diagnosis of PCD. The average age of verification of this disease is an important indicator of the effectiveness of the healthcare system in detecting a rare pathology in children [1,6]. Thus, according to A.A. Novak (Moscow, 2024), the average age of verification of the disease in the Russian Federation is 5.8 years, in the Australian cohort of patients, the diagnosis is established at the age of 6.4 years, in China-8.2 years, and in South Korea-11.8 years [3,13,7,8].

Due to the relatively low frequency of the KS, the variety of phenotypes, the lack of screening, low awareness and alertness of doctors, the diagnosis of PCD is often postponed for years, which significantly reduces the quality of life of such patients [12]. According to the clinical recommendations of the Russian Federation, as well as the diagnostic recommendations of the European respiratory and American thoracic societies, patients with constant productive coughing, the anomalies of the location of the internal organs and congenital heart defects are subject to an additional comprehensive examination using high -tech diagnostic tests for the verification of PCD [10,9].

In the case presented from the first days of life, the child was diagnosed with dectrocardia, incomplete intestinal rotation and ring-shaped pancreas. From the age of 1.5, the child is regularly observed in medical institutions with repeated inflammatory diseases of the upper and lower respiratory tract, and periodically undergoes for diseases of the urinary system. From the age of 8, chronic bronchitis was diagnosed. This child, despite the frequency of outpatient visits and inpatient hospitalizations, was not comprehensively examined, and did not take into account the dispensary accounting for chronic bronchitis.

Conclusion. The presented clinical case clearly demonstrates the problems of the differential diagnosis of the KS. An increase in the awareness of doctors about this disease can help in quick diagnosis, timely treatment and improve the quality of life of such patients.

The authors declare no conflict of interest.

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A FAMILY CLINICAL CASE OF COMBINATION OF TWO MENDELIAL DISEASES: SPINOCEREBELLAR ATAXIA TYPE 1 AND HYPOPHOSPHATEMIC RICKETIS

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The combination of two genetic syndromes in a single patient is a rare occurrence. This article describes a clinical case of a rare combination of two Mendelian diseases: spinocerebellar ataxia type 1 and hypophosphatemic rickets in a single Yakut family. Given the low incidence of both diseases, this finding is of scientific and practical interest. The paper discusses a clinical observation of family members examined in 2012 and 2025. This clinical example is also relevant for practicing physicians. It is necessary to develop algorithms for monitoring complications of spinocerebellar ataxia and phosphate diabetes and to identify pathogenetic therapy.

Keywords: spinocerebellar ataxia type 1, hypophosphatemic rickets, bone deformity, phosphate diabetes, family case.

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Introduction. Spinocerebellar ataxia type 1 (SCA1) is a heterogeneous neurodegenerative disorder with an autosomal dominant inheritance pattern, characterized by progressive cerebellar ataxia, dysarthria, and gradual deterioration of bulbar function [5]. In the early stages of the disease, patients may experience gait disturbances, slurred speech, balance problems, brisk deep tendon reflexes, hypermetric saccades, nystagmus, and mild dysphagia. Later symptoms include slowing of saccade velocity, development of upward gaze palsy, dysmetria, dysdiadochokinesia, and hypotonia. In late stages, muscle atrophy, decreased deep tendon reflexes, loss of proprioception, cognitive impairment (e.g., frontal dysfunction, verbal memory impairment), chorea, dystonia, and bulbar dysfunction are observed [3, 7]. The disease typically presents between the ages of 30 and 40 years, although cases have been reported in childhood and the elderly. Patients whose disease onset is after 60 years may have a purely cerebellar phenotype. The interval from disease onset to death ranges from 10 to 30 years; patients with juvenile onset have more rapid progression and a more severe course of the disease. Axonal sensory neuropathy, detected by electrophysiological testing, is common; brain imaging typically shows cerebellar and brainstem atrophy [3, 8].

Hypophosphatemic rickets (phosphate diabetes) is a hereditary tubulopathy with a defect in phosphate reabsorption in the proximal tubules and high resistance to normal doses of vitamin D, resulting in hyperphosphaturia, hypophosphatemia, and clinical features of rickets [6]. The relevance of studying phosphate diabetes is associated with many unresolved issues in patients suffering from this pathology. Issues of diagnosis, drug therapy, dispensary observation, and rehabilitation of patients with complications remain open [2]. Late diagnosis of hypophosphatemic rickets is associated with a great similarity of the clinical features with other genetically determined metabolic disorders and diseases of mineral-bone metabolism [1]. A small number of publications with clinical examples of phosphate diabetes in recent years also leads to late detection of this pathology in clinical practice [4].

