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Half and half nails: an important sign in the diagnosis of systemic diseases

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Abstract:

Half-and-half nails, also called Lindsay's nails, are a highly specific nail abnormalities for chronic kidney disease; however, the occurrence of half-and-half nails in the course of zinc deficiency, liver cirrhosis, pellagra, Kawasaki disease, Crohn's Disease, Behcet's Disease, citrullinemia, hyperthyroidism, systemic cancer therapy, and yellow nail syndrome, as well as in healthy people was also reported. Half-and-half nails can occur on both, fingernails and much less often on toenails, and are usually described as the proximal white part and the brown, pink or red distal band which are sharply demarcated by the transverse line. The pathogenesis of half-and-half nails is still unclear. Factors that may be involved in the pathogenesis of half-and-half nails include an increase in the thickness and number of capillaries in the nail bed, zinc deficiency, hypoalbuminemia, azotemia, and the accumulation of toxic metabolism products in the body.

Keywords: half-and-half nails; nails changes; chronic kidney disease; systemic diseases

Introduction

Half-and-half nails, also called Lindsay's nails, are a specific nail abnormalities mainly associated with chronic kidney disease (CKD), with a prevalence of 15-50% in patients with CKD [1] compared with 1-2% among all hospitalized patients [2]. Half-and-half nails can occur on both, fingernails and much less often on toenails [3], and are usually described as the proximal white part and the brown, pink or red distal band which are sharply demarcated by the transverse line. The distal band usually occupies 20-60% of the length of the nail [4,5]. Additionally, it was noted that these nails changes do not disappear with the pressure of the nail plate [6]. Bean et al. in 1963 first described nail changes corresponding to half-and-half nails in 2 patients with renal failure; [3] however, Lindsay in 1967 used the term "half-and-half nails" as first [7]. The youngest reported patient was a 7-year-old girl with half-and-half nails associated with chemotherapy; [4] while the two oldest patients were 79-year-old men with renal disease [7]. The incidence of half-and-half nails in addition to CKD was also described in the course of zinc deficiency, liver cirrhosis, pellagra, Kawasaki disease, Crohn's Disease, Behcet's Disease, citrullinemia, hyperthyroidism, systemic cancer therapy, and yellow nail syndrome, as well as in healthy people [2,4].

Pathogenesis of half-and-half nails

The pathogenesis of half-and-half nails is still unclear [1]. These nail abnormalities do not disappear with the increase of the nail plate, which suggests that the pathogenesis of this syndrome is associated with the nail bed, and not with the nail plate or nail matrix [6,8]. Two facts may confirm this hypothesis. First, in the nail bed of the nails with the half-and-half nails syndrome an increase in the thickness and number of capillaries was observed [6]. Secondly, the occurrence of half-and-half nails in patients with Behcet's disease, in whom enlarged capillaries were also observed in capillaroscopy [9]. Studies conducted by Leyden and Wood, in which a nail biopsy was performed, showed accumulation of melanin in the distal nail band [4]. This may suggest that toxic metabolites accumulated in the body in the course of chronic renal failure may stimulate the production of melanin due to the activation of melanocytes present in the nail matrix and resulting in increased release of B-melanocyte-stimulating hormone [6,10]. The influence of azotemia on the pathogenesis of half-and-half nails remains unclear. It was demonstrated that the length of nail band is not related to the severity of CKD [11], the level of azotemia, proteinuria, total albumin and protein levels, as well as serum creatine concentration [3,7]. However, the explanation of the importance of azotemia in the pathogenesis of half-and-half nails is important due to the high prevalence of half-and-half nails

in CKD, suggesting a significant association between half-and-half nails occurrence and the high levels of laboratory renal function markers. Lindsay hypothesized that the occurrence of distal band of the nail is related to the constriction of veins that drain blood from the nail bed [7]. In patients with half-and-half nails observed in the course of Crohn Disease (CD) zinc deficiency and hypoalbuminemia were noted; however, the role of zinc and albumin levels in the pathogenesis of half-and-half nails remains unclear [12,13]. So far, the cause of occurrence of half-and-half nails in healthy people has not been recognized. The persistence of half-and-half nails in patients on dialysis, in relation to the disappearance of this symptom after successful kidney transplantation is also unclear. Further research are necessary to fully understand the pathogenesis of half-and-half nails.

