Painful Facial Disfiguring Swelling in A 33 Year-Old Male with End-Stage Kidney Disease: A Case Report of Sagliker Syndrome With 2-Year Follow-Up Outcomes

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Abstract
Dialysis-dependent stage 5 chronic kidney disease with renal osteodystrophy can develop a rare and extreme form of cranial deformities called Sagliker syndrome, a condition driven by extreme parathyroid hormone production and characterized by disordered skeletal remodeling resulting in severe facial abnormalities, dental deformities, and possible psychological changes. This paper reports a 33-year-old African American male with end stage kidney disease on maintenance hemodialysis secondary to systemic lupus erythematosus, who presented with severe Sagliker syndrome features in 2019. Herewith, we are describing his course after surgical parathyroidectomy and subsequent course with excessive propensity for hypocalcemia and interval need for medical therapy, biochemical control and the evolution of facial symptoms and disfiguring abnormalities over the next 2 years’ duration.

Keywords: Hypocalcemia; Parathyroidectomy; Parathyroid hormone; Sagliker syndrome

Introduction
Severe facial distortion is a rare but severe complication of severe secondary hyperparathyroidism in End-Stage Kidney Disease (ESKD) patients, almost exclusively observed in those receiving kidney replacement therapy [1]. This uglifying and physically disabling scenario represent an immediate indication for surgical parathyroidectomy [2,3]. However, long-term outcomes after surgical parathyroidectomy, including the persistence or resolution of facial disfiguration remains insufficiently understood.

Case report
A 33-year-old African American male with ESKD on hemodialysis (thrice weekly for 7 years prior to presentation), tertiary hyperparathyroidism, and history systemic lupus erythematosus presented in 2019 with severe facial pain, swelling, and deformity with associated tooth loss. Symptom onset was relatively sudden, with development over a 1-month period prior to evaluation. He denied odynophagia, dysphagia, shortness of breath or neck symptoms, but evaluation was positive for speech difficulties and severe headaches. He reported inscons-
tent cinacalcet (30 mg daily) dosing over the year prior to presenta-
tion; the cost being the limiting factor.

On physical exam, significant facial deformity consisting of
maxillary and mandibular enlargement with associated hyper-
trrophic gums, widening of the dental spaces and tooth loss was
noted. A CT scan showed extensive osseous expansile hyperos-
ostosis with marked extension into the buccal spaces (Figure 1-
a-c). Laboratory studies revealed markedly increased intact
parathyroid hormone level between 1,483-4,000 pg/mL (nor-
mal: 18.4 - 88.0 pg/mL) over a 40-week period prior to inter-
tervention (Table 1). Other lab results included a corrected serum
calcium of 9.16 mg/dL, serum 25-hydroxy-vitamin D of 9.8 ng/
(25.00 - 80.00 ng/mL), serum phosphorus of 7.1 mg/dL, and
alkaline phosphatase of 581 U/L (35-150) with normal liver en-
zymes within 2 weeks of intervention (Table 1). Per radiologic
evaluation via parathyroid scan, there was retained radiotracer
uptake within the superior aspect of the left thyroid lobe and
inferior aspect of the right thyroid lobe consistent with parathy-
roid adenomas. Diffuse musculoskeletal sequela of hyperpara-
thyroidism was also noted.

Urgent subtotal parathyroidectomy with autotransplanta-
tion of the right superior parathyroid into the left sternocleido-
mastoid muscle was completed. Intraoperative parathyroid hor-
mones corrected from 2,500 pg/mL to 170 pg/mL. High calcium
bath (3.5 mEq/L) on hemodialysis preceded parathyroidectomy
in preparation for hypocalcemia after surgery, but severe hungry
bone syndrome ensued post-operatively. Corrected calcium
decreased from 9.7 mg/dL the day prior to parathyroidectomy
in post-operative day one as well as hemodialysis with calcium
bath of 3 mEq/L, with increase in corrected calcium to 8.2 mg/-
dl immediately post-operatively with a nadir of 7.1
mg/dL approximately 10 hours post-operatively. Magnesium
and phosphorus dropped to 1.7 mg/dL and 5.3 mg/dL, respect-
ively. To account for hypocalcemia, the patient was treated with
calcium acetate 2,001 mg with meals, calcium carbonate 1,500
mg four times daily, and calcium gluconate 2 mg IV on
post-operative day one as well as hemodialysis with calcium
bath of 3 mEq/L, with increase in corrected calcium to 8.2 mg/-
dl by then end of post-operative day one.