Materials and methods. Family V., a member of the Yakut ethnic group living in a rural area, was studied. An increase in the number of trinucleotide (CAG) repeats up to 42 in one of the alleles of the 6p21.3 locus in the ataxin-1 (*ATXN1*) gene and a deletion of exon 15 of the PHEX gene were detected.

Research methods:

1. Molecular genetic testing to determine mutations in the ataxin-1 *(ATXN1*) and PHEX genes;
2. Montreal Cognitive Assessment (MoCA);
3. Hospital Anxiety and Depression Scale (HADS);
4. Morse Falls Risk Scale;
5. Hendrick Fall Risk Model II;
6. Scale for the Assessment and Rating of Ataxia (SARA);
7. Magnetic resonance imaging;
8. Spirometry;
9. Radiography;
10. Biochemical research methods.

Clinical observation. Patient V., 43, was admitted to the neurology department of the Center for Neurodegenerative Diseases (CND) of the Yakut Scientific Center for Complex Medical Problems (YSC CMP) in 2025. Complaints upon admission included unsteadiness and instability when walking, deterioration of handwriting, slurred speech, occasional choking on solid and liquid food, stiffness and weakness in the legs (which suddenly become "wobbly"), general weakness, increased fatigue, and occasional loose stools.

Medical History and Past Medical History: Patient V. was born the third of four children. The author identified the patient in 2012 as part of a mobile team in the Lensky District, in the village of Tolon. Examination revealed short stature (127 cm), varus deformity of the femoral shafts (more on the left), and shortened lower limbs. Since she began walking independently as a child, she developed leg deformities, which required repeated surgical treatment from 1987 to 2004. She was diagnosed with chondrodysplasia and has been disabled since childhood.

The patient has two sons, both of whom have short stature, rickets-like skeletal changes, knee and ankle deformities, and varus deformities of the lower extremities.

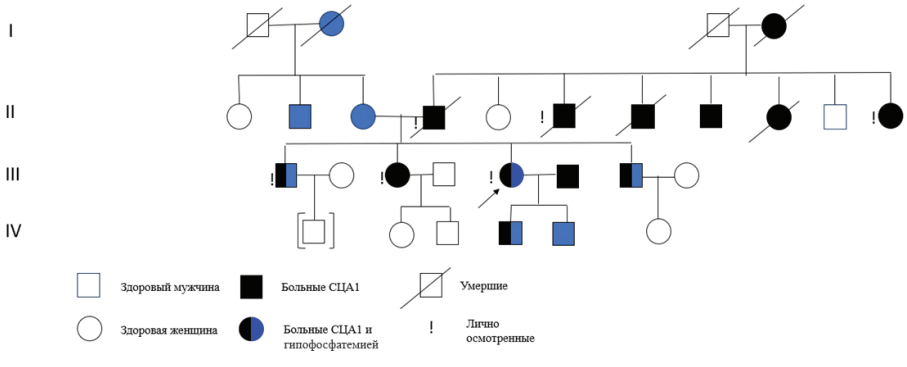

Fig 1. Pedigree of proband V

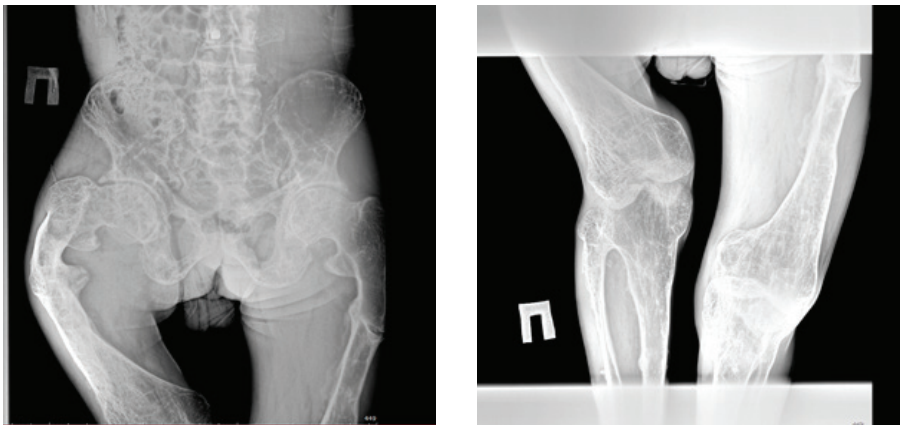

Fig. 2. X-ray of proband V's sibling

The diagnosis of phosphate diabetes was confirmed in both sons using molecular genetic testing. A heterozygous mutation—a deletion of exon 15 of the PHEX gene—was also detected in the mother and her siblings.