Occurrence of half-and-half nails in the course of systemic diseases

Chronic kidney disease (CKD)

Half-and-half nails are highly specific for CKD. In the course of CKD, numerous skin manifestations including xerosis, nephrogenic systemic fibrosis, acquired perforating dermatosis, access site infections, and acquired perforating dermatosis were observed [6]. Frequent nails changes in the course of CKD are: half-and-half nails, splinter haemorrhages and absent lunula [14]. Half and half nails were reported in patients with both, IV and V stage of chronic kidney disease [3,14]. The occurrence of half-and-half nails has been reported in patients with renal failure occurring in the course of diabetes mellitus [1,2], hypertension [11], diabetes mellitus with hypertension [15], diabetes mellitus with HCV infection and secondary liver cirrhosis [16], polycystic kidney disease [17], and systemic lupus erythematosus [3]. The youngest patient with CKD, in whom half-and-half nails were observed was a 10-year-old boy with lesions on all 20 nails; [18] while the oldest patients were two 79-year-old men [7]. In hemodialyzed patients, half-and-half nails are occur with frequency of 70% [14]. To date, no correlation has been demonstrated between the severity of azotemia and the expanse of the distal color band of half-and-half nails [1]. The symptom may persist despite regular dialysis; however, it has been resolved after successful kidney transplantation [1] within two to three weeks [4]. In 1963 Bean et al. reported the occurrence of nail lesions corresponding to half-and-half nails in two patients with renal insufficiency; while in 1967, Lindsay described the occurrence of half-and-half nails in 25 patients. In 24 patients, renal disease was diagnosed, of which 21 patients had azotemia, 2 patients had cylindruria without azotemia, and one patient had reduced creatine clearance without azotemia [7].

Crohn's disease (CD)

Crohn's disease (CD) is a chronic, autoimmune inflammatory disease that can affect various parts of the gastrointestinal tract, as well as other organs [19,20]. Extraintestinal manifestations of CD include eyes, joints, pulmonary system, kidneys, biliary tracts, skin, and others [19,20]. It is estimated that cutaneous manifestations occur in 9-23% of patients with CD [19]. In a study conducted on a group of 124 patients, which included 53 healthy individuals and 71 patients with inflammatory bowel disease (CD or CU), the presence of nails changes in patients was examined. The incidence of half-and-half nails was found only in the group of patients with CD, with a prevalence of 4,5% [19]. To date, five cases of half-and-half nails in patients with CD have been reported [12,13,19]. In 2006, Zagoni et al. described the occurrence of half-and-half nails in the course of CD. They presented case reports of four male patients with normal renal function aged 27-29, with an average CD duration of 5.25 years (6-13 years). All patients had zinc deficiency; however, there was no iron deficiency or hypoalbuminemia. It is worth emphasizing that nail changes were maintained in all patients regardless of the treatment used, as well as the disease activity [13]. Pellegrino et al. described the case of a 53-year-old man with a CD duration of 23 years, with half-and-half on both, fingernails and toenails, with additional erosive lesions of the right big toe. During the diagnostic process, the microbiological background of nail plate changes, liver and kidney function disorders were excluded, and no anti-dsDNA antibodies were found. The results of urine tests, thyroid hormones, blood counts were also correct. The level of zinc in the serum was normal, the only abnormality in the laboratory tests was a slight hypoalbuminemia. Histological examination of the nail plates revealed areas of Malpighian hypertrophy and verruciform hyperplasia [12].

Behcet's Disease (BD)

Behcet's disease (BD) is a rare disease of unknown etiology that belongs to the group of systemic vasculitis and is most common in the third and fourth decade of life. The clinical manifestation includes the triple symptom complex which consists ocular lesions, oral aphthous ulcers, and genital sores [21]. Studies on patients with BD have shown that the dominant lesions observed in the capillaroscopy were enlarged capillaries (26%) and hemorrhages (16%). Loss of capillaries was observed in 0.8% of patients. 70% of patients did not show any changes in the capillaroscopy [9]. The first case of half-and-half nails in 31 year-old man with BD was described by Sahin et al. The first symptoms of Behcet's disease appeared at the age of 15, and the final diagnosis was made after 12 years. In addition, the patient had artery aneurysm. The patient was treated with colchicine, which he took irregularly; however, changes corresponding

