A case of severe long-term secondary hyperparathyroidism (Sagliker syndrome) in a patient treated with intermittent hemodialysis

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In a 50-year-old man malocclusion of the upper and lower jaws, lower height than in the previous years, peculiar appearance of the fingertips - upward curved development of phalanges (Sagliker syndrome) developed during 25-years of treatment with intermittent hemodialysis as a result of severe secondary hyperparathyroidism (sHPT) complicating end-stage renal disease. Serum concentration of intact parathyroid hormone during 2004-2010 (up to 6 results each year) was 1180 ± 514 pg/ml (mean ± SD). At present, a poor general condition of the patient disqualified him from parathyroid gland surgery. Some improvement in laboratory indices of sHPT severity was obtained with combined medication with calcium carbonate, active vitamin D and cinacalcet hydrochloride.

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Słowa kluczowe:
• przewlekła niewydolność nerek
• cynakalcet
• hemodializa
• zespół Saglikera
• wtórna nadczynność przytarczyc

Key words:
• chronic kidney failure
• cinacalcet
• hemodialysis
• Sagliker syndrome
• secondary hyperparathyroidism

Przypadek ciężkiej długotrwającej wtórnej nadczynności przytarczyc (zespół Saglikera) u chorego leczonego powtarzaną hemodializą

U 50-letniego mężczyzny w ciągu 25 lat leczenia powtarzaną hemodializą rozwinęły się zmiany kostne (zniekształcenie twarzoczaszki, obniżenie wzrostu, zniekształcenie końcówek palców), będące skutkiem ciężkiej wtórnej nadczynności przytarczyc (sHPT), wikłającej schyłkową chorobę nerek (zespół Saglikera). Stężenie natywnego parathormonu w surowicy w latach 2004-2010 (do 6 wyników rocznie) wynosiło 1180 ± 514 pg/ml (średnia ± SD). Obecnie zły stan ogólny chorego nie kwalifikuje go do wykonania chirurgicznego usunięcia przytarczyc. Poprawę laboratoryjnych wskaźników sHPT uzyskano w wyniku skojarzonego leczenia węglanem wapnia, aktywnym preparatem witaminy D i chlorowodorkiem cynakalcetu.

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Introduction

Chronic kidney disease and progressive renal failure are associated with phosphate retention and impaired formation of active vitamin D, leading to hypocalcemia, increased secretion of parathyroid hormone (PTH), and hyperplasia of the parathyroid glands. Elevations in PTH occur early in renal insufficiency (at creatinine clearance of 60 mL/min) in a physiologic attempt to normalize calcium, phosphorus, and vitamin D levels [9]. Chronic secondary hyperparathyroidism (sHPT) produces deleterious effects on bone and mineral metabolism. Renal osteodystrophy, loss of bone mineral density, bone pain, and fractures are common complications of sHPT [11].

In the XX century ugly facial changes with leontiasis ossea as an extremely rare form of renal osteodystrophy have been occasionally reported in the literature [2,3]. Sagliker and his co-workers have demonstrated that in the XXI century, despite great advances in medicine it is still possible to meet patients with ugly face appearances and other disturbances of the skeletal system, which emerged in the course of untreated or inadequately treated sHPT. Their efforts in looking for such patients resulted in 2004 in a creation of a new syndrome - Sagliker syndrome (SS), which is defined as uglifying face appearance in severe and late sHPT in the course of chronic renal failure [14]. Incidence of SS in hemodialysis (HD) patients was evaluated to be approximately 0.5%. In 2008, Sagliker et al. [13] have encountered 40 cases of SS by performing an international study in Turkey, India, Romania, Egypt, Maleysia, Tunis, and China.

In 2006, abnormalities in cephalometric evaluation (malocclusion of the upper and lower jaws) [15] and neurologic manifestations (the most frequently headache, polyneuropathy, cranial neuropathy, fatique) [6] in patients with SS were presented. Recently (2008-2010), quality of life [12], psychiatric manifestations (depression, hopeles-

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Figure 1
Appearance of the patient in the first year of treatment with intermittent hemodialysis.
Wygląd chorego w pierwszym roku leczenia powtarzaną hemodializą.

