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Review Article

The face of Sagliker's syndrome in maxillofacial aspect: a brief review

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ABSTRACT

In the world of nephrology, Sagliker syndrome is a unique rarity whose mechanism of occurrence is still not known. A rare bone disease characterized by secondary hyperparathyroidism in patients with chronic renal failure, caused by improper treatment in the early stages of the disease with retention of phosphorus, vitamin D deficiency, and disturbed calcium-phosphorus metabolism, which result in increased parathyroid hormone levels. Patients present with short stature, severe changes of the skull and jaws as well as other skeletal deformities, dental anomalies, "brown tumors" in the mouth, hearing loss, and neuropsychiatric disorders. This review briefly covers the maxillofacial aspect and core of Sagliker's syndrome.

Keywords: Sagliker's syndrome, Chronic renal failure, Browns tumour, Secondary hyperparathyroidism

INTRODUCTION

Sagliker syndrome (SS), also known as an "uglifying human face syndrome," is one of the prominent manifestations of chronic kidney disease occurring severely in patients with uncontrolled secondary hyperparathyroidism. Patients with SS eventually develop a short stature, maxillary and mandibular bone overgrowth, nasal bone changes and cartilage destruction, auditory loss, widely spaced teeth with anterior positioning, soft tissue tumors in the oral cavity, neurological and psychological features.

SS is a rare clinical condition originally described in 2004 by Sagliker and colleagues pioneerly.[1] Early in 1864, Virchow described a patient with enlargement of the facial bones as having a condition called "leontiasis ossea".[2] Over time, people realized that leontiasis ossea was not itself a disease but a rare medical condition fairly associated with Paget's disease, fibrous dysplasia, and gigantism. Cohen et al, in 1953, firstly described the symptoms of secondary hyperparathyroidism (SHPT) in chronic renal failure (CRF) as uremic leontiasis ossea (ULO), characterized by disfiguring facial deformity due to progressive bony overgrowth in the craniomaxillofacial region, resulting in a lion-like face. Other studies have shown that this syndrome has also been associated with a large head or swollen face. Sagliker et al, named it as Sagliker syndrome (SS) to inform and draw attention to this novel disease, and further defined it in detail.

The prominent clinical features of SS are remarkable protrusion of maxilla and mandible, destruction of the nasal bones, dental abnormalities, hyperplasia of the soft tissue inside the mouth, a short stature, fingertip changes, and even severe psychological manifestations.[1] Studies have shown that high levels of alkaline phosphatase and parathyroid hormone in patients with secondary hyperparathyroidism, who suffered from chronic kidney disease (CKD) for a long time, play a major role in SS induction.[6]

Moreover, it is proven that hyperplasia and hypertrophy of the parathyroid gland cells are associated to chronic renal failure, resulting in progressive production of parathyroid hormone (PTH). Following PTH rising, phosphorus clearance is decreased, resulting in

hyperphosphatemia, which is the main cause of SHPT.[7] Therefore, despite the low prevalence of SS syndrome (approximately 0.5%) amongst chronic renal failure patients, it should be considered in the differential diagnosis of renal osteodystrophy.[8] Even though renal transplantation stops the progression of musculoskeletal change, occurrence of established deformities due to SS are not reversible and thus affect the patient' quality of life. Hence, consequent monitoring of SS in young aged patients with CKD seems to be appropriate.[9] This review briefly covers the insights and core of the maxillofacial aspect of Sagliker's syndrome.

CORE OF THE SYNDROME

The mechanisms by which certain CKD patients develop SS is still unknown. Some authors suggest that it may be due to a genetic alteration triggered during dialysis sessions of CKD patients. An international study suggested that the gene responsible for promoting the genesis of SS is the GNAS1 gene and due to its mutation, SS can occur. Evolved SHPT, delayed and inappropriate treatment may play an important role in the appearance of SS.[11,12]

In hyperparathyroidism, facial changes are exclusively associated with patients who are suffering from advanced CKD, and their degree of association depends largely on the severity of the disease and its duration.[1] Cinacalcet is an extremely expensive drug, and, in patients whose parathyroid glands show nodular hyperplasia and a volume >500 mm^3, it seems to be highly associated with resistance to the treatment.[11]

