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Short communication

Lindsay's Nails and Terry's Nails in End Stage Renal Disease - Case Series

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Abstract

Introduction. Nail changes occur as part of a single organ disease, multisystemic diseases or because of the intake of some medications. Chronic kidney disease (CKD) is associated with various nail abnormalities. To identify Lindsay's nails and Terry's nails in patients with end stage renal disease (ESRD) on maintenance hemodialysis (HD) and to determine the common anamnestic, clinical and/or laboratory parameters that would help elucidate the etiopathogenesis of these nail pathology.
Methods. Twenty patients with ESRD on hemodialysis were included into the study. Dermatological examination took place during the dialysis session. Lindsay's nails were identified when the distal part of the nail bed is red/rose-brown, clearly separated from the proximal part of the nail bed, occupying 20-60% of the entire length of the nail bed. The proximal part of the nail bed is whitish, resembling grounded glass. When pressing the nail, the discoloration of the distal part of the nail bad does not fade completely. Terry's nails were identified by a 0.5-3.0 mm wide distal band, pink-brown in color, with a proximal part of the nail bed that is white and occupies 80% of the entire nail bed. Data on demographic characteristics, history of the disease and the laboratory values were noted for each patient.
Results. Out of 20 patients, all males, we diagnosed Half-and-Half nails, also called Lindsay's nails, and Terry's nails in 6(30%) patients [5 Half-and-Half nails (25%), and 1 with Terry's nails (5%)]. All patients had sideropenic-free anemia, elevated urea and creatinine values and elevated parathyroid hormone (PTH) values (>190 pg/L, range 190.3-387.5 pg/L).
Conclusion. After searching the relevant literature (MEDLINE, PubMed), we found this is the first study to link elevated PTH values and Half-and-Half nails (also called Lindsay's nails), and Terry's nails in patients with ESRD on HD.

Keywords: Lindsay's nails, Terry's nails, end stage renal disease, hemodialysis, etiopathogenesis

Introduction

Nail changes can be associated with or may be due to systemic disorders. These disorders occur as part of some single organ disease, multisystemic diseases or because of the intake of some medication. Chronic kidney disease is associated with various nail abnormalities such as Half-and-Half nails, absence of lunula, onychomycosis, leukonychia, onycholysis, splinter hemorrhage, Terry nails, subungual hyperkeratosis, Mees' lines or acropachy. The representation of these changes in CKD patients ranks from 52% to 71% [1-3].
One of the most common nail pathologies in patients with ESRD on chronic HD is Half-and-Half nails or Lindsay's nails. For the first time, Half-and-Half nails were described by Bean, 1963 [4] in two patients with renal insufficiency and azotemia. In published literature, Lindsay's work [5] is more cited, defining Half-and-Half nails as clearly limited discoloration with red/rose-brown color of the distal part and affection of 20–60% of the length of the nail bearing. The discolorration of the distal part does not fade completely after pressing the nail. The proximal part of the nail bearing is white, resembling coiled glass. One or all of the fingernails and toenails may be affected. The prevalence of Half-and-Half nails in HD patients in various studies ranged from 7.7% to 50.6% [2, 6-10]. Lindsay nails are not a specific phenomenon in CKD patients, but also occur in other diseases such as Morbus Crohn (with or without associated zinc deficiency), Morbus Behcet, in patients receiving isoniazide, cytostatic therapy or may be idiopathic [11-15]. Half-and-Half nails have been observed in a patient with a severe clinical picture of COVID-19 infection [16].
Similarly, Terry's nails have been also found in HD patients. The essential difference in the clinical picture is that in Terry's nails, the distal band is less than 20% of the total length of the nail bed presented as 0.5-3.0 mm wide distal band, pink-brownish painted, and a proximal part of the nail bed that is whitened and covers 80% of the entire surface of the nail bed. Although promoted as one of the signs of hepatic cirrhosis [17] and an

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early sign of autoimmune hepatitis [18], Terry's nails are often associated with chronic congestive heart failure, chronic renal insufficiency, hematological diseases and adult diabetes mellitus, but may also occur in healthy individuals as part of the physiological aging process [19]. Pathophysiology responsible for nail transverse discoloration in HD patients is not fully clarified. Proximal white band is thought to be a consequence of chronic anemia, and distal rosemary or brown band is the result of melanin deposition, probably stimulated by uremic toxins.
The aim of our paper was to determine common history, clinical and/or laboratory parameters that would help disclosing the etiopathogenesis of Half-and-Half nails and Terry's nails in patients with ESRD on HD.

