Clinical Observation and Follow-Up of Subungual Splinter Hemorrhages of Toenails in Chinese Adults

Jing Gao1, Changbing Shen2,3, Randy Ko4, Yajun Guo1, Xue Shen5, Yong Cui2,3, Chunjun Yang1

Abstract

Background: Subungual splinter hemorrhage (SSH) is a common nail disorder and is difficult to differentiate from other nail diseases because of their similar characteristics. The epidemiological study of SSH is lacking and it is unclear whether SSH needs treatment or not. Aims: The aims of this study were to observe the clinical characteristics of SSH of toenails in Chinese adults and to provide a reference for the diagnosis and prognosis of patients with SSH. Materials and Methods: We collected and followed up 63 SSH patients who were diagnosed through dermoscopic examination. The clinical and dermoscopic characteristics, disease course, and recovery results were recorded. Data sets were analyzed through the use of SPSS 16.0. Literature concerning SSH were reviewed and compared with the results in this study. Results: Sixty-three SSH patients were included with an age range of 17–58 years. Nearly 93.7% of SSH patients occurred in the right, left, or right and left first toenails; 66.7% of SSH patients occurred only in one toenail; there were 60.3% of SSH patients with a clear stimulus causing it and 31.8% of SSH patients with five types of comorbidities. The common characteristics of dermoscopy showed a reddish brown or brown stain with a clear boundary visible under the nail in which the color gradually faded outward from the center, with no blue or white structure. After following up for 24 weeks, the disappearance of hemorrhage was observed in 95.2% of SSH patients. For the recovered SSH patients, data analysis showed no significant difference in the course of SSH in males and females (P = 0.645); the statistical analysis showed that there was no significant correlation (r² = −0.002) between age and course in recovered SSH patients (P = 0.986). Conclusions: It is unnecessary to do any special treatment during the 1st year. Measures ought to be taken for SSH patients if the course of the disease exceeds more than 1 year.

Key Words: Chinese adults, clinical observation, subungual splinter hemorrhage, toenail

Introduction

Subungual splinter hemorrhage (SSH) is a common nail disease, it has been estimated that the prevalence of SSH is around 19%,[1] and there are statistically greater incidence in male than in female and in African-Americans than in White healthy individuals.[2] Notably, SSH was documented in a range of 11%–20% in hemodialysis patients.[3,4] Usually, SSH was regarded as an early sign of thrombocytopenia,[5] and a new sign of the antiphospholipid coagulopathy.[6] In the clinic, it is difficult to differ SSH from other nail diseases, especially subungual malignant melanoma and melanonychia due to their similar characteristics. Because of the malignancy severity and the early metastasis of subungual malignant melanoma, it is highly valued, and the aim is to distinguish subungual malignant melanoma from SSH.

In the past years, the diagnosis and differential diagnosis of SSH mainly depended on pathological examination.[7] Dermoscopy was previously only used for the assessment of nail pigmentation. Recently, it has been widely utilized for the diagnosis and evaluation of nail disorders, permitting a better visualization of symptoms.[8] For SSH patients, it is unclear whether they need a treatment or not. Here, we conducted a clinical observation of patients with SSH on toenails in Chinese adults and reviewed the relative literature about SSH, in order to provide references for the diagnosis and treatment of patients with SSH.

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Materials and Methods

Study subjects
In total, 63 patients with SSH located in the toenails were collected from December 2014 to December 2017, at the Department of Dermatology, the Second Affiliated Hospital, Anhui Medical University. The SSH patients' demographics, onset time, clinical manifestations, comorbidities, and dermoscopic characteristics were recorded and collected through a face-to-face interview by dermatologists. A follow-up was conducted to record the recovery status of SSH patients in the outpatient clinic as well as by telephone. All included SSH patients signed the informed consent form.

The selection and recovery criteria of subungual splinter hemorrhage patients
Inclusion criteria of this study were as follows: (a) patients must have undergone examination through dermoscopy; (b) all patients were diagnosed by at least two dermatologists; and (c) patients' age range must be from 18 years to 60 years. Exclusion criteria of this study were as follows: (a) patients' age <18 years or >60 years and (b) patients with some conflicting nail diseases, such as subungual malignant melanoma and melanonychia. Recovery criteria were as follows: (a) SSH patients did not receive any treatment during the follow-up period and (b) the hemorrhage spots completely disappeared from the observation by naked eye.

The definition and calculation of onset and recovery time
In this study, we calculated the onset time and recovery time by weeks. Some SSH patients recalled their disease course by months and we interpreted 1 month as 4 weeks. Other SSH patients recalled their disease course by days and we calculated 7 days as a week. Because the course of SSH in a patient is relatively long, if the number is not an integer, the remaining days left were regarded as a week. In addition, if the onset or recovery time was <1 week, it was also regarded as a week.