According to the kidney disease improving global outcomes (KDIGO) clinical guidelines, patients who show moderate deterioration of kidney function (G3a) to kidney failure (G5d), along with significant secondary hyperparathyroidism failing to respond to medical treatment, should undergo parathyroidectomy.[13]

Therefore, inadequately treated patients with CKD and SHPT14 should undergo parathyroidectomy without delay, before the onset or signs of SS.[15] In a case report published by Rubio-Manzanares, A 35-year-old man with CKD secondary to glomerulosclerosis on dialysis for 9 years, reported with unusual changes in his facial features in recent years. He suffered from complete loss of residual renal function in 2007. One year earlier, a progressive increase in parathyroid hormone (PTH) levels was detected.[15]

So, the patient received calcimimetics, phosphate binders and vitamin D, but despite this, the PTH levels continued to rise. In 2008, the patient received a cadaveric renal transplant. During this time period, PTH values came to near normal levels. In 2010, due to poor adherence to immunosuppressive therapy, a decrease in kidney graft function was observed. Initially, the patient refused to enter the haemodialysis program, although in 2012 he finally agreed to rejoin the program. At that time, PTH levels had risen to 1000 pg/ml (Figure 1).

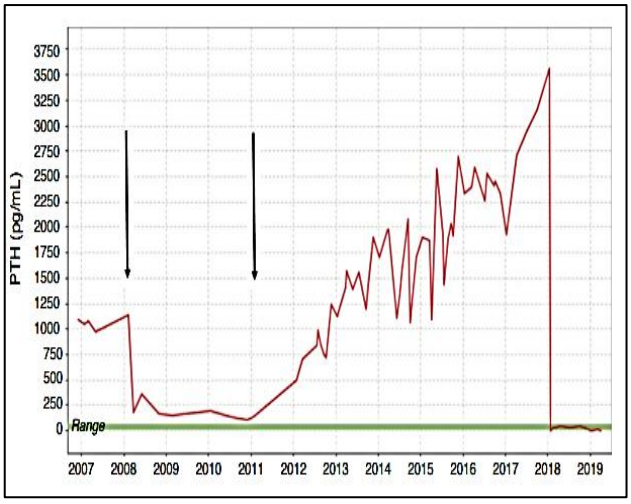

Figure 1: fluctuation in PTH levels from 2007 to 2019. The arrows indicate kidney transplantation performed in 2008 and the acute renal graft rejection before reinitiating the haemodialysis program. Pharmacological preparations for SHPT (calcimimetics, phosphate binders and vitamin d) were used over the course of dialysis.

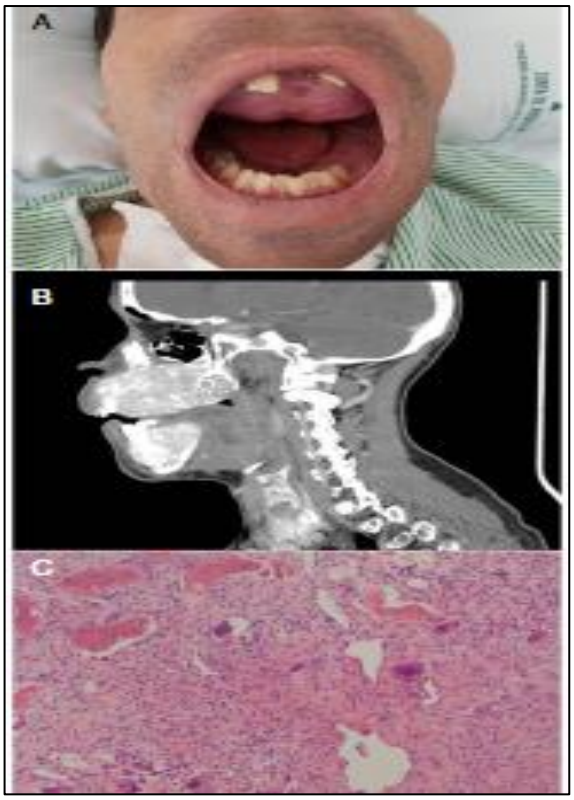

Figure 2: A) deformity of the maxilla and mandible. Brown tumor on the upper palate. B) CT scan of the skull showing diffuse bone disease characterized by obvious deformity of the upper and lower jaw, demineralization of the axial skeleton, and extensive lytic-appearing lesions. C) mesenchymal and multinucleated giant cells, typical of brown tumor (H&E, T50).