Materials and methods

This is an observational descriptive study conducted at the University Clinic for Nephrology, Skopje, N. Macedonia. We have examined a series of six patients with ESRD on chronic HD program with a clinical picture of Half-and-Half nails or Lindsay's nails and Terry's nails. The inclusion criteria were: patients with glomerular filtration rate (GFR) <15 ml/min/1.73m^2 being on chronic HD > 3 months, age ≥18, with a written informed consent for participation in the study. The exclusion criteria were: patients with Morbus Crohn and Behcet, those receiving isoniazid or cytostatic therapy, or those with congenital, systemic or primary skin disorders that contribute to nail change, the use of any colors/paints, nail injuries or infection, Carpal Tunnel Syndrome, ischemic syndrome secondary to arterial-venous fistula.
A clinical examination was performed of the fingernails and toenails in 20 patients with ESRD on a chronic hemodialysis program in the University Clinic for Nephrology. The dermatological examination to evaluate nail changes of the type of Half-and-Half nails and Terry's nails took place in the dialysis centre during the dialysis session. The room was illuminated by natural daylight, ceiling electric lighting, and a hand-held additional lamp was used for the examination of the nails when needed. Half-and-Half nails or Lindsay's nails and Terry's nails were diagnosed clinically based on diagnostic definitions for both nail changes.
Data on demographic characteristics (age and gender) were provided for each patient, the history of the disease (primary cause for ESRD, standard therapy, HD duration) and for laboratory values of medical histories [hemoglobin, ferritin, calcium, phosphorus, albumins, creatinine, urea and parathormone (PTH)], (Table 1).

Table 1. Demographic data, disease history data and laboratory parameters

	Patient 1	Patient 2	Patient 3	Patient 4	Patient 5	Patient 6
Age (years)	67	47	53	66	58	74
Sex	Male	Male	Male	Male	Male	Male
HD duration	8	6	6	8	25	9
Primary cause for ESRD	MesPGN	HTN	APKD	Bilat. Nx due to kidney cancer	UND	Bilat. RPD
Hemoglobin (g/L)	113	103	88	113	131	110
Ferritin (μg/L)	697.2	605.7	296.4	679.1	73.9	469.2
Urea (mmol/L)	20.3	20.2	29	16.5	24.1	16.8
Creatinine (μmol/L)	731	713	1019	709	868	88
Albumin (g/L)	45	45	35	47	41	41.8
Parathormone (pg/ml)	387.5	265.9	268.2	190.3	264.9	277.6
Medications	Fe, ESA, CaCO3, vit. D3, CCB, ACT, statin, BB, DIU	Fe, ESA, CaCO3, vit. D3, ACT, CCB	Fe, ESA, CaCO3, vit. D3, ACT, CCB	Fe, ESA, CaCO3, vit. D3, ACT, CCB	Fe, ESA, CaCO3, vit. D3, ACT, vit. C, BB, statin, PDN, ASA	Fe, ESA, CaCO3, vit. D3, statin, PPI, NSAID
Nail changes	Terry's nails	Half-and-Half nails	Half-and-Half nails	Half-and-Half nails	Half-and-Half nails	Half-and-Half nails

Abbreviations: MesPGN= Mesangial proliferative glomerulonephritis; HTN=Hypertensive nephropathy; APKD=Adult polycystic kidney disease; Bilat Nx= Bilateral Nephrectomy; UND= Undifferentiated; RPD=Renal parenchymal disease; ESA=Erythropoietin-stimulating agent; $CaCO_3$=calcium carbonate; Fe= Iron; vit=vitamin; CCB= calcium channel blocker; ACT= Anticoagulant Therapy; Statin= HMG-CoA reductase inhibitors; BB= Beta blocker; DIU= Diuretic; PDN= Prednisone; ASA= Aminosalicylate;PPI= Proton pump inhibitor

Results

In 6 out of 20 patients with ESRD on hemodialysis, n=20 (14 men, 6 women) who underwent a dermatological examination, nail changes of type Half-and-Half nails and Terry's nails were diagnosed (30%). Half-and-Half nails were diagnosed in 5 patients (25%), and only 1 patient was diagnosed with Terry's nails (5%). The images with nails changes of fingernails and toenails are presented in Figure1.

