



# Neurological Face of the Paget's Disease of Bone: A Case Report and Literature Review

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## Abstract

This is a case of Paget's Disease of Bone (PDB) with a quick, progressive clinical course, initially presented with neurological symptoms which is rare in previously presented literature. Also, it occurred in a region unusual for PDB. This diagnosis should be considered in the clinical states of an unusual neurological presentation such as the one presented here.

**Keywords:** Paget's Disease of Bone (PDB); Neurological symptoms; Bone turnover; Alkaline phosphatase; Bisphosphonates

## Introduction

The second-most common metabolic disorder of the bone, after osteoporosis, is Paget's Disease of Bone (PDB), also known as osteitis deformans. A defect in osteoclasts causes greater bone destruction, which in turn prompts osteoblastic new bone production. Because the natural balance between the two processes is impaired, this condition is characterized by an unorganized bone turnover [1]. As pagetic bone is more vascular, less compact, and enlarged, it is more prone to deformities and fractures. Bone or joint pain, fractures, bone abnormalities and enlargement, and even malignant transformation are common symptoms and manifestations [2]. Elevated serum alkaline phosphatase, distinctive radiographic features, and bone nuclear scintigraphy are used to diagnose it [1].

There are monostotic and polyostotic forms of PDB, with the former being the more prevalent [3]. Typically, PDB appears in people who are middle-aged or older. According to post-mortem and radiographic investigations, the prevalence of PDB is 3% to 3.7% worldwide [4-6]. Great Britain, Australia, New Zealand, North America, and Western Europe have the greatest prevalence rates [7,8].

## Case Presentation

A 67-year-old female was admitted to our clinic due to double vision, bilateral deafness and progressive skull deformation. She stated that double vision had been present for one month. In that period, her hearing became progressively worse. From family medical history, we found that her father suffered from Parkinson's disease and brother is suffering from bilateral deafness. Her mother had polydactyly.

Physical examination showed craniomegaly with diffuse alopecia (Figure 1a, 1b). Neurological examination showed sixth cranial nerve palsy on the right, hypoacusis on both sides and waddling



Figure 1a and 1b: Craniomegaly with diffuse alopecia.

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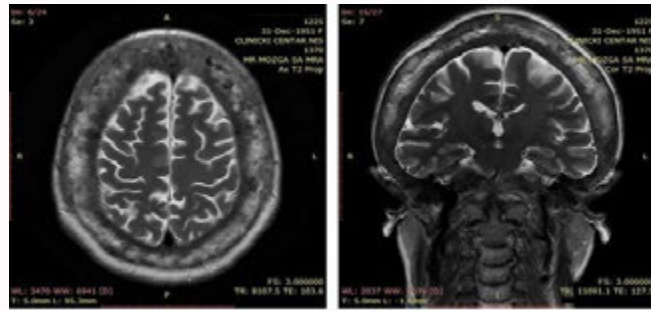


Figure 2a and 2b: MR of endocranium - axial section (a), and coronal section (b).

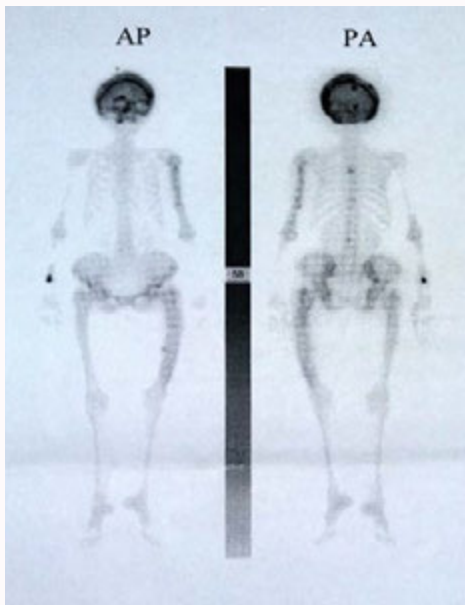


Figure 3: Bone scintigraphy with 99mTc-DPD.

elevation of alpha 2 fraction (13.4%, Normal range 7% to 11%). Magnetic Resonance (MR) of endocranium showed diffuse thickening of calvarial bones and skull base, with pons compression by thickened clivus and suspect compression of sixth cranial nerve (Figure 2a-2c). Direct X-ray of pelvis showed an osteosclerosis of pelvic bones and proximal halves of both femurs. Skull deformities, deafness, radiology findings and increase in the serum alkaline phosphatase were sufficient for the diagnosis of PDB. Serum parathyroid hormone level was more than twice times higher than upper limit of the reference range (132.1 pg/mL, normal range 10 to 65 pg/mL), while Vitamin D was lower (3.4, normal range >30 ng/mL). Specific marker of bone resorption, serum beta – Cross Laps was 2.3 pg/mL (normal range 50 to 450 pg/mL). Treatment was commenced with a single intravenous infusion of 5 mg zoledronic acid associated with oral calcium intake.