In 2015, following a referral from the Medical Genetic Center of the Republican Hospital No. 1 - National Center of Medicine, she was hospitalized for the first time at the FSBI "NMRC of Endocrinology" of the Ministry of Health of Russia, where she was diagnosed with E83.3 X-linked dominant hypophosphatemic rickets. Deletion of exon 15 of the PHEX gene. Bow-shaped deformity of the lower extremities (post-surgical correction). Osteoarthritis of the left and right knee joints. Somatic short stature. Secondary hyperparathyroidism. Decreased BMD. Vitamin D deficiency.

The diagnosis of phosphate diabetes was confirmed in both sons by molecular genetic testing. A heterozygous mutation—a deletion of exon 15 of the PHEX gene—was also detected in the mother and her siblings.

In 2012, patient V. underwent DNA testing at the molecular genetics laboratory of the Medical Genetics Center of Republican Hospital No. 1, which revealed an increase in the number of trinucleotide (CAG) repeats to 42 in one allele of the 6p21.3 locus in the ataxin-1 (*ATXN1*) gene. She had no symptoms of SCA type 1 at the time of testing.

Family history of hypophosphatemic rickets and spinocerebellar ataxia type 1. Figure 1 shows the pedigree of patient V. for both conditions. She has a strong maternal family history of phosphate diabetes. The proband was born the third of four children. All four suffer from this hereditary disorder. A genealogical study of the proband revealed that three of the four siblings suffer from these two hereditary disorders: the proband and two brothers (Fig. 3). The older sister was diagnosed with only type 1 spinocerebellar ataxia; no heterozygous mutation (deletion of exon 15 of the PHEX gene) was detected. The remaining three children were found to have two concurrent mutations in the genes that cause hypophosphatemic rickets and type 1 spinocerebellar ataxia.

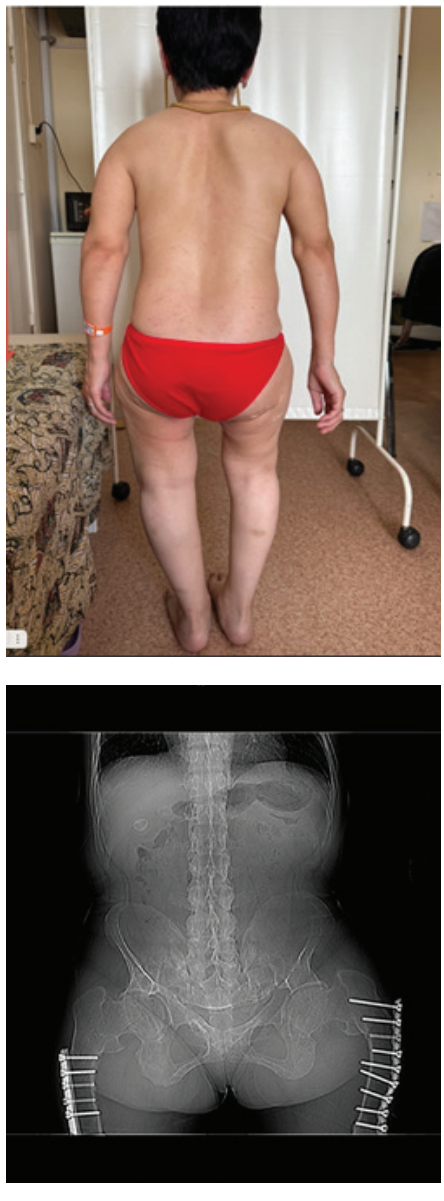

Fig. 3. Patient B. Typical changes in the skeleton and lower extremities in hypophosphatemic rickets

A family history of spinocerebellar ataxia type 1 was identified on the paternal side. The father, at age 42, developed unsteadiness when walking and speech impairment. He was bedridden for the last five years due to unsteadiness and died at age 67 from aspiration pneumonia. According to his daughter, molecular genetic testing was performed on the father, which revealed a mutation in the ATXN1 gene with a repeat count of 32/48. The father's mother had the disease and died at age 55. She had the disease for 15 years, walking with assistance due to unsteadiness. The father was the eldest child. Of the father's eight siblings, two currently have spinocerebellar ataxia type 1, and four have died from spinocerebellar ataxia type 1.

