

Case report



EXTENSIVE INTRACRANIAL CALCIFICATION WITH NEUROLOGICAL AND OPHTHALMOLOGICAL COMPLICATIONS IN A PATIENT WITH IDIOPATHIC HYPOPARATHYROIDISM: A CASE REPORT.

Maya P. Danovska¹, Diana L. Marinova¹, Igor Mladenovski¹, Emilia M. Ovcharova¹, Vesela Ivancheva², Nachko Totsev³, Lyubomir Tzankov³,

1) Department of Neurology, University Hospital, Medical University, Pleven, Bulgaria

2) Department of Ophthalmology, University Hospital, Medical University, Pleven, Bulgaria

3) Department of Neuroimaging, University Hospital, Medical University, Pleven, Bulgaria.

ABSTRACT

Background: Idiopathic hypoparathyroidism is a rare endocrine disorder caused by the deficiency of parathyroid hormone. It typically has a progressive course and is characterized by accumulations of calcium deposits in the basal ganglia bilaterally. In untreated patients, the intracranial calcification may also affect the thalamus, dentate nuclei, cerebral cortex, grey-white junctions and the cerebellum. Different locations can mimic multiple neurological diseases making the diagnosis of that rare disease a challenge.

Purpose: To present a clinical case with untreated idiopathic hypoparathyroidism, extensive intracranial calcifications and neurological and ophthalmological complications.

Material and methods: We present a 50-year-old man with untreated idiopathic hypoparathyroidism who was diagnosed in 2015 with massive intracranial calcifications located in the basal ganglia and outside the extrapyramidal structures. The neurological examination showed involuntary choreoathetotic movements of the right arm, progressive severe cognitive decline, generalized tonic-clonic seizures, gait imbalance and visual disorders. Abnormalities in the calcium-phosphorus metabolism and renal function tests were found. CT scans demonstrated extensive brain calcifications. The ophthalmological examination showed diminished visual acuity and mature cataract. The histopathological result did not demonstrate ragged red fibres. Some differential diagnostic opportunities like Fahr's disease or Kearn Sayre's syndrome were also considered.

Results: The patient was diagnosed with untreated childhood idiopathic hypoparathyroidism with extensive intracranial calcifications and neurological and ophthalmological complications – a rare clinical case. This was confirmed by his medical history, general, neurological and ophthalmological examinations, laboratory, histopatho-

logical and neuroimaging investigations.

Conclusion: The CT findings demonstrating extensive intracranial calcifications in the basal ganglia and the extrapyramidal structures make the presented clinical case a diagnostic challenge.

Keywords: Idiopathic hypoparathyroidism, brain calcifications, Kearn Sayre's syndrome.

BACKGROUND

Idiopathic hypoparathyroidism is a rare endocrine disorder associated with deficiency of parathyroid hormone causing decreased blood levels of calcium and higher phosphorus [1, 2]. Basal ganglia calcification was first described by Eaton in 1939 as part of chronic hypoparathyroidism [3]. It is a progressive disorder despite the maintenance of normal calcium levels [3]. Repeated CT scans show the accumulation of calcium deposits by detecting new and increased volume of old calcification sites. Brain calcifications are frequently spread in the basal ganglia bilaterally: the lentiform (putamen and globus pallidus) and the caudate nuclei [2]. Calcifications are rarely spread over the dentate nucleus, corona radiata, subcortical white matter and thalamus [2]. Up to 1.5% of the patients with hypoparathyroidism have calcifications in the thalamus, dentate nuclei, cerebral cortex, gray-white junctions and the cerebellum [3]. The exact mechanism of extensive intracranial calcification has not been clarified yet. It could stem from lower PTH level, but also from the hypocalcaemia and hyperphosphatemia duration [4]. Scientific research shows that hyperphosphatemia is important for the ectopic brain calcifications and the superoxide production of mitochondria in patients with idiopathic hypoparathyroidism and intracranial calcifications [4]. Bilateral symmetrical calcification is typical for Fahr's disease, however, the patient's biochemical profile is normal [2].