All six patients were men. The mean age of patients was 60.83±9.99 years (ranging from 47 to 74 years). The mean hemodialysis duration was 10.33±7.28 years (in the rank of 6 to 25 years). Half-and-Half nails were equally present on both hands and feet in patients of our series. None of the patients knew how to indicate a time or an event related to the nail changes. All 6 had the same comment that they had noticed nail changes over the years, but before the dermatological examination they were not even aware that it could be of any importance related to CKD and/or dialysis. The cause of CKD was different in each individual patient. All patients had anemias without sideropenia, low-hemoglobin and elevated ferritin levels, expectedly elevated urea and creatinine levels, and no patient had hypoalbuminemia. Chronic medication therapy was identical in all 6 patients. PTH levels were elevated (>190 pg/L, range 190.3-387.5 pg/L) in all 6 patients, as well.

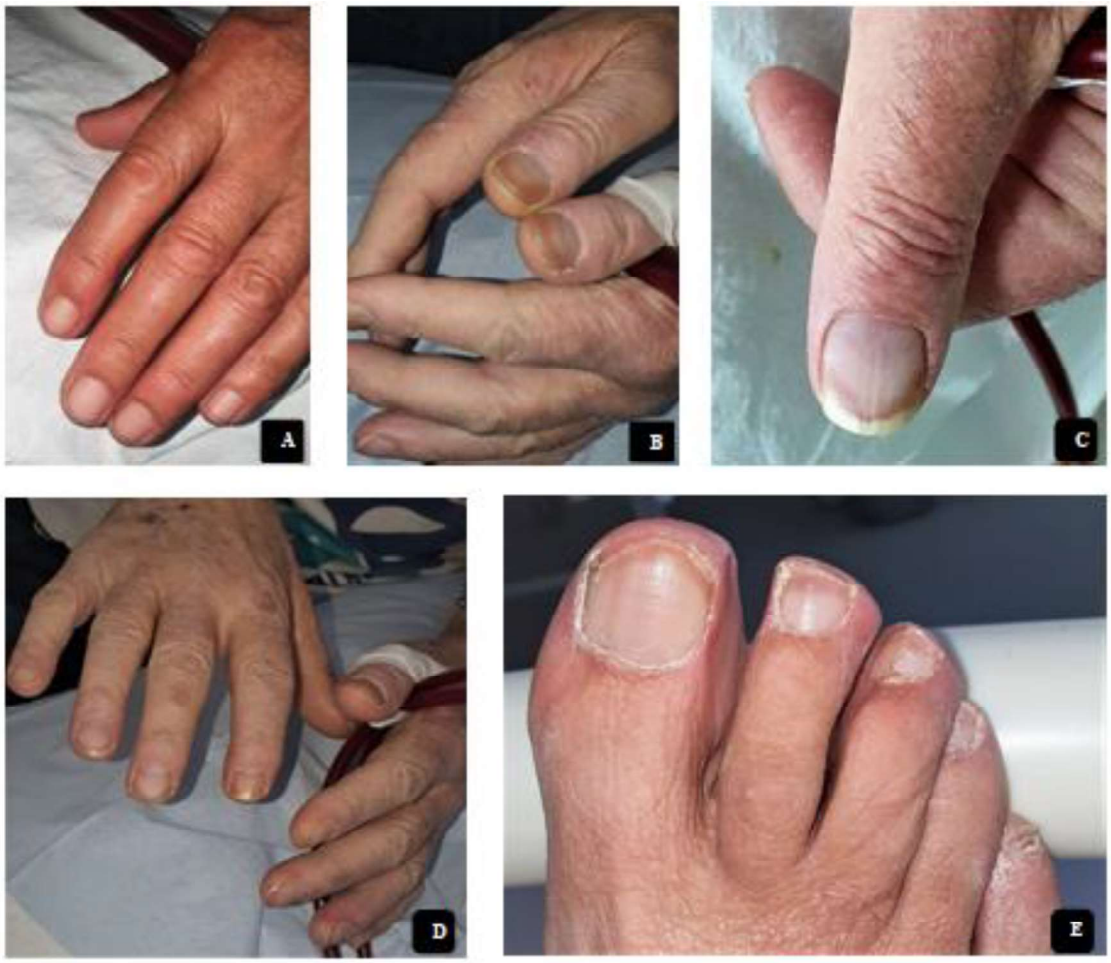

Fig. 1A. Terry's nails - a 1 mm wide distal band with brown color and a distal whitish part that covers 90% of the entire surface of the nail bed. **B.** Half-and-Half nails - red/brown color of the distal part of the nail bed, covering 60% of the entire length of the nail bed and a proximal part of the nail with grounded glass color. **C.** Half-and-Half nails - a clearly expressed demarcation zone between distal and proximal discoloration. **D., E**. Half-and-Half nails - more fingernails and toenails are affected