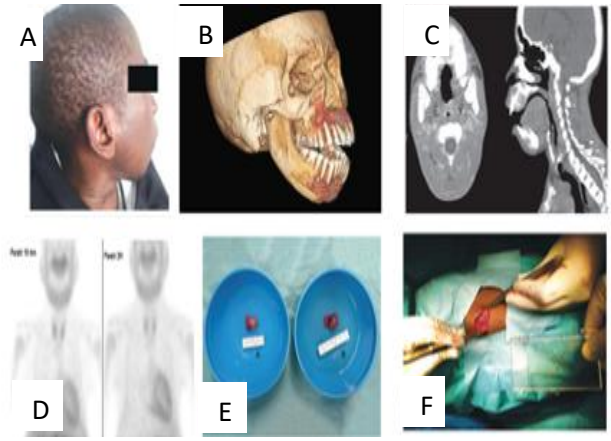

Figure 3: A) Craniofacial appearance of the patient. B) Craniofacial three-dimensional CT-scan reconstruction. C) Benign tumor of the hard palate (arrow) D) Preoperative Tc-MIBI scintigraphy. E) Total parathyroidectomy: (A) Left parathyroids (superior and inferior); ((B) Right parathyroids (superior and inferior)) F) Right forearm parathyroid auto transplant.

Figure 4: 24-year-old woman had obvious facial deformity. (A) Normal appearance four years prior. (B) and (C) Frontal and side photos, respectively, of the craniofacial deformity before parathyroidectomy. (D) Increasing width of dentition with alveolar bone neoplasia. (E) and (F) Frontal and side photos of craniofacial deformity with partial relief 4 mo after parathyroidectomy.[10]

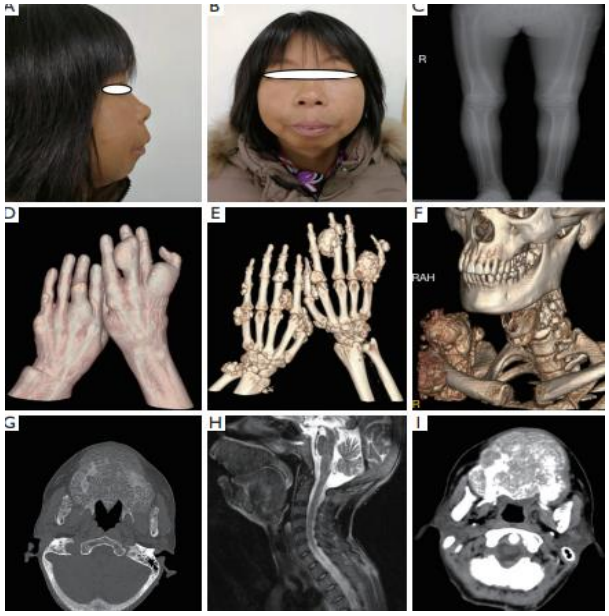

Figure 5: Signs of patient with hyperparathyroidism. (A, B) Maxillary and mandibular bone changes, and dental malocclusion. (C) Long bone deformities. (D, E, F) Multiple ectopic calcifications (G) Skull bone tomography showing salt-and-pepper syndrome in a patient with SS. (H, I) Tumor-like tissue growths in the upper oral cavity under computed tomography and MRI.[16]

During the following 6 years, PTH levels continued to rise from 1000 to 3500 pg/ml despite intensive treatment with sevelamer (3200 mg/8h), paricalcitol (9 mg/IV/3 times a week) and cinacalcet (90 mg/8h). The patient reported headache, fatigue, joint pain and changes in the tips of the fingers. His face displayed a notable frontal protrusion and obvious deformities of both the maxilla and the mandible. Both bones had expanded noticeably losing their normal architecture, causing the teeth to move into an irregular arrangement (Figure 2A). Cranial computed tomography showed diffuse involvement of the cranial base and vault (Figure 2B).

Cervical ultrasound revealed two extra nodular lesions of thyroid below the lower pole of the right thyroid lobe and the lower pole of the left thyroid lobe. On SPECT/CT scan, the only finding was pathological retention of the radiopharmaceutical over the lower end of the left thyroid lobe, suggestive of parathyroid adenoma. In 2017, post biopsy of the upper palate, the presence of a brown tumor was confirmed (Figure 2C).