CASE DESCRIPTION

The patient was admitted to the Neurology Clinic twice (in 2015 and in 2017) with a history of rare generalized seizures and abnormal involuntary choreoathetotic movements of the right arm since the age of 15. During the first hospitalization, he was diagnosed with untreated idiopathic hypoparathyroidism. The CT scan performed in 2015 visualized multiple massive calcifications, up to 50 mm in size, localized in the basal ganglia, frontal brain parenchyma and the cerebellum. The neuropsychological tests showed a cognitive decline with severe disturbances in short-term, episodic and semantic memory. Both eyes had normal ocular adnexa and extraocular movements. The right eye had visual acuity (VA) = 0.2 - 0.3, cortical cataract, vital optic disc, diminished foveal reflex, no signs of macular degeneration, blood vessels with sclerotic changes (Gun I), no pigment deposits. The left eye had VA=PPLC due to mature cataract, which did not allow fundoscopy. The patient had aphasia during the second hospitalization impeding neuropsychological testing. The neurological

examination demonstrated ptosis and amblyopia of the left eye, involuntary movements of the right arm resembling choreoathetosis and gait ataxia. The ophthalmological status was similar to that from 2015, VA was not tested. The right eye's fundoscopy showed vital optic disc, diminished foveal reflex, blood vessels with sclerotic changes, no pigment deposits. The left eye didn't allow fundoscopy due to mature cataract. The laboratory results presented hypocalcaemia and hyperphosphataemia with progressive renal dysfunction.

The thyroid hormone levels in 2015 were: TSH 1.0; FT3 4.9; FT4 17.0; Parathormone (PTH) 67.47 pg/ml; Cortisol 425 nmol/l, urine calcium 0,07mmol/l and phosphorus 22,71mmol/l. The electroencephalogram revealed a focal activity of spikes and complexes (spike-slow waves) fronto-temporally in the left hemisphere with secondary bilateral synchronization. The repeat non-contrast 2017 CT scan visualized extensive intracranial calcification spread in the basal ganglia, frontal brain parenchyma and cerebellum bigger in size compared to the 2015 CT scan.

Table 1. Laboratory investigations of the patient

| No. | Parameters | 2015 y | 2017 y |
|-----|-----------------------------------|------------|-------------|
| 1. | Serum total calcium (mmol/l) | 1.15; 1.13 | 1.21 |
| 2. | Serum ionized calcium (mmol/l) | - | 0.59 |
| 3. | Serum phosphorus (mmol/l) | 2.11 | - |
| 4. | Serum magnesium (mmol/l) | 0.71 | - |
| 5. | Serum parathyroid hormone (pg/ml) | 67.47 | - |
| 6. | Urea | 7.2 | 12.83; 20.0 |
| 7. | Creatinin | 93 | 136.48; 163 |

Fig.1. Non-contrast CT showing calcification in the region of the basal ganglia (2015).

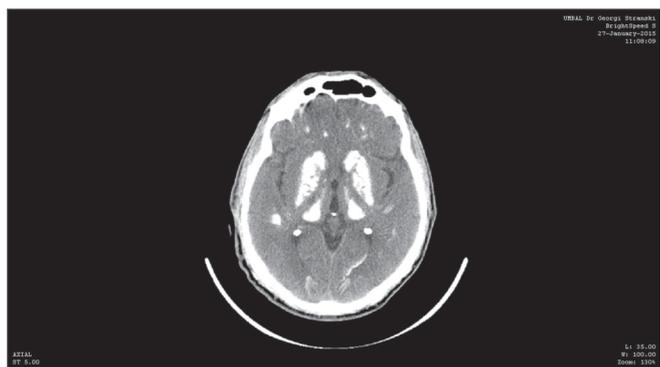


Fig.2. Non-contrast CT showing calcification in the region of the basal ganglia (2017).