Discussion

Our case series of patients with Half-and-Half nails and Terry's nails represented 30% of total ESRD patients on HD that underwent examination This proportion fits with numbers in the reports from other studies where the prevalence of this type of nail changes in HD patient stages from 7.7% to 50.6% [2]. There is also evidence that in certain cases these nail abnormalities withdraw after several months of successful kidney transplantation, while in others the prevalence is higher in transplanted patients compared to patients on hemodialysis [20]. Half-and-Half nails can occur on one or all fingernails and toenails. However, this condition is more common on the fingernails. In our study, Half-and-Half nails were observed equally on both fingernails and toenails, all 6 patients being males. In the literature, the ratio males/females is reported as 2:1, while another case control study did not observed any gender difference [2]. There were various causes for renal insufficiency: mesangial proliferative glomerulonephritis (MesPGN), hypertensive nephropathy or nephroangiosclerosis (NAS), adult polycystic kidney disease (APKD), bilateral nephrectomy due to urothelial cell carcinoma (TCC) on the left and hydronephrosis on the right kidney, undifferentiated chronic kidney disease, and unknown bilateral renal parenchymal disease. All patients received identical therapy, although the duration of HD and age varied widely. Anemia, elevated urea and creatinine levels, and secondary hyperparathyroidism (sHPTH) with PTH values >190 pg/L were present in all patients. These findings are similar to the findings of the Study of Dyachenko et al. from 2007, which indicates the prevalence of nail changes in patients with CKD is not significantly dependent on age, gender, duration of CKD, medication or underlying disease that caused ESRD. This study of Dyachenko *et al*. established a significant correlation between these particular nail changes and PTH > 220 µlEq/mL or 2.06 (1.34-4.52).

Lindsay's nails and Terry's nails pathogenesis is not fully clarified so far. There is an opinion that the red-brown distal tape is due to melanin deposition in the nail plate and/or increased capillary density [21,22]. In the study Fernandez-Somoa *et al*. from 2021, capillaroscopy has not determined an increased amount of melanin. Instead, a dilation of the venous plexus from the nail bed has been found [23]. It is considered that proximal white band is caused by chronic anemia, increased thickness of capillary walls and excessive growth of the connective tissue between the nail and bone.

After searching the relevant literature (MEDLINE, PubMed), we found no study describing the connection of sHPTH to Half-and-Half nails and Terry's nails. sHPTH is a common disorder in patients with HBB and is characterized by increased levels of PTH in serum, parathyroid hyperplasia and calcium and phosphorus metabolism disorder. sHPTH develops in the early stages of CKD and worsens by the reduction of renal function. PTH is the major uremic toxin responsible for long-term consequences such as renal osteodystrophy, vascular calcification, alterations in cardiovascular structure and function, immune system dysfunction and anemia. These adverse effects contribute to increased mortality and morbidity from cardiovascular disease in patients with ESRD patients [24]. PTH has a vasorelaxant effect on smooth muscle cells of the blood vessels and is a potent activator of endothelial nitrogen oxide synthesis [25]. Thus leading to vasodilation of small blood vessels. The elevated PTH levels in all patients in our case series leads to the hypothesis that sHPTH in ESRD patients on HD might be responsible for red/brown color of the distal part of the nail plate due to the vasorelaxation of the blood vessels and the increased synthesis of endothelial nitrogen oxide resulting in an enlarged venous plexus of the nail bed. Anemia and deposits of calcium in blood vessels caused by the elevated levels of PTH create a microenvironment of hypoxia responsible for the proximal white coloration of the nail plate.

Conclusion

This study was designed to determine common history, clinical and/or laboratory parameters that would help disclosing the etiopathogenesis of the Half-and-Half nails and Terry's nails in patients with ESRD on HD. All patients from this case series had low hemoglobin and elevated PTH levels. sHPTH originates the hypothesis that PTH with its vasorelaxant and vasodilatation effect is responsible for the presence of dilated venous plexus in the nail bed and red-brown discoloration of the distal part of the nail. Conversely, the white color of the proximal part of the nails may be due to the anemia and calcium deposits of calcium in the blood vessels wall caused by the increased PTH, which create hypoxia and the growth of connective tissue between the bone and the nail plate. To prove this hypothesis, studies with a larger number of ESRD patients on HD are needed to determine PTH levels, capillaroscopic evaluation of blood vessels and high-frequency ultrasonography to evaluate calcium deposits of blood vessels.

Conflict of interest statement. None declared.

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