After being discharged from the hospital treatment, her symptoms worsened within a month. There was a ptosis of the right eyelid, paresthesia of the right half of the face and mild to occasionally severe headache. The neurological examination also showed total ophthalmoplegia on the right side with mydriasis. She was admitted to our clinic for the second time. Serum alkaline phosphatase was fifteen times higher than the upper limit value (1930 U/L), while serum phosphorus and calcium were normal. Repeated MR imaging did not show a significant difference concerning the previous finding. Ill-defined lucent and sclerotic areas, as well as thickening of the calvarium, were presented on skull X-ray. Bone scintigraphy with <sup>99m</sup>Tc-DPD demonstrated increased diffuse uptake in the calvarial, parietal and supraorbital parts of the frontal bone (Figure 3). The patient was treated with symptomatic therapy.

Further, in the next month due to a neurologic worsening patient was admitted again to our clinic. Neurological findings showed the existence of previous, residual findings with the appearance of a left-side pyramidal deficiency. The serum alkaline phosphatase was 2059 U/L. Computerized Tomography (CT) of the endocranium showed

manner of walking.

Laboratory reports revealed progressive increase in the serum alkaline phosphatase (1120 U/L, Normal range 30 to 120 U/L), lactate dehydrogenase (455 U/L, Normal range 100 to 190 U/L), while serum calcium and phosphorus were normal. Urine calcium concentration in a 24 h sample was decreased, while concentration of urine phosphorus was normal.

Since that Multiple myeloma and PDB show certain similarities such as increased osteoclastic activity and bone resorption, serum protein electrophoresis was performed, which showed moderate



Figure 4a and 4b: Computerized Tomography (CT) of endocranium.

diffuse lytic bone lesions and multiple neoplasm-like structures that infiltrate brain parenchyma (Figure 4). The symptomatic therapy was applied.

## Discussion

PDB is common in the Caucasian population [9]. Based on the available literature, PDB appears to be rare in the Balkans and Serbia. The usual course of PDB has three phases [10]. The first phase is osteolytic, the second is mixed osteoblastic/osteolytic, where the mineralization of new bone matrix is ineffective, and the third phase is sclerotic [10]. At the time of first admission, our patient was in the second phase with dominantly osteoblastic hyperplasia, according to the magnetic resonance, direct X-ray and bone scintigraphy. Common initial symptoms of the disease include bone pain, bone deformities, symptoms of fractures, decreased hearing and headache [1]. Our patient was admitted to our clinic because of undefined diplopia in the first line. Although neurologic symptoms are uncommon, their appearance is possible during the evolution (exacerbation) of the disease [11]. However, according to the literature, the disease has been rarely previously reported to initially manifest with neurological presentation as well as diplopia. Diagnosis is based on characteristic radiographic findings and by nuclear scintigraphy of the bone [1]. Magnetic Resonance (MR) of the endocranium showed diffuse thickening of calvarial bones and skull base, and compression of the sixth cranial nerve, which could be the reason for six nerve palsy. Bone scintigraphy demonstrated increased diffuse uptake in the calvarial, parietal and supraorbital parts of the frontal bone, as a confirmation of the finding of the skull X-ray. Scintigraphy has an important role in the diagnosis of PDB because of its high sensitivity for the detection of increased osteoblastic activity [13]. The biochemical markers of this disease are numerous, but one of the most commonly used is serum alkaline phosphatase, which reflects osteoblast activity [1]. Our patient showed high serum alkaline phosphatase levels at the time of admission to our clinic, while serum calcium and phosphorus were normal. The alkaline phosphatase can also be considered to be a sensitive marker for the therapeutic monitoring of PDB [9]. Urinary calcium is an indicator of bone resorption [9]. The concentration of calcium in a 24-h sample of urine was decreased, which also confirms the second stage of the disease.

Remedies of choice for the treatment of this disease are bisphosphonates, which reduce osteoclast-induced resorption and osteoclastic maturation [13]. Furthermore, bisphosphonates achieve a rapid reduction in bone turnover in PDB by inhibiting osteoclast resorption [14]. The treatment started with a single intravenous infusion of 5 mg zoledronic acid associated with oral calcium. Patients should be followed by measuring bone markers every three to six months depending on the activity of the pagetic lesions and the

drug used [15]. However, in our patient, the applied therapy has led to favors of osteoblastic activity which can be the cause of expansive changes of the calvarial bone that exert pressure on the brain tissue on this way leading to neurological worsening (Figure 4).

This is a case of PDB with a quick, progressive clinical course, initially presented with neurological symptoms, which is rare in previously presented literature. Also, it occurred in a region unusual for PDB. This diagnosis should be considered in the clinical states of an unusual neurological presentation such as this one presented here.

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