



# Saglikler Syndrome: Uglifying Human Face Appearance in Late and Severe Secondary Hyperparathyroidism in Chronic Renal Failure

Yahya Saglikler,<sup>\*,†</sup> Mustafa Balal,<sup>\*</sup> Piril Saglikler Ozkaynak,<sup>†</sup> Saime Paydas,<sup>\*</sup> Cemal Saglikler,<sup>†</sup> Hasan Sabit Saglikler,<sup>†</sup> Necati Kiralp,<sup>‡</sup> Siddik Mumin Adam,<sup>‡</sup> Ilhan Tuncer,<sup>\*</sup> Gulfiliz Gonlusen,<sup>\*</sup> Mustafa Esenturk,<sup>§</sup> Erdal Gocmez,<sup>§</sup> Hulya Taskapan,<sup>||</sup> Mehdi Yeksan,<sup>¶</sup> Ersin Kobaner,<sup>#</sup> Ozan Ozkaya,<sup>\*\*</sup> Musa Yuksekgonul,<sup>‡</sup> Idris Emir,<sup>††</sup> Nurdan Cengiz,<sup>‡‡</sup> Ismet Onder Isik,<sup>§§</sup> Omer Bilginer,<sup>§§</sup> Turgay Guler,<sup>|||</sup> Hasan Yakar,<sup>|||</sup> Nedim Sarsmaz,<sup>‡</sup> Serkan Dilaver,<sup>‡</sup> Balim Akoglu,<sup>‡</sup> Mustafa Basgumus,<sup>¶¶</sup> and Ercin Chirik<sup>##</sup>

Almost every patient with chronic renal failure (CRF) eventually develops secondary hyperparathyroidism (SH) unless they are treated with proper and novel medications in advanced medical centers by skilled medical personnel. Every kind of bone abnormality including skull deformities has been described in detail by almost every concerned researcher and textbook, but descriptions of this phenomenon are limited in the medical literature to the years from 1973 to 1977. To our knowledge, extensive data regarding uglifying human face appearances have not been defined so far in the literature. We are therefore making this addition to the clinical nephrology field by accumulating such data. After we found 2 consecutive peculiar and unique patients with uglifying human face appearances in 2000, we attempted to inform and draw attention to this new entity to all hemodialysis (HD) centers in Turkey, as well as in other developing countries around the world to collect data on this phenomenon. Accordingly, we visited dialysis centers and patients' houses to collect detailed information, including medical clinical histories, physical examinations, laboratory data, biographies, current medications, and so forth. We found 25 patients who had CRF, SH, short stature, extremely severe skull changes, maxillary and mandibular bone changes, teeth/dental abnormalities, and soft and innocuous tumoral tissues in the mouth (hence, uglifying the appearance of the face), fingertip changes, severe psychologic problems, and depression. It appears that patients with CRF may have a new syndrome of bone deformities that have long been neglected, ignored, and forgotten since the mid-1970s when they were first described. This is vital and critical information for the clinical status of patients who suffered from the syndrome that we have named *Saglikler syndrome (SS)*, and we believe there are many more patients in the world who are suffering from it.

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Almost every chronic renal failure (CRF) patient, and especially those in developing countries, will develop hyperparathyroidism (SH) if not treated correctly in the early

phases of the disease. Serum levels of phosphorus (P) increase and levels of calcium (Ca) decrease in these patients.

\*Cukurova University Medical Faculty, Adana, Turkey.

†Saglikler Nephrology-Hypertension Unit, Adana, Turkey.

‡Fresenius Medical Centers, Adana, Turkey.

§Malatya State Hospital, Malatya, Turkey.

||Inonu University Medical Faculty, Malatya, Turkey.

¶Selcuk University Medical Faculty, Konya, Turkey.

#Beysehir State Hospital, Beysehir, Turkey.

\*\*19 Mayis University Medical Faculty, Samsun, Turkey.

††Emir Dialysis Center, Antakya, Turkey.

‡‡Baskent University Medical Faculty, Adana, Turkey.

§§Kahramanmaraş State Hospital, Kahramanmaraş, Turkey.

|||Osmaniye State Hospital, Osmaniye, Turkey.

¶¶Olmezler Dialysis Center, Konya, Turkey.

##Cukomes Radiology Center, Adana, Turkey.

Address reprint requests to: Yahya Saglikler, MD, Professor of Medicine, Saglikler Nephrology and Hypertension Unit, Ziyapasa Bulvari, Ciritcioğlu Apt., Kat 1, Adana, Turkey. E-mail: sagerya@superonline.com



**Figure 1** Top row showing current uglified human face appearances. Bottom row shows previously taken normal facial photographs.