The characteristic deformities of the face along with the appearance of a brown tumor confirmed the diagnosis of SS. The patient underwent total parathyroidectomy with auto transplantation of a fragment of one of the glands and thymectomy. During the postoperative period, the patient developed hypocalcaemia that was difficult to control, requiring calcitriol, oral calcium carbonate, and intravenous calcium gluconate for 5 days.

After one year of follow-up, his calcium level remained stable and his PTH level was 14 pg/ml. The patient reported feeling subjectively better and there was a slight improvement in his facial features, although he was unable to close his mouth. The postponement of parathyroidectomy for years clearly contributed to the appearance of the functional and cosmetic alterations of his face and hands, and to the presence of difficult to control hungry bone syndrome with a prolonged postoperative stay.[15]

A case reported by Castro et al of a 26-year-old African male from Angola with CKD since he was 15-year-old, and on peritoneal dialysis in the last 6 years, presented to their institution in Portugal to treat his SHPT after bilateral femur fracture. The patient had short stature (152 cm), severe craniofacial and dental deformities (Figures 3A & B), benign tumor of the hard palate (Figure 3C), and obstructive sleep apnea due to his maxillofacial deformity. His serum PTH was >5,000 pg/ml with a seric calcium of 10.2 mg/dl.[17]

After starting haemodialysis and treatment with calcimimentics (cinacalcet 60 mg 1id), phosphate binders (sevelamer 800 mg 3id), and vitamin D analog (alfacalcidiol 0.25 mg 2id), serum PTH is decreased to 1,300 pg/ml. TC-99m MIBI scintigraphy showed bilateral cervical capitation corresponding to the four parathyroid glands and no ectopic foci of capitation (Figure 3D). After adequate preparation, he underwent total parathyroidectomy (Figure 3E) with parathyroid auto transplant on the right forearm (Figure 3F). Intraoperative decrease of serum PTH to 136 pg/ml was verified after 30 minutes of excision of all four parathyroid glands. On the first postoperative day was identified hypocalcemia, even though the patient was receiving prophylactic endovenous calcium carbonate (hungry bone syndrome). The seric calcium level was stabilized on the 5th postoperative day with oral calcium supplementation only.

A study done by Ping et al shows that patients with SS exhibit facial and biochemical anomalies compared to patients with SHPT. Female sex, duration of dialysis, and high serum levels of iPTH and ALP may be potential risk factors for SS (Figure 5).[16]

CONCLUSION

Sagliker syndrome is assumed to be the result of insufficient treatment of SHPT in early stages of CRF. This syndrome is usually observed in developing countries where people are negligent and lack access to necessary medical treatment and do not receive timely treatment for renal insufficiency. Our country, is economically compromised, has the drawbacks in various aspects that could lead to the appearance of SS. Some classic features of SS include progressive CKD, secondary or tertiary hyperparathyroidism with parathyroid hormone-intact levels in the thousands, elevated bone-specific alkaline phosphatase, hypocalcaemia, and hyperphosphatemia.

Physical and radiological changes include short stature, accumulation of facial & skull bones, irregular scattering of bone tumors, maxillary and mandibular expansion of bone resulting in the lateral spreading of teeth, severe destruction of the nasal bones showing a flattened nasal bridge, benign soft tissue growths in the upper part of oral cavity, upwardly curved third phalanx of the fingers, x- or o-type knee deformities, and crippled walking. Brown tumors, a result of parathyroid hormone–driven osteoclastic activity with sclerosis causing abnormal remodelling of the bone, can be seen on imaging but needs to be confirmed with biopsy. Neurologic manifestations, hearing difficulty, and depression are other symptoms occurring frequently.

The universal acceptance of this syndrome is still debated topic, because many characteristics are extreme manifestations of uncontrolled secondary hyperparathyroidism. Currently, the precise pathophysiology of SS remains unknown; although the root pathology is likely to be multifactorial complication of a genetic propensity, combined with late or inadequate advanced CKD and hyperparathyroidism treatment. In the USA where citizens are eligible for Medicare and have access to adequate dialysis, nutrition counselling, and guideline-driven treatment of renal osteodystrophy, hence the development of SS is quite rare. Most case reports are from developing countries and describe young patients who are compromised to receive optimal CKD therapy. Treatment includes aggressive care from the first display of symptoms of SS. Parathyroidectomy is recommended, because most patients have a parathyroid hormone-intact level above 1500 pg/ml.