During examination and assessment of the neurological status, the following was revealed: short stature - 120 cm, with varus deformity of the lower limbs, shortening of the right lower limb by 1.5-2.0 cm, weight 40 kg (Fig. 2). Consciousness is clear, orientation in space and time, in one's own personality is not impaired. CN: sense of smell is not impaired, pupils D = S, photoreaction is brisk, no limitation of the visual fields was revealed by the control-comparative method, double vision does not bother. Eye movements are full. Convergence is insufficient. Trigeminal points are painless upon pal-

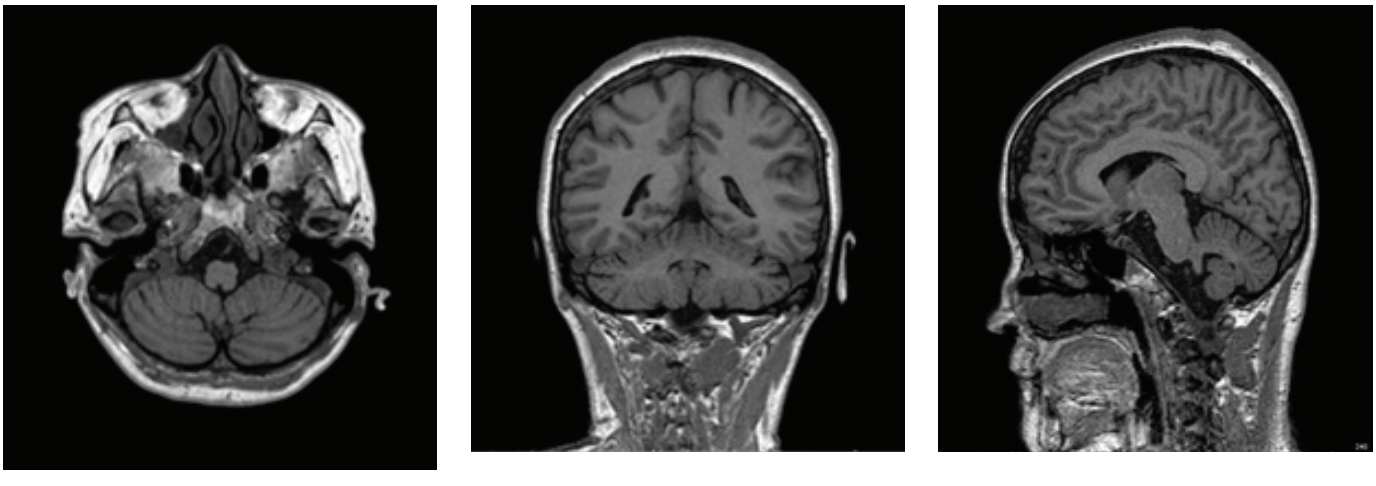

Fig. 4. MRI picture of isolated cerebellar atrophy

pation, sensitivity on the face is normal. Asymmetry of the nasolabial folds is mild - smoothed on the left. Tongue slight deviation to the right, uvula is mobile, to the right. Speech is slightly altered according to the type of cerebellar dysarthria. Mild dysphagia for liquid and solid food. Pharyngeal reflex is slightly reduced. The patient can distinguish whispered speech from left to right at a distance of 6 meters. The sternocleidomastoid and trapezius muscles are intact. Motor function: wide-legged gait with the aid of two canes, similar to cerebellar ataxia.

Muscle tone: D=S, increased in the arms. Contractures in the extremities are present at the hip joints on both sides, with movement limited at the knees when lying horizontal. Muscle strength in the extremities is equal proximally to 5.0 points, equal distally to 5.0 points, equal proximally to 4.0 points, equal distally to 4.0 points. Tendon reflexes in the upper and lower extremities: D=S, high, with widened reflexogenic zones. Abnormal foot signs (-) on both sides. In the Romberg position, there is moderate unsteadiness, which increases with eye closure. The patient performs the finger-to-nose test with ataxia on both sides; heel-to-knee tests are impossible due to deformities in the lower extremities. There is no impairment of deep sensory sensation in the fingers or toes. No impairment of superficial sensory sensation was objectively detected. Pelvic functions are normal.