Statistical analysis
In this study, continuous data were presented as mean ± standard deviation (SD) and qualitative data were presented as number (percent). Data were analyzed using SPSS version 16.0 (SPSS Inc., Chicago, Illinois, USA). The course difference between male and female SSH patients was tested by t-test, and Pearson correlation test was used for detecting the correlation between age and course of recovered SSH patients. All tests were two-tailed; the level of statistical significance was set at P < 0.05.

Results

Baseline characteristics of the subungual splinter hemorrhage patients
Sixty-three Chinese adult patients with SSH on toenails were included, and basic information was recorded. Among the 63 SSH patients, there were 22 males and 41 females, and the age ranged from 18 to 58 years, whereas the mean age was 32.22±10.09 years. There were 59 patients (93.7%) in which SSH occurred in the right, or left, or both first toenails, 42 patients (66.7%) where SSH occurred in only one toenail, and 21 (33.3%) patients where SSH occurred in more than one toenail (including 3 patients with more than 2 toenails).

Clinical and dermoscopic characteristics of subungual splinter hemorrhage
To the naked eye, hemorrhage spots were found in the medial or lateral deck. The SSH patients generally presented with clinical manifestations of dark red or brown spots, a clear border, and a round or irregular shape. The common characteristics of dermoscopy were as follows: reddish brown or brown stain, a clear boundary that was visible under the toenail, the color gradually faded outward from the center, and no blue or white structures were observed.

The predisposing factors and comorbidities of subungual splinter hemorrhage patients
We collected the possible predisposing factors of each SSH patient. There were 38 (60.3%) SSH patients with clear stimulus causing the disease, including 20 SSH patients that had a clear history of extrusion, 12 patients with trauma, and 6 patients with other factors. Interestingly, there were 20 (31.8%) SSH patients with 5 kinds of comorbidities, including tinea pedis (10 patients), onychomycosis (7 patients), pemphigus vulgaris (1 patient), paronychia (1 patient), and systemic lupus erythematosus (SLE, 1 patient). We also searched and summarized the comorbidities of SSH patients from the literature [Table 1].

The onset time and recovery time of subungual splinter hemorrhage
The onset time and recovery time of each SSH patient varied in length [Figure 1c includes 60 recovered SSH patients]. Figure 1a (includes 63 SSH patients) shows the frequency of SSH patients' onset time, ranging from <1 week to 28 weeks. The proportions of SSH patients' onset time in a month and in 3 months are 63.5% and 90.5%, respectively. All SSH patients participated in a follow-up observation without special treatment for 6 months (24 weeks). The patients were also informed to avoid trauma, wear comfortable loose shoes, and not to walk long distances. The disappearance of hemorrhage was observed in a total of 60 patients (95.2%), whereas only 3 SSH patients did not recover during the follow-up...
Table 1: Comorbidities of subungual splinter hemorrhage patients from the literature

| Comorbid disease            | Location                  | Population | Patients (n) | Report year | References |
|-----------------------------|---------------------------|------------|--------------|-------------|------------|
| Pemphigus vulgaris          | Fingernails and toenails  | Chinese    | 1            | 1998        | [9]        |
|                             | Fingernails and toenails  | Chinese    | 1            | 2005        | [10]       |
|                             | Fingernails               | Chinese    | 1            | 2007        | [11]       |
|                             | Fingernails and toenails  | Chinese    | 1            | 2007        | [12]       |
|                             | Fingernails and toenails  | Chinese    | 2            | 2012        | [13]       |
|                             | Fingernails and toenails  | Chinese    | 1            | 2017        | [14]       |
| Onychomycosis               | Fingernails               | Chinese    | 1            | 2006        | [15]       |
| Hypertension                | Fingernails               | Chinese    | 1            | 2013        | [16]       |
| Psoriasis                   | Fingernails               | Chinese    | 1            | 2009        | [17]       |
|                             | Fingernails               | Italian    | 1            | 2015        | [19]       |
| Systemic lupus erythematosus| Unclear                   | Puerto Rican| 11           | 1992        | [18]       |
|                             | Unclear                   | Egyptian   | 2            | 2008        | [19]       |
|                             | Fingernails               | Moroccan   | 3            | 2014        | [20]       |
| Chronic renal failure       | Unclear                   | Puerto Rican| 11           | 1992        | [18]       |
|                             | Unclear                   | Egyptian   | 2            | 2008        | [19]       |
| Acral erythema              | Fingernails               | Unclear    | Unclear      | Unclear     | 1993       | [21]       |
| Punctate keratoderma        | Unclear                   | Unclear    | Unclear      | 1993        | [22]       |
| Antiphospholipid syndrome   | Fingernails               | European   | 1            | 1992        | [23]       |