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REFERENCES

1. Sagliker Y, Balal M, Sagliker OP. Sagliker syndrome: uglifying human face appearance in late and severe secondary hyperparathyroidism in chronic renal failure. Semin Nephrol. 2004;24:449–55.
2. Evans J. Leontiasis ossea; a critical review, with reports of four original cases. J Bone Joint Surg Br. 1953;35:229–43.
3. Cohen J, Diamond I. Leontiasis ossea, slipped epiphyses, and granulosa cell tumor of testis with renal disease; report of a case with autopsy findings. AMA Arch Pathol. 1953;56:488–500.
4. Lee VS, Webb MS, Martinez S, McKay CP, Leight GS. Uremic leontiasis ossea: "bighead" disease in humans. Radiologic, clinical, and pathologic features. Radiology. 1996;199:233–40.

5. Fisher D, Hiller N, Drukker A. Nephroquiz for the beginner: A swollen face in a girl on haemodialysis. Diagnosis: renal osteodystrophy. Nephrol Dial Transplant. 1999;14:1797–8.
6. Shakeri S, Moghadam SZ, Sadeghi R, Ayati N. Sagliker syndrome in a patient with secondary hyperparathyroidism and chronic renal insufficiency: a case report. Asia Oceania J Nuclear Med and Biol. 2018;6(2):167.
7. Mohebi-Nejad A, Gatmiri SM, Abooturabi SM, Hemayati R, Mahdavi-Mazdeh M. Diagnosis and treatment of Sagliker syndrome; a case series from Iran. Iran J Kidney Dis. 2014;8(1):76–80.
8. Yavascan O, Kose E, Alparslan C, Sirin Kose S, Bal A, Kanik A, et al. Severe renal osteodystrophy in a pediatric patient with end-stage renal disease: Sagliker syndrome J Ren Nutr. 2013;23(4):326–30.
9. Lopes ML, Albuquerque AF, Germano AR, Queiroz LM, Miguel MC, Silveira EJ. Severe maxillofacial renal osteodystrophy in two patients with chronic kidney disease. Oral Maxillofac Surg. 2015;19(3):321–7.
10. Yu Y, Zhu CF, Fu X, Xu H. Sagliker syndrome: A case report of a rare manifestation of uncontrolled secondary hyperparathyroidism in chronic renal failure. World J of Clinical Cases. 2019;7(22):3792.
11. Chen XH, Shen B, Zou J, Ding X, Liu Z. Clinical status of Sagliker syndrome: a case report and literature review. Ren Fail. 2014;36:800-3.
12. Yildiz Y, Sagliker O, Demirhan E, Tunc N, Inandikliogl. International evaluation of unrecognizably uglifying human faces in late and severe secondary hyperparathyroidism in chronic kidney disease Sagliker syndrome. A unique catastrophic entity, cytogenetic studies for chromosomal abnormalities, calcium-sensing receptor gene and GNAS1 mutations striking and promising missense mutations on the GNAS1 gene exons 1, 4, 10, 4. J Ren Nutr. 2012;22:157-61.
13. Kidney Disease: Improving Global Outcomes (KDIGO) CKD-MBD Update Work Group. 2017: 1-59.
14. Mejía Pineda AM, Aguilera ML, Meléndez HJ, Lemus JA. Sagliker syndrome in patients with secondary hyperparathyroidism and chronic renal failure: case report. Int J Surg Case Rep. 2015;8:127-30.
15. Dorado MR, Díaz VP, Fontillón-Alberdi M, Padillo-Ruiz J, Martos-Martínez JM. Síndrome de Sagliker. Cirugía española: Organo oficial de la Asociación Española de Cirujanos. 2020;98(7):414-6.
16. Mi JP, He P, Shi K, Feng SY, Chen XZ, He QQ, et al. Cephalometric craniofacial features of patients with Sagliker syndrome: a primary analysis of our experience. Annals of Translational Medicine. 2021;9(12):67-9.
17. Castro LB, Mendes R, Coelho FB, Capella V, Silva AB. Sagliker syndrome: A case report on a rare case of severe renal osteodystrophy due to untreated secondary hyperparathyroidism. World J Endocrine Surg. 2020;12:38-40.

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