitamin-D resistant osteomalacia or rickets, and when the causal relationship will be persumed surgical resection of the tumors may be essential way of treatment.

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국문초록

치은부에 발생한 거대세포육아종에 의한 골연화증

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김여갑 · 류동목 · 이상철

비내분비성 골종양이나 연조직종양에서 유래되는 구루병이나 골연화증은 매우 드문질환으로 1947년 이래로 14명의 환자만이 보고되고 있다.

이 질환의 본태는 아직 밝혀지지 않았으나 종양에서 생성하는 인산염뇨유발성 물질이 신세뇨관에 영향을 주고 저인산염혈증을 일으키며 골조직의 석회화에 장애를 일으키는 것으로 생각된다.

본 증례의 환자는 약 4년 전부터 지속된 심한 전신동통과 근육위축, 현저한 신장의 감소를 주소로 내원한 41세 남자로 상악우측 치은부의 종양에 의한 전신적 골연화증의 진단하에 종양의 외과적적출을 시행하였으며 술후 환자의 혈청과 뇨의 생화학적결과는 12일 후에 정상으로 회복되었고 임상증상은 수술후 6주에 회복되었으며 4달후에 촬영한 치과 방사선상 놀랄만한 골재생과 새로 형성된 치조백선의 형성이 관찰되었다. 적출된 종물은 거대세포육아종의 조직소견을 보였으며 종물의 적출에 의하여 골연화증의 치유소견이 관찰 되었기에 종양에 의한 골연화증의 희유한 증례로 사료되어 이에 보고하는 바이다.