These changes occur initially because of phosphate (P) retention and later because of vitamin D deficiency. Hence, serum alkaline phosphatase levels increase and, eventually, parathyroid hormone levels increase. As a result of these fluctuations, SH takes place and, consequently, skeletal changes develop. These latter changes in patients with CRF include renal rickets, growth point changes in bones in children, subperiosteal changes in nearly all bones, osteosclerosis, untidy parallel bone changes noticeable when wearing sleeveless shirts (rugger jersey appearance), smooth tissue accumulations (brown tumors), ground-glass appearance, salt and pepper skull, and so forth. Osteoporosis and aluminum-induced bone changes in patients with CRF who consume aluminum-based phosphate binders also can occur.

There are numerous reports and pictures showing multiple types of changes in almost every part of the skeleton including the ulna, clavicles, spine, hand, and long bones.<sup>1-7</sup> There are also some texts and pictures that draw attention to skull changes in patients with SH and CRF,<sup>5-7</sup> but they date back to early years of nephrologic reports. It may be possible to find a few cases of skull and face changes in the literature, but to our knowledge, there are meager data on the subject of uglifying human face appearance.

## Methods

After encountering 2 consecutive patients in 2000 in the Division of Nephrology-Hypertension at the Cukurova University

Medical Faculty, we attempted to inform and draw attention to this subject by giving 5 different conferences on this matter in different cities such as Izmir, Mersin, Adana (Turkey), Taormina (Italy), and Varna (Bulgaria), and have been invited to give lectures in 2 other cities (Karachi, Pakistan, and Kosice, Slovak Republic) to collect data on patients with these types of abnormalities, including extremely severe changes to the skull and face. Beginning in March of 2003, we sent approximately 1,500 letters and e-mails to almost all hemodialysis (HD) centers in Turkey. We also sent similar e-mails, particularly to HD centers in developing nations such as Pakistan, India, Iran, Egypt, and Singapore, as well as to most of the European countries and some states in the United States. We inquired whether or not patients with these types of skull and facial appearance changes, particularly in uglifying fashion, have been encountered in HD centers. We encouraged and advised HD centers to request previous pictures of the patients' faces taken several years earlier to compare them with pictures taken recently. We received about 20 letters or e-mails from approximately 20 HD centers indicating that they have encountered these types of peculiar and unique cases.

We personally visited with a 5-person team composed of 2 doctors and one nurse all of the HD centers that had responded. In addition, we also visited the patients in their houses and met their family members. We took their current contemporary face and body pictures and requested copies of their previous pictures and family photo albums, which in-

**Figure 2** Picture showing differences in heights between brothers (patient on the right is 9 years old; in the middle is his healthy younger brother aged 8, and on the opposite side is the youngest brother aged 7).



cluded pictures of other family members. We also took medical histories, performed physical examinations, requested available medical data, collected the patients' biochemical values, radiographs and tomographies of their bones, and evaluated their current treatment modalities.

## Results

These efforts yielded the discovery of 25 patients with moderate to severe bone deformities. The first 4 patients had severe uglifying human face appearances and had an unbelievably different facial appearance in current photographs as compared with those taken several years earlier (Fig. 1). The other 21 patients also had almost as severe a degree of uglifying human face appearance. They all had very short stature and were shorter than their younger brothers or sisters (Fig. 2).

Skull tomographies taken from the patients showed extremely unique and peculiar irregularities and bone density

changes, both in the sagittal views and from the temporal angle (Fig. 3). There also was maxillary, mandibular, and nasal bone destruction (Fig. 4). Their teeth were irregularly shaped and located (Fig. 5). Most of them had soft, large, tumor-like tissue accumulations, particularly in the upper side of the oral cavity (Fig. 6). Although expecting to find the typical soft-tissue calcification pattern of SH in CRF, we have encountered only fairly regular and benign mucosal epithelial cell hyperproliferation of the mucosal cavity, caused solely by the compression from the upper maxillary side of the bones in the oral cavity.