Due to further downward corrected calcium (7.9 mg/dL)
trends on post-operative day two, the patient was started on
p.o. calcitriol 2 mcg twice daily and, with a further drop in cor-
rected calcium (7.5 mg/dL), intravenous calcium gluconate infu-
sion for the next 2 days. Calcium acetate 2,001 mg with meals and
calcium carbonate 1,500 mcg four times daily were contin-
ued in the interim, as well.

On post-operative day three corrected calcium levels were
measured at 7.7 mg/dL in the morning. Calcium carbonate was
increased to 2,000 mg four times daily and calcium gluconate 2 g
IV twice daily was added to his regimen. He also underwent high
calium bath (3 mEq/L) hemodialysis and continuation of the
8,000 mg/L calcium gluconate infusion. He remained on calci-
um acetate 2,001 mg with meals. Corrected calcium levels were
measured at 10 mg/dL at the end of post-operative day three.

On the morning of post-operative day four, corrected calcium
levels were measured at 7.8 mg/dL. The patient received calci-
um acetate 2,001 mg with meals, calcium carbonate 2,000 mg
four times daily, calcitriol 2 mcg twice daily, and completed the
last day calcium gluconate infusion. The patient also received
two different doses of IV calcium gluconate for symptomatic
hypocalcemia, one 1 g dose and a second 2 g dose. The patient
also underwent high calcium bath (x3) hemodialysis with cor-
corrected calcium levels of 10.5 mg/dL and 9.6 mg/dL by the end
of post-operative day 4.

He was discharged on post-operative day 5 on calcium ac-
etate 1,334 mg with meals, calcium carbonate 2,000 mg four
time daily, ergocalciferol 50,000 units (1 capsule every 7 days)
and calcitriol 2 mcg twice daily as an outpatient. He was also
scheduled outpatient dialytic sessions with high calcium hemo-
dialysis baths.

The subsequent two years were characterized by tremen-
dous need for both intra-dialytic and home supplementation
of activated vitamin-D with calcitriol. Over the first-year post-
parathyroidectomy, daily needs of calcitriol oscillated between
2 and 8 mcg per OS three times per week with dialysis and 1
mcg on non-dialysis days. The need for calcitriol supplementa-
tion peaked at 8 mcg with dialysis 22 weeks post-parathyroidec-
tomy, with gradual decline back to 1.5 mcg over the next year.
Alkaline phosphatase over the 2-year post-operative period av-
eraged 146 U/L after gradually declining from 500s U/L pre-op-
eratively and 397 U/L within a 1-month post-operative period.
PTH remained suppressed in keeping of post-parathyroidecto-
my state (Table 1). At 2-year follow-up laboratory studies revealed corrected se-
rum calcium of 7.5 mg/dL, serum phosphorus of 6.2 mg/dL, and
intact parathyroid hormone of 36 pg/mL. Data beginning prior
to his hospital admission in 2019 through 2021 is displayed in
Figure 2. On interview with the patient at 2-year follow-up, his
facial pain persisted, but with improvement. Pain is especial-
ly present with eating and talking; restricting food intake and
preventing consumption of hard foods. He has lost 3 additional
teeth since his parathyroidectomy. Facial swelling persists with
only minimal improvement per his assessment. There does appear
be improvement in swelling based on initial versus follow-up imaging (Figure 1-a; Figure 3). He has reduced vision
in the left eye; per ophthalmology, this attributed to orbital
compression of Sagliker syndrome. He also has difficulty with
mobility and standing.

Figure 1: Gross appearance and radiology before surgical
parathyroidectomy.

Figure 2: 2-year follow-up laboratory studies revealed corrected se-
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### Table 1: Summary of key bone-mineral metabolism parameters.

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Parathyroidectomy

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**Figure 2:** Parathyroid hormone, calcium, and phosphorus levels over time: 39 weeks prior to and 98 weeks post-parathyroidectomy.

**Figure 3:** Facial swelling and dental abnormalities 2-year post-parathyroidectomy.
Discussion

Sagliker syndrome was first described in publication in 2004 by Sagliker et al. defining the characteristic findings of diagnostic cumulatively seen together in patients with chronic kidney disease and severe secondary hyperparathyroidism[1]. Classic symptoms include maxillary and mandibular deformities and enlargement associated with class II malocclusion of the jaws, dental abnormalities including widely and irregularly spaced teeth with possible tooth loss, benign soft tissue hyperplasia and tumors of the oral cavity, hearing loss, short stature with ambulation difficulties, bone density loss, scapular deformities, fingertip curvature, as well as psychiatric and neurologic disorders[1,4-6].