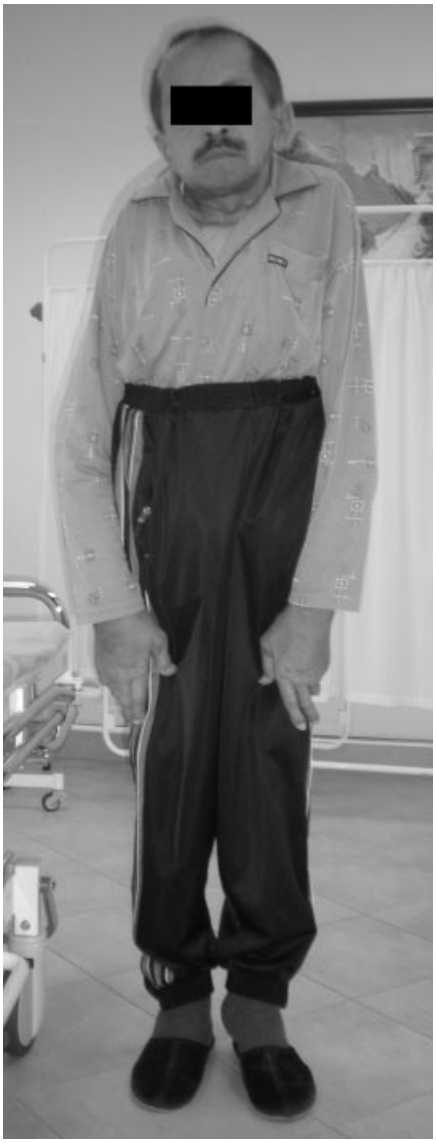
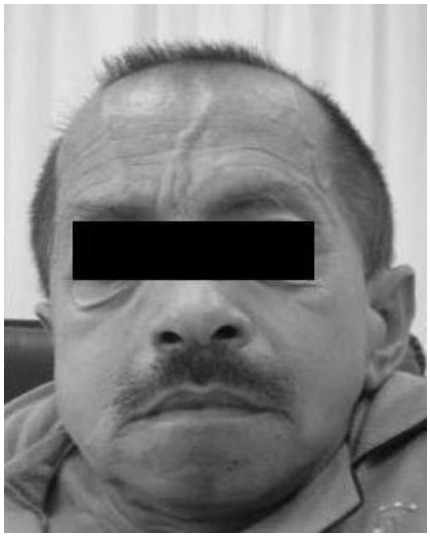


Figure 2
Appearance of the patient in the 25th year of treatment with intermittent hemodialysis.
Wygląd chorego w 25-tym roku leczenia powtarzaną hemodializą.



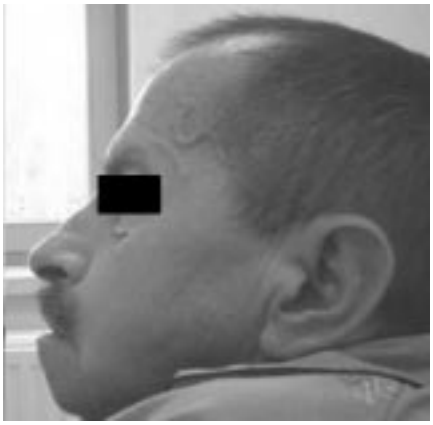


Figure 3
Face appearance shown in the patient in the 25th year of treatment with intermittent hemodialysis.
Wygląd twarzy chorego w 25-tym roku leczenia powtarzaną hemodializą.

sness) [10] and audiological findings (hearing loss) [4] were described in these patients.

Although there is a great advance in diagnosis and treatment of sHPT in end stage renal disease (ESRD), new cases of marked facial changes [1, 5] and full-symptom SS are still found [16]. Detailed signs and symptoms of SS we have presented in the last issue of Nefrologia i Dializoterapia Polska [7]. At present, we would like to show a case of SS found in Poland in 2010.

A case report

A Caucasian male patient, at present 50.0 years old, started intermittent HD at November 1, 1985 in the university department of nephrology, located 148 kilometers from his house, due to ESRD in the course of chronic glomerulonephritis (Fig. 1). In 1987, he underwent renal transplantation from a dead donor, but due to severe acute rejection a transplant never took up a proper function and the patient continued HD treatment.