Results:

Montreal Cognitive Assessment (MoCA) - 30 points (normal).

Hospital Anxiety and Depression Scale (HADS): Anxiety - 4 (normal), Depression - 5 (normal).

Morse Falls Risk Scale - 80 points, indicating a high risk of falls.

Hendrick Fall Risk Model II - 5 points, also indicating a high risk of falls.

Scale for the Assessment and Rating of Ataxia (SARA) - 16 points (maximum 40 points).

Magnetic resonance imaging (MRI) of the brain: signs of mild cerebellar and brainstem atrophy (Fig. 4).

Needle electroneuromyography: needle EMG revealed... Left, Vastus lateralis, Femoralis, L2, L3, L4 – no spontaneous activity detected; interference EMG – horizontally extended turn-amplitude cloud, increased average MUAP frequency to 600/s; MUAP examination revealed EMG stage IIIa (intermediate type). Clinically, no evidence of primary muscular or primary neuronal disorders was detected.

Spirometry, conclusion: moderate decrease in vital capacity. Moderate restrictive VFL impairment.

Blood tests showed thrombocytopenia: 11 *10 10 9/L upon admission, rising to 74 *10 10 9/L by discharge; parathyroid hormone – 27.2 pg/ml. Thyroid hormones: TSH - 0.20, free T4 - 8.41, free T3 - 3.12, antibodies to TPO - 34.6 IU/ml.

Discussion. In this case report, we describe a previously unreported case of two concurrent hereditary diseases transmitted in an autosomal dominant manner from both parents. The mother suffered from hypophosphatemic rickets, and the father from spinocerebellar ataxia type 1. As a result, the couple had children with both conditions. All affected siblings developed symptoms of hypophosphatemic rickets in childhood, and all were recognized as disabled from childhood. Symptoms of spinocerebellar ataxia type 1 began at the age of 39-40 years.

Molecular genetic analysis revealed a heterozygous mutation—a deletion of exon 15 of the PHEX gene—and a pathological expansion of 40 CAG repeats in the ATXN1 gene in both patient V. and her siblings.

The patient developed SCA type 1 symptoms at age 40 in 2021: unsteadiness when walking and slurred speech. Due to unsteadiness and limited mobility in her legs, she cannot walk down stairs independently and only walks short distances. She has noted a worsening of her condition over the past year and uses a wheelchair for longer distances.

The onset of SCA type 1 in her older brother and older sister also occurred at age 40. Both brothers were diagnosed with a mutation in the ATXN1 gene with a pathological expansion of 40 CAG repeats.

The older sister was diagnosed with an expansion of 29/42 CAG repeats in the ATXN1 gene, but was not diagnosed with a heterozygous mutation (deletion of exon 15 of the PHEX gene) and has no signs of chondrodysplasia. At the same time, she is also registered with a rheumatologist with the following diagnosis: Rheumatoid arthritis, seropositive, anti-CCP?, late stage, low DAS28CRP-2.72 activity, erosive arthritis, radiographic stage III, functional class 1. Partial ankylosis of both wrist joints. Secondary gonarthritis II-III.

Thus, based on the family history, molecular genetic testing for type 1 SCA and hypophosphatemic rickets, neurological status, and clinical examination data, the final clinical diagnosis was:

Primary: G11.2 - Late-onset cerebellar ataxia: Spinocerebellar ataxia type 1, autosomal dominant inheritance pattern (mutation in the ATXN1 gene, increased CAG repeats 29/42), with cerebellopyramidal and mild bulbar syndrome, moderately progressive course.

Concomitant: E83.3 - Disorders of phosphorus and phosphatase metabolism: X-linked dominant hypophosphatemic rickets. Deletion of exon 15 of the PHEX gene. Bow-shaped deformity of the lower extremities (condition after multiple surgical corrections). Osteoarthritis of the left and right knee joints. Somatic short stature. Secondary hyperparathyroidism. Decreased BMD. Vitamin D deficiency.

Varus deformity of the lower extremities (post-severe surgical corrections). Osteoarthritis of the left and right knee joints. Biconcave deformity of the bodies of the Th5 (grade 1), Th6 (grade 2), Th7 (grade 2), Th8 (grade 2), Th9 (grade 2), Th1O (grade 1), L1 (grade 1), L2 (grade 1), L3 (grade 2), L4 (grade 2), and L5 (grade 3) vertebrae.

