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# Adefovir Dipivoxil-induced Osteomalacia: A Rare Case of Misdiagnosis due to Concurrent Thyroid Tumor

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**Abstract: Background:** Both the administration of adefovir dipivoxil and the elevation of primary parathyroid hormone can result in serum electrolyte abnormalities and the development of metabolic bone disease. Adefovir dipivoxil-induced osteomalacia is a clinical disease that is rarely seen and often leads to misdiagnosis. **Case presentation:** In this case, the patient developed osteomalacia due to renal tubular toxicity caused by chronic use of adefovir dipivoxil. The drug indirectly affected the secretion of parathyroid hormone (PTH). Coincidentally, the patient also had a tumor below the thyroid, leading to a misdiagnosis. **Conclusion:** Osteomalacia caused by adefovir dipivoxil is a clinically rare disease, and it is important not to overlook it as it may lead to misdiagnosis. Hence, in cases where laboratory tests reveal abnormal parathyroid hormone levels, it is crucial to inquire about the patient's detailed medication history. This is applicable even in situations where there is evidence suggesting primary hyperparathyroidism.

**Keywords:** Adefovir dipivoxil; Hyperparathyroidism; Osteomalacia; Case report

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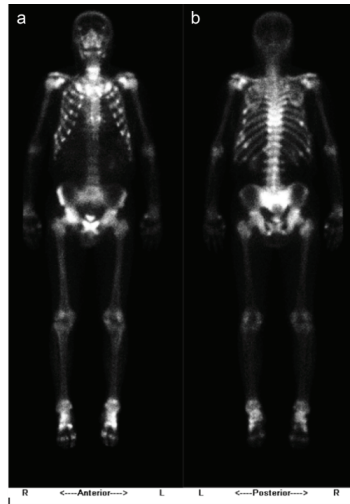
## 1. Introduction

Adefovir dipivoxil (ADV) is a nucleotide-like inhibitor used clinically to inhibit various viruses, including hepatitis B virus (HBV) and human immunodeficiency virus (HIV)<sup>[1]</sup>. Recent studies have shown that ADV can cause proximal renal tubular injury and reabsorption dysfunction, resulting in decreased blood phosphorus and secondary metabolic bone disease<sup>[2-4]</sup>. Parathyroid hormone (PTH) is a single-stranded polypeptide hormone secreted by the main cells of parathyroid glands. PTH primarily acts on the bone lattice and kidney, regulating calcium and phosphorus metabolism<sup>[5]</sup>. It promotes the renal tubular excretion of phosphate, leading to increased blood calcium levels and decreased blood phosphorus levels. PTH secretion is mainly regulated by plasma calcium concentration; when the concentration decreases, PTH secretion increases<sup>[6]</sup>. Whether due to long-term use of ADV or excessive PTH secretion, the ultimate effect is the disruption of calcium and phosphorus metabolism, resulting in elevated blood calcium and phosphorus levels and eventually leading to bone metabolism abnormalities and metabolic bone disease<sup>[7]</sup>. In this case, we report a patient who developed metabolic bone disease due to long-term use of adefovir dipivoxil. Coincidentally, the patient also had a nodule in the lower right pole of the thyroid gland, leading to a misdiagnosis of osteomalacia caused by parathyroid adenoma.

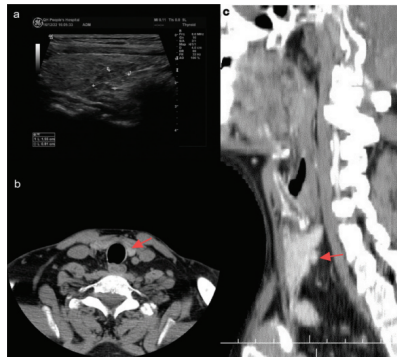
## 2. Case presentation

A 69-year-old male presents with bilateral knee, bilateral hip, and sacral pain persisting for 2 years. Physical examination reveals multiple areas of tenderness in both lower limbs. Laboratory examinations show parathyroid hormone levels at 81.2 pg/ml, blood phosphorus at 0.47 mmol/L, and blood calcium at 2.14 mmol/L. Imaging examinations, including whole body bone imaging, reveal multiple abnormalities in the ribs, sacroiliac joints, bilateral hip joints, and ankle joints (Figure 1). Thyroid CT and B ultrasound show the presence of nodules below the thyroid gland in the right lobe (Figure 2).