In some patients, we also found peculiar and unique findings in the fingertips, with upward curves in the third phalanges (Fig. 7). Among the most striking common patterns for these patients were psychologic problems and depression. All patients had typical biochemical serum Ca values averaging 6 to 7 mg/dL, P levels of 7 to 8 mg/dL, increased levels of alkaline phosphatase (120-240 U/L), and at least 3.5 times greater values than normal for intact parathyroid hor-



**Figure 3** Radiographs of the skull showing salt and pepper appearance and round and large radiolucent areas.

mon levels (180-240 pg/mL by immunoradiometric assay [IRMA] assay) before entry to HD treatments and current values were fluctuating around normal values. None of the patients had high aluminum levels. All patients were taking calcium acetate or carbonate orally, 1.25 (OH)<sub>2</sub> vitamin D<sub>3</sub> preparations either orally or intravenously, or 1-alfa analogues of vitamin D regimen orally. None of the patients were taking aluminum preparations. Two of the patients had parathyroid surgery. None of the HD centers that reported these patients had high aluminum levels in their dialysis fluids and they all used a reverse-osmosis water purification system.

## Conclusions

Patients who have CRF who are not treated early with proper medications and in the proper way eventually develop varying degrees of changes in their skull as described in the literature.<sup>5-7</sup> To our knowledge, such peculiar and unique uglifying human face appearances caused by maxillary, mandibular, dental, and nasal bone changes and destructions have not been described widely. The last available pictures of skull deformities was found in texts dating back to the mid-1970s (1973 to 1977) and this phenomenon largely has been neglected, ignored, and forgotten in clinical nephrology texts. These bone changes include: short stature, extremely

severe skull changes, extremely severe maxillary and mandibular changes, severe teeth/dental abnormalities, soft and benign tumor-like tissue accumulations in the mouth, uglifying human face appearance, and fingertip changes.

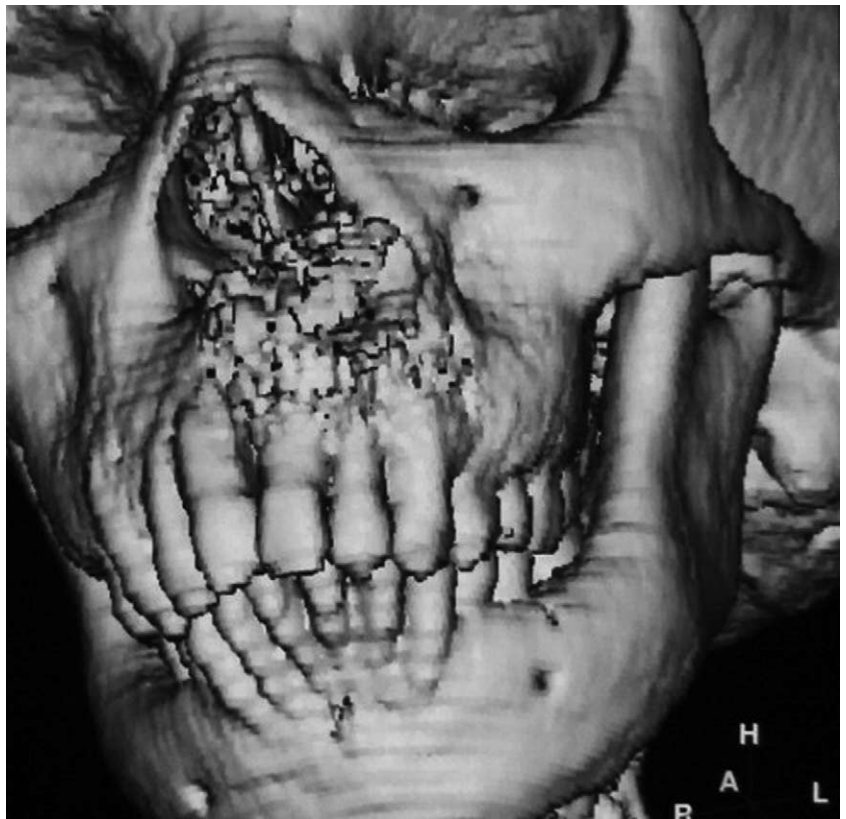
The patients also may develop psychologic problems and suffer from depression because of these deformities. These bone changes may collectively be called the *Sagliker syndrome*.

We believe there are still hundreds of hidden and silent patients with such signs and symptoms throughout the world, particularly in developing countries where therapy of secondary hyperparathyroidism is not optimal. The incidence of *Sagliker syndrome* may be approximately 0.5% because of the detection of these 25 patients in a population of 5,000 patients currently undergoing hemodialysis treatment in Turkey.

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**Figure 4** Tomograph taken with modern technology showing nasal and left maxillary destructions.



**Figure 5** Irregularly developed upper and lower teeth.



**Figure 6** Photograph taken from the mouth showing 4 separate soft and benign, mucosal, cellular hyperproliferations of the upper part of the mucosal space such as tumoral tissue and opportunistic ulcerations.

**Figure 7** Peculiar appearance of the fingertips, upward curved development of the third phalanges.



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