BPPV syndrome. Left-sided nodular goiter, euthyroidism. D69.5 - Secondary thrombocytopenia: mixed genesis, due to severe secondary immunodeficiency; H52.2 - Astigmatism: Simple myopic astigmatism OU.

Conclusion. The authors present a family case of a previously undescribed combination of two genetic syndromes. The combination of two hereditary pathologies in this clinical description presents a very challenging diagnostic challenge for neurologists due to the rare nature of the two hereditary disorders and the fact that the symptoms of hypophosphatemic rickets may overlap with those of ataxia, which can complicate timely diagnosis. This family case should alert the medical community and health authorities not only of the Lensky District but also of the entire Republic of Sakha (Yakutia) and should direct the efforts of the medical organization toward public education regarding hereditary diseases, taking into account the bioethical issues that inevitably arise when discussing this area of medicine.

The authors declare no conflict of interest.

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PAGET'S DISEASE OF BONE AS A RARE CAUSE OF HEADACHE

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УДК 616.71-003.93

Headache is one of the most common complaints encountered in clinical practice. Although primary headaches (such as migraine and tension-type headache) are most prevalent, timely identification of secondary headaches is essential, as they require distinct diagnostic and therapeutic approaches. This paper presents a clinical case of Paget's disease of bone with isolated skull involvement, manifested solely by chronic headache. Based on elevated serum alkaline phosphatase levels, further examination was performed in a 47-year-old patient initially diagnosed with tension-type headache. Magnetic resonance imaging (MRI), computed tomography (CT), and bone scintigraphy confirmed the diagnosis of Paget's disease of bone, after which pathogenetic therapy was initiated.

Keywords: headache, secondary cephalgia, Paget's disease of bone, alkaline phosphatase.

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Introduction. Headache is one of the most common reasons for seeking medical care [1, 8]. According to the Global Burden of Disease (GBD, 2022) study, the overall prevalence of headache was 52.0% (95% CI: 48.9–55.4), migraine – 14.0% (95% CI: 12.9–15.2), and tension-type headache – 26.0% (95% CI: 22.7–29.5). Chronic headaches lasting 15 or more days per month were reported in 4.6% (95% CI: 3.9–5.5) of cases [16]. Headache significantly reduces quality of life and often leads to temporary or permanent disability [14].

In most cases, primary headaches—migraine, tension-type headache, and cluster headache—are observed. However, secondary headaches are not uncommon; these are symptoms of other, often more serious disorders, requiring specific diagnostic approaches [8].

Paget's disease of bone (PDB, also known as deforming osteitis) is a chronic, slowly progressive skeletal disorder characterized by focal abnormalities in bone remodeling [2]. Excessive osteoclastic resorption, coupled with disorganized osteoblastic bone formation, results in structurally weakened, deformed, thickened, and hypervascularized bone [3]. PDB typically affects older individuals, particularly men, and occurs in approximately 1–5% of people over 50 years old [5]. There is marked geographic variation, with the disease being more common in populations of European descent and relatively rare in Asians [11]. Although its exact cause remains unclear, PDB is thought to develop in genetically predisposed individuals, as a positive family history is reported in 5–40% of cases [9]. Environmental factors, including viral infections (especially paramyxoviruses) and vitamin D deficiency, have been proposed as contributing factors [3].

Clinically, the disease manifests with bone pain (73.8%), bone deformities (18.1%), hearing loss (7.9%), and pathological fractures (5.7%). However, in up to 22% of patients, PDB may remain asymptomatic [15]. Neurological complications include hearing loss (76%), neck pain (2–5%), cranial nerve palsies (0.2–41%), and peripheral nerve involvement (2–5%) [13]. Although headache is frequently reported in PDB, it is a nonspecific symptom [4]. Typically, headaches are localized in the posterior head and are aggravated by increased intracranial pressure, such as during coughing or defecation. Possible mechanisms include skull hypervascularization, basilar impression, hydrocephalus, compression of trigeminal nerve roots, thickening of facial bones, and intracranial hemorrhage [7].

Thus, although rare, Paget's disease of bone should be considered in the differential diagnosis of chronic headache. We present a clinical observation of a patient in whom headache was the only manifestation of Paget's disease of bone.

Case Description. A 47-year-old man was admitted in August 2025 to the neurology department with persistent dull and aching headaches localized in the temporal and infraorbital regions (VAS score 7), unaccompanied by nausea or vomiting.

History of present illness. The patient had been experiencing headaches since

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