The frequency of occurrence is 0.5% in patients with chronic kidney disease and severe secondary untreated hyperparathyroidism[1,7]. Although the exact cause leading to the development of Sagliker syndrome in a subset of those with chronic kidney disease is unknown, several studies have been carried out on Sagliker populations in an attempt to identify genetic abnormalities or other factors that may place individuals with chronic kidney disease at risk. Within their studied population sample, Demirhan et al. found mutations in the stimulatory alpha subunit of the Guanine Nucleotide-Binding Protein Gene (GNAS1) a signal transduction modulator (73.9% of patients), fibroblast-derived growth factor-23, and fibroblast-derived growth factor-FGFR3(7). Yıldız et al. also found GNAS1 missense gene mutations in 40% of Sagliker patients within the population they studied[5]. No gene abnormalities within the calcium-sensing receptor exons 2 or 3, nor any significant hormonal or biochemical abnormalities were identified[5]. Multiple studies have found no notably different in thyroid function (including thyroid stimulating hormone, free thyroxine and triiodothyronine levels), growth hormone levels, or sex hormone levels (luteinizing and follicle stimulating hormone levels) in those with Sagliker syndrome and those without[5,6,8].

Commonalities between case studies seem to indicate a young age of onset to be more typical and point towards longer duration of dialysis, female gender, and higher serum parathyroid hormone, phosphate, and alkaline phosphatase levels as potential risk factors[9-12]. Early lack of treatment for chronic kidney disease is also a significant factor, with financial difficulties many times being the underlying cause of delayed treatment[5]. Prior to starting chronic renal replacement therapy, Sagliker syndrome patients typically have serum calcium levels ranging between 6-7 mg/dL, while phosphate and alkaline phosphatase range between 7-8 mg/dL and 120-240 U/L respectively and with intact parathyroid hormone levels at least 3.5 times higher than normal[4,6]. Sagliker syndrome is more typical in anuric subjects, as even minimal renal function can provide phosphate balancing capabilities that prevent extreme parathyroid hormone levels[6,13]. Radiologic appearance may even imitate multiple myeloma and the expected “brown tumor” may not be uniformly present of treated severe secondary hyperparathyroidism, with medical therapy of high-dose cinacalcet and activated vitamin-D products in the current era[14,15].

Sagliker syndrome is treated via parathyroidectomy to reduce parathyroid gland mass; with partial, total, or total with auto-transplantation all being viable surgical options. While partial parathyroidectomy and total with auto-transplantation preserve calcium balance, they place patients at small risk of recurrence[6,10]. Total parathyroidectomy with prior nuclear scan to localize all parathyroid tissue may be the best option, especially for those with indeterminate follow-up potential due to financial concerns[6,10]. Post-operative hypocalcemia can be excessive, necessitating prolonged course of inpatient I.V.calcium, prolonging length of inpatient stay[16]. Previous reports have suggested cessation of further disfigurement or clinical symptoms post-parathyroidectomy[10]. However, as outlined in this case-report, our patient suffered the loss of multiple additional teeth as well as delayed onset orbital compression in the two-year period following parathyroidectomy. Many literature sources report disfigurement attained prior to parathyroidectomy to be permanent, and some patients report only minimal or mild improvement in facial deformity[10,11]. As seen with our patient, swelling persisted, but was overall reduced during the 2 years follow-up. The differential diagnosis, especially for those who fail to improve after surgical parathyroidectomy, should include co-morbid Paget’s disease. Indeed, is possible that the presence of co-morbid severe tertiary hyperparathyroidism is modulating both the course and severity of co-existing Paget’s disease, which may be difficult to recognize if other peripheral manifestations are missing[17].

One peculiar feature of this case was the extend and severity of hypocalcemia and the amount of calcitriol needed to maintain low-normal range of calcium. While hypocalcemia is common, indeed the rule after surgical parathyroidectomy in end-stage kidney disease[18], the duration and severity with calcitriol requirements were unlike we have seen before. While excessive hypocalcemia may be a feature of pharmacologic acid suppression or achlorhydria, interfering with effective absorption of calcium carbonate he did not receive proton-pump inhibitor therapy[19,20]. Moreover, after approximately 1.5 years of high-dose therapy, his calcitriol requirements normalized to a customary and expected range[14].

Conclusion

We have documented persistence of facial abnormalities and excessive nature of post-parathyroidectomy hypocalcemia and calcitriol requirement in an ESKD patient with phenotypical features of Sagliker syndrome.

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Dr. Fülöp is current employee of the United States Veterans Health Administration. However, the views and opinions expressed herewith do not reflect the official views or opinion or endorsed by the United States Veteran Health Administrations.