to half-and-half nails were observed before starting the therapy with colchicine. Similar nail changes also occurred in the close relatives of the patient. There were no abnormalities of liver and kidney function, as well as other abnormalities in laboratory tests. A fungal etiology of nail changes was also excluded [22]. The case of a 38-year-old man with BD and a HIV infection, in which half-and-half nails were observed, was reported by Mahajan et al. Laboratory tests revealed anemia (8g/dl), as well as a high level of ESR (115mm), in addition a significant reduction in the CD4 to CD8 ratio (0.07, N: 0.6-2.8) was observed, the others results of laboratory tests were normal [23]. In 2014, Gonul described the case of a 27-year-old woman with BD, in whom half-and-half nails were observed in all the fingers of the hands. Due to hypothyroidism, the patient has been using thyroid hormones for 3 years. The results of laboratory tests, including renal and hepatic function, were normal [24].

Chemotherapy

In studies conducted on a group of 150 patients aged 12-73 years undergoing cancer chemotherapy, nails changes were observed in 50 patients, and were the most common in patients receiving platinum based agents (54%). The most frequent lesions of the nail plate were changes in pigmentation (16.1%). Half-and-half nails were most frequently observed in patients receiving cyclophosphamide- hydroxydaunorubicin- oncovin- prednisone (CHOP) chemotherapy [10]. The case of a 7-year-old girl with half-and-half nails in the course of the chemotherapy was described by Afsar et al. The nails changes occurred one month after the therapy according to the modified Berlin-Frankfurt-Munster protocol and the maintenance therapy in which 6-mercaptopurine and methotrexate were used. The results of laboratory tests, including kidney function, were normal [4].

Pellagra

Pellagra is a systemic disease whose primary cause is a deficiency of niacin or tryptophan [25], while the secondary form of the disease may be caused by drugs, e.g. isoniazid. Typical symptoms of pellagra are described as "4D" and include: diarrhea, dermatitis, dementia and death as the final stage [25]. The case of half-and-half nails in a 23-year-old man in the course of pellagra induced with isoniazid has been described by Ma et al. Five months earlier the patient started anti-tuberculosis treatment due to secondary tuberculosis of the gastrointestinal tract. The patient denied alcohol abuse. The results of laboratory tests including kidney function were also correct. The nails changes were accompanied by brown-red symmetrical changes on the skin of the face, neck, hands, forearms, and feet . After discontinuation of isoniazid and

treatment, skin lesions resolved after 3 weeks, and resolved half-and-half nails after the next 4 months [26]. A similar case of half-and-half nails in the course of pellagra in a patient with a deficiency of vitamin B3 has also been described [27]. In both cases, the changes resolved after treatment with nicotinamide. The case of a patient with half-and-half nails who did not develop a full-blown pellagra during the use of isoniazid has also been described [28].

Yellow nail syndrome (YNS)

Yellow nail syndrome (YNS) is a acquired condition characterized by the presence of a triad of symptoms: lymphoedema, thickened yellow nails, and symptoms associated with respiratory tract involvement. To date, less than 400 cases have been reported. The etiology of YNS has not been recognized, and the occurrence of this syndrome was observed in the course of cancers, autoimmune disorders, as well as diseases of the lymphatic system [29]. The case of half-and-half nails in a 24-year-old woman with YNS without lymphoedema was described by Scher and Farel. The examination showed half-and-half nails of all 20 fingers. In addition to YNS, hyperthyroidism and chronic sinusitis was noted. This was the first case of half-and-half nails in a patient with YNS, as well as the first case of half-and-half nails coexistence with thyroid disease [30].

Citrullinemia

Citrullinemia is an autosomal recessive disease. Typical symptoms include elevated levels of ammonia and citrulline in the blood serum, as well as psychiatric and neurological symptoms [31]. To date, one case of the occurrence of half-and-half nails in the course of citrullinemia has been reported [32]. Nail changes occurred in a 56-year-old woman with hypouremia, hypermonemia, hypercitrullinemia and a reduced level of arginine-succinic synthetase in skin fibroblasts. Vomiting and two episodes of coma were also noted. The patient's skin was atrophic with visible vessels. In addition to the occurrence of half-and-half nails, fingers were clubbed. It was the first case of skin involvement and appendages in the course of citrullinemia.