In March 19, 1993, he changed a dialysis center for a new one, situated 24 kilometers from his house. Chest x-ray examination showed at that time a symmetric pectoral cavity. In January, 1994, his left arm was broken in the traffic accident. In 1994-1995, serum activity of total alkaline phosphatase was 1950-1235 IU/L, respectively. In October, 1995, he suffered from fragile fracture of the left femoral neck. In April, 1996, he was sent to the university department of nephrology for diagnosis of sHPT. Bone scintigraphy showed an increased tracer uptake in plane bones, skull, mandible, spine, sacral bone, and extremities of long bones. Serum PTH concentration was 378.6 pg/ml (normal range 8 - 76 pg/ml). (99m)Tc-MIBI scintigraphy did not reveal enlargement of parathyroid glands and due to this fact and relatively not very high serum PTH concentration he was not qualified for parathyroidectomy. The next available serum level of intact PTH (1681 pg/ml) was from January 30, 2004 (normal range 15 - 63 pg/ml).

In December 17, 2005 he changed dialysis center again for a new one built in the town he lives. Serum concentration of intact PTH during 2004 - 2010 (up to 6 results each year) was 1180 ± 514 pg/ml (mean ± SD). In 2010 the dialysis center was visited by a physician who has known the patient from the university department of nephrology. The difference in the patient appearance was striking. Osteoporotic fractures of bone spine, right-sided scoliosis and kyphosis resulted in a decrease of height from 176 cm to 151 cm.

