Abstract. Aim: To present a case of Sagliker syndrome (SS), a rare syndrome caused by long-term heavy tertiary hyperparathyroidism (HPT) in end-stage renal disease (ESRD). Case report: In the year 2000, the 38-year-old man was diagnosed with ESRD. He is currently of low height, paraplegic, pigeon and barrel chested, with elongated upper extremities, deformed fingers, mandibular and maxillary asymmetric deformities with teeth malformations. Due to extremely high serum parathormone (PTH), resistant to pharmacological treatment, subtotal parathyroidectomy (PTx) was performed in 2007. However, he underwent parathyroid resurgery in 2010 for persistently high PTH of more than 2500 pg/mL (upper normal limit 69). In 2012, imaging found two suspected parathyroid glands and one of them was surgically removed. Postoperatively, the expected decrease in calcium and PTH serum concentrations did not occur. Ten years after the diagnosis of ESRD, the patient began to notice more pronounced skeletal deformities (upper, lower jaw, extremities, deformities of fingers, kyphoscoliosis) along with depressive disorder. Laboratory findings still show extremely high PTH (1994 pg/mL), low calcium, 1.89 mmol/L (normal range 2.14–2.53), and high alkaline phosphatase, 837 U/L (normal range 60–120), despite continuous pharmacological treatment. Conclusion: SS was firstly recognized by Yahya Sagliker in 2004 and it has not been described in Croatia to date. Pervasiveness and knowledge of the syndrome is still poor. The most efficient way of treating/preventing SS is early total PTx in severe secondary HPT related to ESRD. However, it can only stop progress of the disease, but cannot return skeletal deformities.

Keywords: facial asymmetry; hyperparathyroidism; kidney failure, chronic


Ključne riječi: asimetrija lica; hiperparatireoidizam; kronično zatajenje bubrega

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INTRODUCTION

Yahya Sagliker was the first to describe unique patients with uglifying human face appearance and associated that phenomenon with tertiary hyperparathyroidism due to chronic kidney disease (CKD)\(^1\).

The diagnosis of the syndrome is established clinically, based on the most common SS signs: maxillary and mandibular disfiguring bone changes (usually progressing throughout the years), pi-
DISCUSSION

Even though there is no exact diagnostic criteria for SS, different studies reported physical diagnostic criteria based on clinical presentation including maxillary, mandibular and dental deformities, skeletal changes like short stature, knee and scapula deformities, benign epithelial hyperplasia, fingertip changes, neurological and psychiatric disorders. In 2019 Muhammad Ajmal Panezai et al. reported a case about a 31-year-old African American man in the USA with ESRD on hemodialysis with severe secondary hyperparathyroidism. He noticed swelling of his gums, facial bones, and cheeks that began to increase in size over several years, which was the same case as in our patient. Other symptoms that occurred in our patient which are also characteristics of SS are deformed fingers, pigeon and barrel chest, hearing loss and depression. Etiology of the syndrome is tertiary hyperparathyroidism of the chronic kidney disease. However, literature does not provide a clear etiopathological pathway for such bone deforming changes so authors try to hypothesize it. Cholakova et al. explains that commensurate increased serum alkaline phosphatase is responsible for this type of skeletal changes. Yu Yu et al. hypothesized that intramembranous ossification is hyperactivated in this syndrome, which then leads to thickening of the maxilla, anterior mandible and skull. Moreover, in the international research of Yahya Sagliker et al. they concluded that the GNAS1 gene missense mutations, which are possibly activated during the hemodialysis, might be responsible for genesis of SS. Laboratory values that are dominant in this syndrome are high serum PTH and ALP. High PTH (2815.07 pg/mL) and ALP (2350 U/L) with lower range of calcium (2.31 mmol/L) were presented for the patient in the case report done by Yu Yu et al. in China. Moreover, similar laboratory results were given in the research done by A. M. Pineda et al. In the both researches total PTx was performed which resulted in rapid decrease in PTH level. After more than four months, post-operative values of PTH were 131.01 pg/mL in one patient and 15.8 pg/mL in the other. On the other hand, due to unchanging high level of PTH, our patient underwent PTx in 2007. Expected decrease in PTH eventually did not occur, thus parathyroid reoperation was performed in 2010 and again in 2012. After that, the level of PTH was still high. According to the stated results, the most efficient way of treating/preventing SS would be total PTx. We consider it to be a better choice than subtotal PTx, which was also confirmed by the study published by Schneider et al. that reported rates of 4.1 % of persistent renal HPT in patients that underwent subtotal PTx compared to 0 % of persistent renal HPT after total PTx without autotransplantation. Furthermore, recombinant PTH (teriparatide) availability could help with deciding for total PTx in the case of SS in the future. Teriparatide is currently one of the growing solutions in treating osteoporosis. In the research of N. Ayati et al. it was reported how the mutations on the GNAS1 gene were some of the main causes of SS. Moreover, in the study of Azin Mohebi-Nejad et al, it was mentioned how genetic researches have detected 4 missense mutations on the GNAS1 gene among 40 % of patients with SS. However, the results of our patient’s genetic testing did not show any changes on GNAS and GNAS-AS1 genes. Even though some other researchers have also mentioned this gene on the 20th chromosome as a potential cause, the exact cause of the syndrome has still not been confirmed.

CONCLUSION

After the syndrome was described for the first time in 2004, only few cases have been described in the world so far and it has not been described in Croatia to date. Pervasiveness and knowledge...
of the syndrome is extremely low, thus there is a possibility of unrecognized patients with the alleged signs. The most efficient way of treating/preventing SS is early total PTx in those with severe secondary or tertiary HPT due to ESRD. However, it can only stop disease progression but cannot return skeletal deformities.

Conflicts of interest: Authors declare no conflicts of interest.

REFERENCES