Idiopathic half-and-half nails

To date, five cases of half-and-half nails in healthy people have been described. Mahajan et al. reported a case of a 25-year-old man with nail changes diagnosed as half-and-half nails. Nails changes occurred in the patient since he was 8 years old. Changes were present on both the fingernails and the toenails. The occurrence of systemic and local diseases related to nails was excluded, and the patient denied nails injuries. The kidney and liver function was normal, and

there were no abnormalities in other laboratory tests [33]. Schers and Kleinpenning reported the case of a 2 year younger man who also had the presence of half-and-half nails. Laboratory tests were normal, which in addition to the correct clinical condition without any pathologies allowed to diagnose idiopathic half-and-half nails [34]. The case of a 25-year-old woman with half-and-half nails of all 20 nails was described by Agrawal et al. Nail changes appeared three months before the presentation. No abnormalities were found in the results of laboratory tests or physical examination [35]. Half-and-half nails in a 57-year-old patient were described by Oanta and Tarean. Nails changes have been present for 17 years, during the diagnosis the presence of diseases that may be associated with the occurrence of half-and-half nails were excluded, as well as fungal etiology [36]. An interesting case of nail changes called longitudinal half-and-half nails, which were found on nails of big toes, was described by Wollina and Bula. Nails changes occured in a 45-year-old healthy woman, mycological examination was ordered to exclude fungal etiology, and the result was negative. The only pathology was the presence of bilateral hallux valgus [37].

Conclusions

Half-and-half nails are an underestimated but very important finding that can be useful in clinical practice. In addition to the high specificity for chronic kidney disease, half-and-half nails may occur in the course of systemic diseases such as Crohn's Disease, Behcet's Disease, pellagra, and others. Improving knowledge about half-and-half nails may facilitate the initial diagnosis of chronic kidney disease as well as other systemic diseases in the course of which half-and-half nails are present. For this reason, it should be remembered that nail examination is an important part of physical examination, especially in patients with diseases that may lead to the development of nephropathy. Further research to understand the pathogenesis of half-and-half nails are required.

References:

[1] Huang WT, Wu C. Half-and-half nail. CMAJ. 2009; ; 180(6): 687

[2] Sahoo JP. Half and half nail. Saudi J Kidney Dis Transpl 2014; 25: 168-9

[3] Cabana MD, Ensor A, Tunnessen WW Jr. Picture of the month: Half-and-half fingernails. Arch Pediatr Adolesc Med. 1998; 152(9): 923–4

[4] Afsar FS, Ozek G, Vergin C. Half-and-half nails in a pediatric patient after chemotherapy. Cutan Ocul Toxicol. 2015; 34(4): 350-1

[5] Patel LM, Lambert PJ, Gagna CE, Maghari A, Lambert WC. Cutaneous signs of systemic disease. Clin Dermatol. 2011; 29(5): 511-22

[6] Gagnon AL, Desai T. Dermatological diseases in patients with chronic kidney disease. J Nephropathol. 2013; 2(2): 104–9

[7] Lindsay PG. The half-and-half nail. Arch Intern Med. 1967; 119(6): 583–7

[8] Markova A, Lester J, Wang J, Robinson-Bostom L. Diagnosis of common dermopathies in dialysis patients: A review and update. Semin Dial. 2012; 25(4): 408–18

[9] Movasat A, Shahram F, Carreira PE, Nadji A, Akhlaghi M, Naderi N, Davatchi F. Nail fold capillaroscopy in Behçet's disease, analysis of 128 patients. Clin Rheumatol. 2009; 28: 603–5

[10] Reddy PKS, Prasad ALS, Sumathy TK, Reddy RV. Nail changes in patients undergoing cancer chemotherapy. Int J Res Dermatol. 2017; 3(1): 49

[11] Chadha S, Nannapaneni S, Shetty V, Shani J. Half-and-Half Nail. AJMS. 2013; 346(6): 513

[12] Pellegrino M, Taddeucci P, Mei S, Peccianti C, Fimiani M. Half-and-half nail in a patient with Crohn's disease. J Eur Acad Dermatol Venereol. 2010; 24: 1359–69