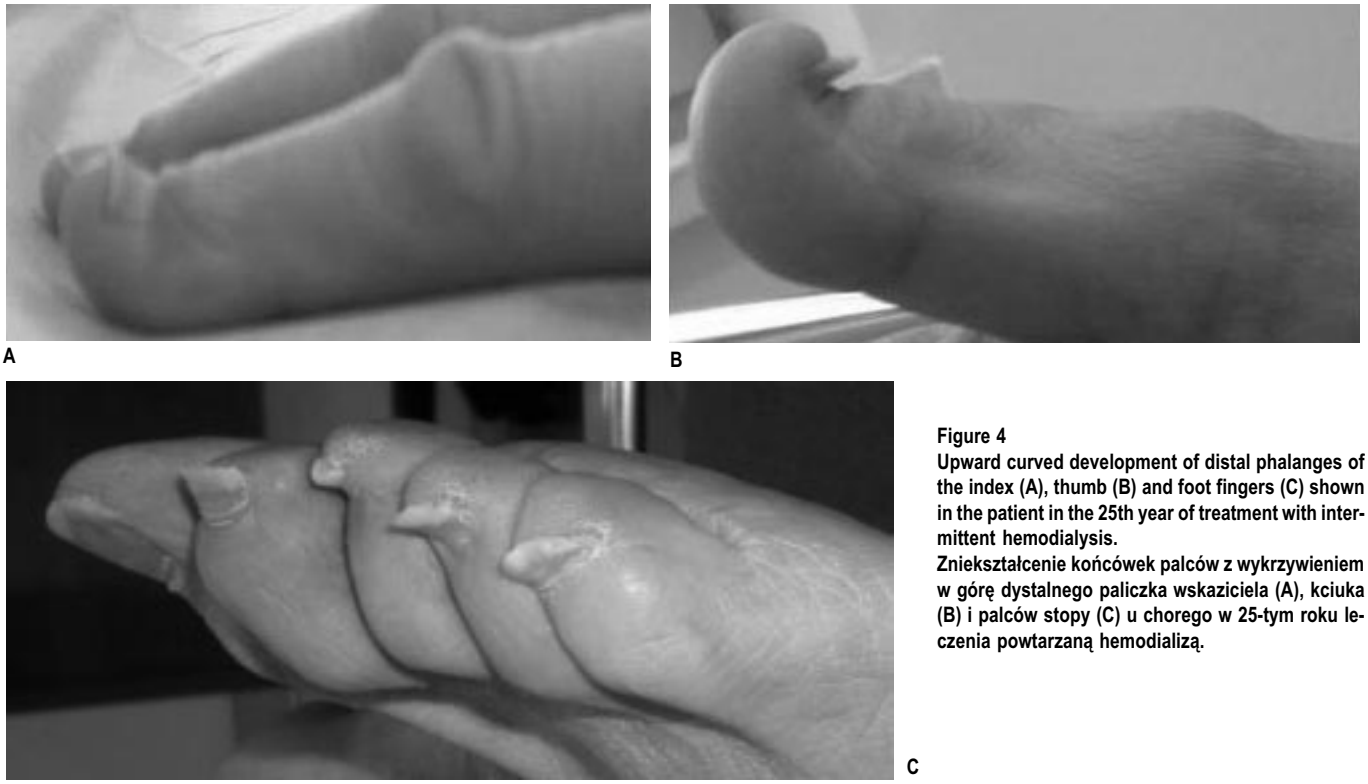


Figure 4
Upward curved development of distal phalanges of the index (A), thumb (B) and foot fingers (C) shown in the patient in the 25th year of treatment with intermittent hemodialysis.
Zniekształcenie końcówek palców z wykrzywieniem w górę dystalnego paliczka wskaziciela (A), kciuka (B) i palców stopy (C) u chorego w 25-tym roku leczenia powtarzaną hemodializą.

Proportions of the body changed (Fig. 2). Body mass decreased from 64 kg to 47 kg. Characteristic face appearance (malocclusion of the upper and lower jaws) (Fig. 3) and peculiar appearance of the fingertips: upward curved development of phalanges (Fig. 4) resulted in a diagnosis of SS.

Only pharmacological medication of sHPT (aluminum hydroxide in past, calcium carbonate, sevelamer hydrochloride, active vitamin D) was used in the course of dialysis treatment in this patient. At present, a poor general condition of the patient, especially respiratory insufficiency with dyspnoea even in the rest, disqualified him from parathyroid glands surgery. In April 2010, cinacalcet hydrochloride in increasing doses (30 mg at the start to 120 mg) was added to medication with calcium carbonate and active vitamin D resulting during April - November in a gradual decrease of serum concentrations of PTH (1501 - 1257 - 825 pg/ml), total calcium (2.25 - 2.06 mmol/l, normal range 2.00 - 2.75 mmol/l) and phosphorus (3.12 - 1.54 mmol/l, normal range 0.97 - 1.51 mmol/l).

Closing remarks

In the XXI century, despite great advances in management of sHPT it is still possible to meet patients with characteristic face appearances and other disturbances of the skeletal system, which emerged in the course of untreated or inadequately treated sHPT.

The experts involved in a preparation of Kidney Disease Improving Global Outcomes (KDIGO) Clinical Practice Guideline for treatment of dialyzed patients with ESRD suggest maintaining PTH levels in the range of approximately two to nine times the upper normal limit for the assay [8]. In patients with elevated or rising PTH, calcitriol, or vitamin D analogs, or calcimimetics, or a combination of calcimimetics and calcitriol or vitamin D analogs are suggested to be used to lower PTH. In patients with severe sHPT who fail to respond to pharmacological therapy, parathyroidectomy is suggested, which performed by an expert surgeon generally results in a marked, sustained reduction in levels of serum iPTH, calcium, and phosphorus. Subtotal parathyroidectomy or total parathyroidectomy with autotransplantation also effectively reduces elevated levels of PTH, calcium, phosphorus, and alkaline phosphatase. However, there is no evidence showing how long is reasonable to wait for potential effects of pharmacological therapy. Waiting to long may result in a development of SS, frequently associated with a poor clinical state unsuitable for surgery. When pharmacological treatment of sHPT does not lead to adequate regulation of parathyroid function, a decision of parathyroidectomy should not be put off. In a long-term HD patient with sHPT, the first fragile bone fracture may be a serious indicator predictive further progression of bone abnormalities and SS development, and perhaps is the last ringing bell for successful parathyroidectomy. In time parathyroidectomy may control and partially ameliorate bone changes shown in SS [17]. Moreover, correctional surgical treatments performed after parathyroidectomy may significantly improve facial appearance and give sustained effect [2].

In the last years, a great advance in the treatment of sHPT was made due to introducing calcimimetic agents, which are recommended by KDIGO Clinical Practice Guideline for treatment of sHPT in dialysis patients [8]. It is unknown if they are able to make SS a history, but calcimimetics may be a hope for at least some SS patients for slowing or stopping progression of bone deformations.

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