Case Report

Osteomalacia Induced by Adefovir in Patient With Hepatitis B

Mayra Nathali Rivas Zavaleta,* Sonia Guayambuco Romero, Marcelo Calabozo Raluy, Fernando Pérez Ruiz

Servicio de Reumatología, Hospital Cruces, Barakaldo, Vizcaya, Spain

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A B S T R A C T

Osteomalacia is defined as a defect in mineralization of the bone matrix. We describe the case of a patient
with chronic hepatitis B infection in whom treatment with adefovir induced renal phosphate loss with
intense and sustained hypophosphatemia which derived in symptomatic osteomalacia.

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Osteomalacia inducida por adefovir en paciente con hepatitis B

R E S U M E N

La osteomalacia se define como un defecto en la mineralización de la matriz ósea. Describimos el caso
de un paciente con infección crónica por virus de la hepatitis B en el que el tratamiento con adefovir
indujo una pérdida renal de fosfato con hipofosfatemia intensa y mantenida que derivó en osteomalacia
sintomática.

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Introduction

Adefovir is an antiretroviral drug used for the treatment of patients with chronic infection with hepatitis B. Among its adverse
effects one finds nephrotoxicity, although this usually occurs when high doses (60–120 mg/day) are employed.1 The currently recom-
ended dose is approximately 10 mg/day PO, which minimizes the risk of nephrotoxicity in patients without a history of renal
disease.2–4 The case presented is that of a patient treated with adefovir at a dose of 10 mg/day which caused abnormalities in the prox-
imal renal tubule, leading to5–9 hypophosphatemic osteomalacia.

Case Presentation

The patient was an 81 year old male with a single kidney, with chronic hepatitis B treated with adefovir for four years

approximately at a dose of 10 mg/day. The patient had poor over-
all condition, fatigue, weakness, bone pain, muscle atrophy and
weight loss which had lasted for a year. He had elevated alkaline
phosphatase (386 U/l; normal <140 U/l) and a bone scan showed
multiple pathological uptake areas (Fig. 1). With the presumptive
diagnosis of Paget’s disease, treatment was begun with bisphos-
phonates (etidronate 30 mg/day for 2 months), calcium and vitamin
D, with no clinical improvement, so the patient was referred to
the Rheumatology department. Laboratory results showed elev-
ated alkaline phosphatase (329 U/l), hypoproteinemia (5.5 g/dl),
 hypoalbuminemia (3.3 g/dl), hypouricemia (1.5 mg/dl) with a frac-
tional excretion of urate of 50% and hypophosphatemia (1.2 mg/dl)
with tubular reabsorption of phosphate 9% (normal >80%). PTH lev-
els were normal as was 25-hydroxycholecalciferol. Regarding renal
function, creatinine was 1.13 mg/dl and the estimated glomeru-
lar filtration rate was 53 ml/min. The patient had proteinuria
(1178 mg/day) and glucosuria (>100 mg/day). A chest X-ray showed
rib fractures on both sides and bone scintigraphy showed multiple
foci of uptake in the ribs, right sacrum, knees and right tibia.

A historical review of the analysis showed that the onset of
disturbances, in particular decreasing phosphate levels, coincided
with the beginning of the administration of adefovir (4 years

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* Corresponding author.
E-mail address: nathali_r17@hotmail.com (M.N. Rivas Zavaleta).

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prior). Adefovir was discontinued and the patient was treated with intravenous phosphate, presenting an increase in phosphate values to 4.1 mg/dl. He was discharged with oral phosphate at a dose of 7 g/day. In the next 6 months, there was a clear, albeit slow, clinical improvement.

Discussion

In the case presented, laboratory abnormalities coincided with the start of the administration of adefovir and were associated with an improvement in phosphate values after drug withdrawal. Adefovir is associated with nephrotoxic effects, which are dose-dependent, leading to dysfunction of the proximal renal tubule and glomerular filtration rate. The lowering effect of the plasma phosphate levels of adefovir has been observed in 22%–50% of patients treated with doses of 30 mg/day for at least 6 months and manifests itself as a progressive increase in serum creatinine, hypophosphatemia or both. While use of 10 mg/day orally is not associated with significant renal dysfunction, in this case a low dose caused a decrease in tubular phosphate reabsorption and resulted in hypophosphatemia, leading to clinically manifested osteomalacia and bone pain, functional impairment and generalized muscle pain.

Predisposing factors were the presence of a single kidney, and a moderately low glomerular filtration rate which contributed to a greater impact of the drug on renal function, as seen in previous cases.

The pathophysiology of renal proximal tubule dysfunction caused by adefovir is due to its concentration in the mitochondria, resulting in mitochondrial toxicity and inhibition of ATP-dependent transporters in proximal tubule cells, leading to altered phosphate reabsorption, decreasing its concentration in plasma and ultimately leading to osteomalacia.

In conclusion, although low doses of adefovir are not usually associated with renal toxicity and hypophosphatemia due to renal phosphate loss, the comorbid conditions present in this case led to a situation of increased susceptibility.

Ethical Responsibilities

Protection of people and animals. The authors state that no experiments were performed on humans or animals.

Data confidentiality. The authors declare that they have followed the protocols of their workplace regarding the publication of data from patients and all patients included in the study have received sufficient information and gave their written informed consent to participate in this study.

Right to privacy and informed consent. The authors state that no patient data appears in this article.

Conflict of Interest

The authors have no conflict of interest to declare.

References