[13] Zágoni T, Sipos F, Tarján Z, Péter Z. The half-and-half nail: A new sign of Crohn's disease? Report of four cases. Dis Colon Rectum 2006; 49: 1071-3

[14] Alston H, Burns A. Half and half nails. NDT Plus. 2011; 4: 361

[15] Gandhi K, Prasad D, Malhotra V, Agrawal D. Half-and-half nails. Indian J Nephrol. 2014; 24: 330

[16] Pitukweerakul S, Pilla S. Terry's nails and Lindsay's nails: two nail abnormalities in chronic systemic diseases. J Gen Intern Med. 2016; 31(8): 970.

[17] Yang CS, Robinson-Bostom L. Lindsay's nails in chronic kidney disease. N Engl J Med. 2015; 372: 1748

[18] Avhad G, and Ghuge P. Half and half nail. Indian Dermatol Online J. 2014; 5: S67

[19] Ekiz Ö, Çelik E, Balta İ, Bülbül Şen B, Rifaioğlu EN, Demir M, Ekiz F, Başar Ö, Yüksel O. Nail changes in patients with inflammatory bowel diseases. Turk J Med Sci. 2016; 46(2):495-500

[20] Freeman HJ. Natural history and long-term clinical course of Crohn's disease. World J Gastroenterol. 2014;20:31–6

[21] Zeidan MJ, Saadoun D, Garrido M, et al. Behcet's disease physiopathology: a contemporary review. Auto Immun Highlights 2016;7:4

[22] Sahin AA, Kalyoncu AF, Selçuk ZT, Cöplü L, Celebi C, Baris YI. Behcet's disease with half and half nail and pulmonary artery aneurysm. Chest. 1990; 97(5):1277

[23] Mahajan VK, Sharma NL, Sharma VC, et al. Behcet's disease with HIV infection: response to antiretroviral therapy. Indian J Dermatol Venereol Leprol 2005; 71: 276–8

[24] Gönül M, HIzlI P, Gül U. Half-and-half nail in Behçet's disease. Int J Dermatol. 2014;53:e26–7

[25] Hegyi J, Schwartz RA, Hegyi V. Pellagra: dermatitis, dementia, and diarrhea.
Int. J. Dermatol. 2004; 43: 1-5
[26] Ma Y, Xiang Z, Lin L, Zhang J, Wang H. Half-and-half nail in a case of isoniazid-induced pellagra. Postepy Dermatol Alergol. 2014; 31(5): 329–31
[27] Cakmak SK, Gönül M, Aslan E, Gül U, Kiliç A, Heper AO. Half-and-half nail in a case of pellagra. Eur J Dermatol. 2006; 16: 695–6
[28] Chadwick A, Thwaites V, Holland M, Shahidi M. Half-and-half nails in a patient on antituberculosis treatment. BMJ Case Rep. 2017; bcr2017219841
[29] Vignes S, Baran R. Yellow nail syndrome: a review. Orphanet J Rare Dis. 2017;12:42
[30] Scher RK. Yellow nail syndrome and half-and-half nail. Arch Dermatol. 1987; 123: 710–11
[31] Woo HI, Park HD, Lee YW. Molecular genetics of citrullinemia types I and II. Clin. Chim. Acta. 2014; 431, 1–8
[32] Bonafe JL, Pieraggi MT, Abravanel M, Benque A, Abravanel G. Skin, hair and nail changes in a case of citrullinemia with late manifestation. Dermatologica. 1984; 168(5): 213-8
[33] Verma P, Mahajan G: Idiopathic 'half and half' nails. J Eur Acad Dermatol Venereol 2015; 29: 1452
[34] Schers HJ, Kleinpenning MM. A young man with discoloured nails. Ned Tijdschr Geneeskd. 2016;160:D448
[35] Agrawal SK, Pandhi D. Idiopathic half-half nail. Indian J Dermatol. 2005; 50: 170
[36] Oanță A, Iliescu V, Țărean S. Half and Half Nails in a Healthy Person. Acta Dermatovenerol Croat 2017; 25(4): 303-4
[37] Wollina U, Bula P. Longitudinal 'half-and-half nails' or true leukonychia. Skin Appendage Disord. 2016; 1: 185–6