Fig. 3. Non-contrast CT showing extensive calcification bilaterally in the cerebral cortex (2015).

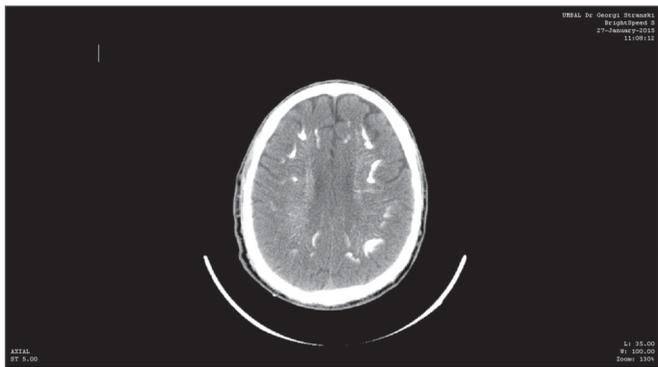


Fig. 4. Non-contrast CT showing extensive calcification bilaterally in the cerebral cortex (2017).

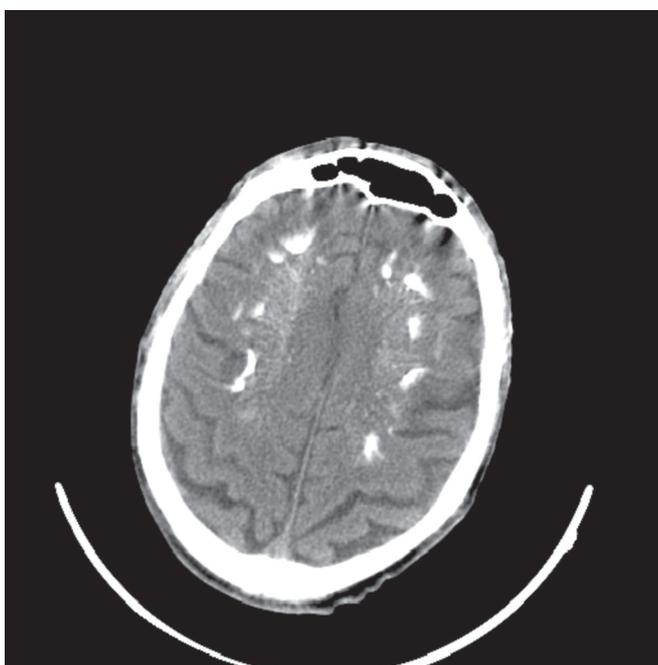


Fig. 5. Non-contrast CT showing extensive calcification in the cerebellum (2015).

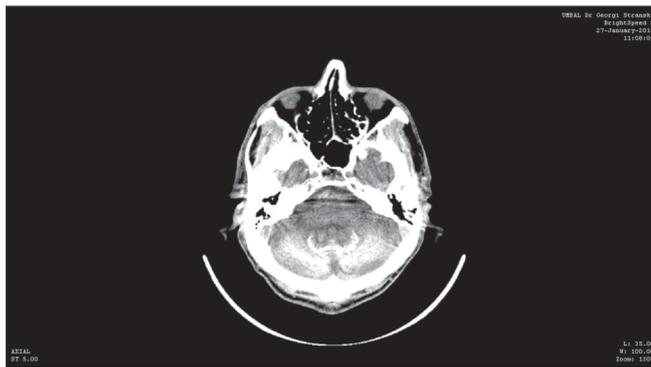
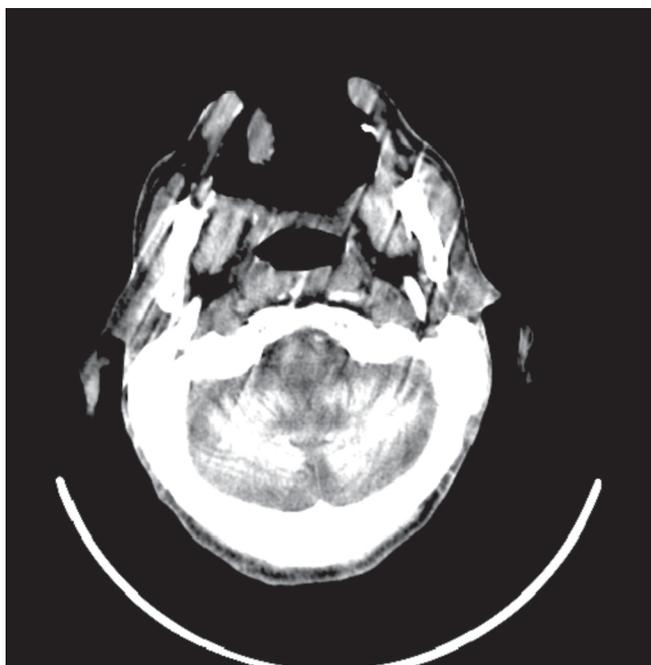