The patient was initially misdiagnosed with hyperparathyroidism caused by parathyroid adenoma, secondary to metabolic bone disease. Treatment involved a lower right inferior parathyroidectomy, with postoperative pathological findings indicating the presence of fat, posterior wall vessels, and a small amount of thyroid tissue.



**Figure 1: The whole body bone imaging showed multiple ribs, sacroiliac joint, bilateral hip joint and ankle joint.**

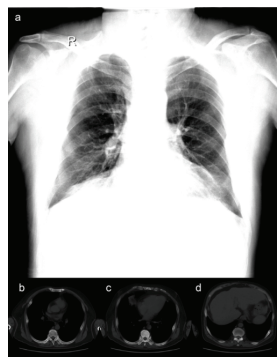


**Figure 2: thyroid CT and B-ultrasound showed that nodules were seen in the outer and inferior thyroid of the right lobe.**

**OUTCOME AND FOLLOW-UP:** One week after the operation, the patient's parathyroid hormone levels were measured at 83.1 pg/ml. Moreover, after six months, the patient's systemic bone pain worsened, leading to difficulty in walking and requiring further treatment. Upon reviewing the medical history, it was discovered that the patient had been taking ADV in a long-term small dose.

History of present illness: The patient has been carrying the Hepatitis B virus for 8 years but has been undergoing regular physical examinations with good virus control.

**FINAL DIAGNOSIS:** Based on the analysis of the medical history and laboratory examination results, the final diagnosis was ADV-related osteomalacia, impaired renal function, and secondary hyperparathyroidism. The patient was advised to discontinue ADV and switch to entecavir (1 tablet/day orally), along with oral potassium citrate, calcium supplements, and Calcitriol. Symptomatic treatment included zolhosphoric acid. After six months of the prescribed treatment, the patient experienced a gradual decrease in self-perceived bone pain, with fractures healing (Figure 3). The patient regained the ability to live a normal life, and subsequent reexamination of blood calcium, phosphorus, renal function, and other indicators showed a gradual return to normal levels (Figure 4).



**Figure 3: The X ray and CT showed fracture healed.**

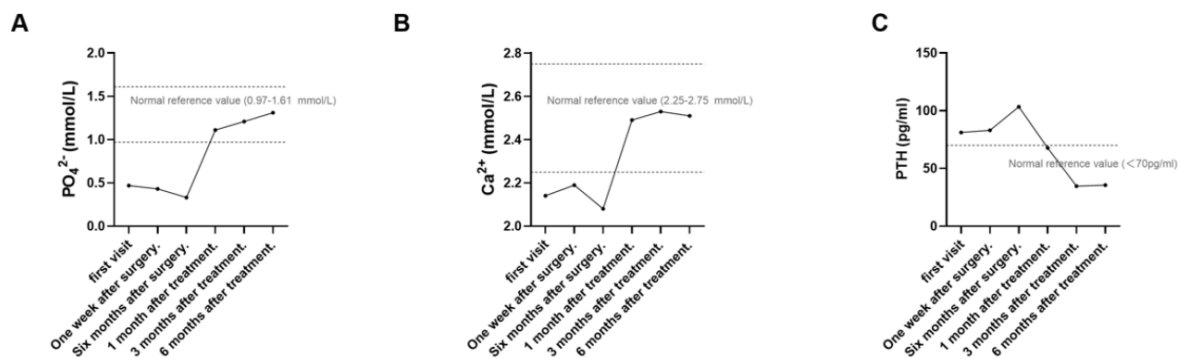


Figure 4: The results of laboratory examination showed that all related blood indexes returned to normal.

### 3. Discussion

Metabolic bone disease caused by ADV is a rare condition in clinical practice, and the patient's medical history plays a crucial role in its diagnosis. This disease is characterized by symptoms such as bone pain and abnormal levels of calcium, phosphorus, and parathyroid hormone in laboratory tests. Thyroid nodules are a common occurrence and can be found in any part of the thyroid gland. It can be challenging to differentiate these nodules from parathyroid adenomas located near the parathyroid gland. Therefore, when considering the clinical diagnosis of metabolic bone disease, it is important to thoroughly inquire about the patient's history of medication use, even if there is evidence of primary hyperparathyroidism, in order to avoid misdiagnosis.

### 4. Conclusion

In conclusion, while Osteomalacia induced by adefovir dipivoxil is uncommon in clinical practice, it is crucial to inquire about the patient's medication history when diagnosing metabolic bone diseases. This is especially important to prevent misdiagnosis, even in cases where primary hyperparathyroidism is suspected.

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