Discussion

SSH is a clinically common nail disease and easily confused with subungual malignant melanoma. For example, onychomatricoma is a subungual tumor of the finger and toenails and often misdiagnosed.[24] The diagnosis and treatment of SSH is still unclear, and the clinical and epidemiological studies of SSH are lacking. Wang et al. has reported that a surgical blade technique is employed to scrape off the deck of the nail bed in order to identify the hemoglobin of the removed brown material, which is used to confirm the brown color.[25] This is useful as this method can differentiate SSH from malignant melanoma. However, this method is cumbersome and difficult to practice in a clinical setting, and it can be considered for patients who are highly skeptical of malignant melanoma.

The goal of most SSH patients going to hospital to visit doctor is to exclude subungual malignant melanoma or melanonychia. In these cases, dermoscopy may be a good choice when making clinical observations. Dermoscopy can initially identify different nail diseases. SSH presents with an irregular black-red or brown-stained appearance, melanonychia with brown or black vertical regular line, and malignant melanomas are characterized by dermoscopy.[26] In this study, we collected 63 SSH Chinese adult patients the majority of them were female (65.1%). In contrast, a previous study found that SSH was significantly more frequent in males than in females in 1980.[27] We may explain this difference by the fact that women participate in more work and activities than previous ages. In this study, we collected SSH patients with a hemorrhage that occurred in toenails. Usually,
SSH has a specific predilection site, and there were 93.7% patients with SSH occurring in the right, or left, or both first toenails. It may be related to a crush injury because the first toenail is most vulnerable.

There was a study that indicated idiopathic atraumatic SSH can occur in healthy individuals. However, most of the SSH occur because of a clear stimulus. The prevalence of SSH was higher in patients with the antiphospholipid syndrome. SSH is also associated with some drugs, such as terbinafine, cabozantinib, sunitinib, and griseofulvin. This study found that SSH patients had a clear stimulus including mainly crush injuries and walking over long distances. There was a clear stimulus causing SSH in 38 cases, which mainly correlated to crush injuries or trauma. Therefore, it is necessary to inform patients to avoid extrusion and trauma to prevent SSH.

Interestingly, there were 20 SSH patients with 5 kinds of comorbidities, including tinea pedis, onychomycosis, pemphigus vulgaris, and SLE. We reviewed published literature about SSH comorbidities, and some comorbidities in this study were also reported, such as onychomycosis, pemphigus vulgaris, psoriasis, and SLE. There were also some other comorbidities, including hypertension, chronic renal failure, acral erythema, punctate keratoderma, and antiphospholipid syndrome. May be there are some potential correlations between SSH and these comorbidities, this will be an important research topic in the future.

All SSH patients in this study did not receive any special treatment but follow-up for 6 months (24 weeks). At different onset times, subhyperdia had different colors, as the early stage of the disease might be dark red or tan. After gradual absorption, brown spots might appear uneven, and the area would gradually become smaller. At last, the disappearance of hemorrhage was observed in a total of 60 patients (95.2%). Though the onset time varied in length, the longest disease course was 11 months (44 weeks), and we concluded that patients with SSH should be followed up for the 1st year.

The onset time and recovery time of SSH patients vary in length, and the average course of recovered male SSH

Figure 1: Details and frequency of onset and recovery time of subungual splinter hemorrhage patients. (a) The frequency of SSH patients’ onset time, (b) the frequency of SSH patients’ recovery time, (c) The onset time and recovery time of each SSH patients vary in length.
patients is higher than that of female SSH patients. However, there is no significance in the average course of between recovered male SSH patients and recovered female SSH patients. For the recovered SSH patients, we wondered whether there was a correlation between age and course length. The result shows there is no significant correlation.

In this study, the study sample size was relatively small, so it will be necessary to expand the sample size to confirm these results. Furthermore, the included SSH patients’ age ranges from 18 years to 58 years, but there are studies showing that nail disorders (including SSH) are frequent among the elderly population.[32,33] Therefore, it will be necessary to observe the SSH patients under 18 years and higher than 60 years in the future study.

Conclusions
The diagnosis of SSH mainly depends on characteristics of dermoscopy. We summarized from this study that follow up is needed and it is unnecessary to do any special treatment during the 1st year. SSH should be noticed and measurements ought to be taken for SSH patients if the disease course exceeds more than 1 year.

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Conflicts of interest
There are no conflicts of interest.
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