Fig. 6. Non-contrast CT showing extensive calcification in the cerebellum (2017).



DISCUSSION

Multiple diagnoses were considered before reaching the conclusion that the patient is suffering from idiopathic hypoparathyroidism. The variety of neurological and cognitive symptoms is seen in Fahr's disease. However, in this case, onset in childhood and calcium metabolism abnormalities caused by idiopathic hypoparathyroidism exclude Fahr's disease. Other diagnostic options were analyzed as possible reasons for the extensive intracranial calcifications: secondary hypoparathyroidism, pseudohypoparathyroidism, hypothyroidism, chronic intoxication with lead, familial idiopathic symmetric calcification, syndrome of Hastings-James (idiopathic lenticular-dentate calcification), Kearns Sayre's syndrome, stroke and brain parasitoses [3, 6]. The CT scan findings are also seen in cases with Kearns Sayre's syndrome, but the absence of chronic progressive external ophthalmoplegia and pigmentary retinopathy exclude the diagnosis. A mature cataract primary or secondary is usually characterized with lenticular opacities caused

by the deficiency of PTH action or secretion [7, 8]. Idiopathic hypoparathyroidism and hypoparathyroid cataracts are relatively rare findings, and their etiology and pathogenesis still remains unclear. Metabolic disturbances, calcitonin reduction, chronic hypocalcemia and hyperphosphatemia, vitamin D insufficiency could also be the causes of the cataract formation [9, 10]. The opacities are typically located in the subcapsular cortical region, lenticular changes originate initially as multiple fine punctuations or vacuoles, replaced later by white irregular laminated opacities [11]. In long standing severe hypoparathyroidism, the risk of cataract is higher and mature cataract develops, as in this case.

Idiopathic hypoparathyroidism and symptomatic epilepsy associated with hypocalcaemia could be one of the clinical manifestations of endocrine dysfunctions seen in cases with Kearns Sayre's syndrome [12]. The original publication of Kearns in 1965 on the clinical presentation of the syndrome also includes some sporadic symptoms

like hearing loss, EEG changes, cerebellar ataxia and hyperproteinorachie. In this case, we found only hyperproteinorachie and neuropathy of the statoacoustic nerve. Muscle biopsy in Kearns Sayre's syndrome reveals ragged red fibers, consisting of the abnormal mitochondrial amount in 80-100%. Based on our review of the literature there is no effective disease-modifying therapy for Kearns Sayre syndrome [12].

CONCLUSION

The patient was diagnosed successfully by a multidisciplinary team who carefully analyzed, considered and excluded multiple diagnostic options. The clinical examination and further tests performed were indicative of idiopathic hypoparathyroidism. However, the extensive intracranial calcifications detected by the CT scan made this clinical case a real diagnostic challenge.

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Address for correspondence:

Dr Diana L. Marinova,
Neurology Clinic UMHAT “Dr Georgi Stranski”
8a, Georgi Kochev str., Pleven 5800, Bulgaria
E-mail: dianamarinova1980@gmail.com,