have developed fibrosing alopecia in a pattern distribution acutely for the first time. Although it is hard to correlate the onset of fibrosing alopecia in a pattern distribution with Covid 19, we propose that in our patients, cytokine storm observed in Covid 19 might have promoted fibrosing alopecia in a pattern distribution by damaging hair follicles which in turn may have led to the expression of cytokines that initiate an inflammatory process. Furthermore, the virus itself might have acted as an antigenic stimulus on hair follicles in immunogenetically susceptible individuals that resulted in a lichenoid tissue reaction. However, it is difficult to estimate whether fibrosing alopecia in a pattern distribution developed as a new condition or existed, albeit unrecognized before and accelerated after Covid 19 Still, fibrosing alopecia in a pattern distribution might have occurred just coincidentally due to a genetic, autoimmune or environmental factor which led to the inflammation of both terminal and vellus hairs.

Our experience in the present two cases suggests that fibrosing alopecia in a pattern distribution may be a new alopecia type which occurs in association with Covid 19. In patients with abrupt onset of severe hair loss months after Covid 19, before making the diagnosis of post-infectious effluvium, we recommend to evaluate the patient regarding the clinical and trichoscopic features of fibrosing alopecia in a pattern distribution and, if necessary, to perform histopathological examination. Thus, with timely diagnosis, appropriate treatment can be instituted to control fibrosing alopecia in a pattern distribution and to prevent permanent alopecia.

Declaration of patient consent
The patient's consent is not required as the patient's identity is not disclosed or compromised.

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There are no conflicts of interest.

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References

1. Trüeb RM, Dutra Rezende H, Gavazzoni Dias MFR. What can the hair tell us about COVID-19? Exp Dermatol 2021;30:288-90.
2. FIvenson D. COVID-19: Association with rapidly progressive forms of alopecia areata. Int J Dermatol 2021;60:127.
3. Miyazato Y, Morioka S, Tsuzuki S, Akashi M, Osanai Y, Tanaka K, *et al*. Prolonged and late-onset symptoms of Coronavirus disease 2019. Open Forum Infect Dis 2020;7:ofaa507.
4. Zinkernagel MS, Trüeb RM. Fibrosing alopecia in a pattern distribution: Patterned lichen planopilaris or androgenetic alopecia with a lichenoid tissue reaction pattern? Arch Dermatol 2000;136:205-11.
5. Griggs J, Trüeb RM, Dias MF, Hordinsky M, Tosti A. Fibrosing alopecia in a pattern distribution. J Am Acad Dermatol 2020:S0190-9622(20)30030-X.

Nail involvement in Langerhans cell histiocytosis and its association with multisystem presentation and lung involvement

Sir,
Langerhans cell histiocytosis is a rare proliferation of cells of the mononuclear-phagocyte system mainly affecting children.[1]

The great heterogeneity of clinical presentation requires histopathological confirmation and a multidisciplinary approach. According to the number of involved sites, Langerhans cell histiocytosis is clinically classified into single-system or multisystem, the latter having a poor prognosis especially when "risk-organs" are involved.[1]

Nail involvement with varying morphology of changes has been reported, though rarely, in Langerhans cell histiocytosis. Nail involvement has also been considered an unfavorable prognostic sign and seems to be more frequent in multisystem-Langerhans cell histiocytosis.[2-4]

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A 41-year-old previously healthy Caucasian man, presented in October 2019, with multiple cutaneous erythematous papules over the scalp, persistent chronic paronychia with onychodystrophy and nail discoloration involving only the fifth finger of the right hand [Figure 1]. Differential diagnoses included onychomycosis, chronic candidiasis, Darier disease and Langerhans cell histiocytosis.

A diagnostic biopsy of both skin and nail was performed. Both the biopsies revealed findings consistent with Langerhans cell histiocytosis. Complete skeletal survey, whole body computed tomography, laboratory, pulmonary and hematological investigations were normal ruling out the involvement of other organs hence depicting a single-system-Langerhans cell histiocytosis. Sequenced BRAF gene revealed wild-type and it was decided to follow up the patient with only symptomatic treatment. The clinical picture is stable even fourteen months into follow up.

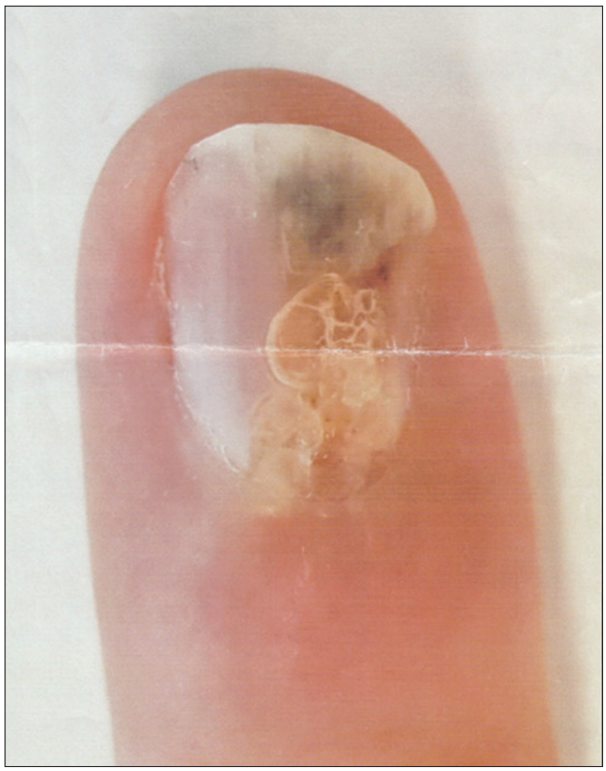

Figure 1a: The patient displayed an involvement of the fifth finger, featuring chronic paronychia with onychodystrophy and a discoloration of the nail lamina.

We queried the PubMed database, searching for all the combinations of the word "nail" and synonyms of Langerhans cell histiocytosis. Deduplication, exclusion of non-relevant records and reference list analysis yielded 34 papers, describing a total of 38 patients.

The medical literature currently reports only 38 cases of Langerhans cell histiocytosis with associated nail involvement [Tables 1 and 2]. Most reported patients were young boys. In all but two cases, patients presented with cutaneous, nail and often systemic involvement.

Nail changes included onycholysis (28/38, 73.7%), subungual hyperkeratosis (23/38, 60.5%), purpuric striae (21/38 55.3%), nail dystrophy (21/38, 55.3%), paronychia (11/38, 28.9%), pachyonychia (8/38, 21.0%) and longitudinal grooving (8/38, 21.0%). In most cases, more than one nail presented with changes and in 21/38 (55.3%) of them, all fingernails were involved. Nail involvement by Langerhans cell histiocytosis was histopathologically proven in nine cases [Table 1]. In 35 (92.3%) of cases, the nail changes were present at disease onset.

Most patients displayed multisystem Langerhans cell histiocytosis, especially in the pediatric sub-cohort (22/28, 92.8% vs. 14/16 87.5% among adult patients). Around half of the cases displayed lung involvement. Bone involvement, diabetes insipidus and risk organ involvement were seen in

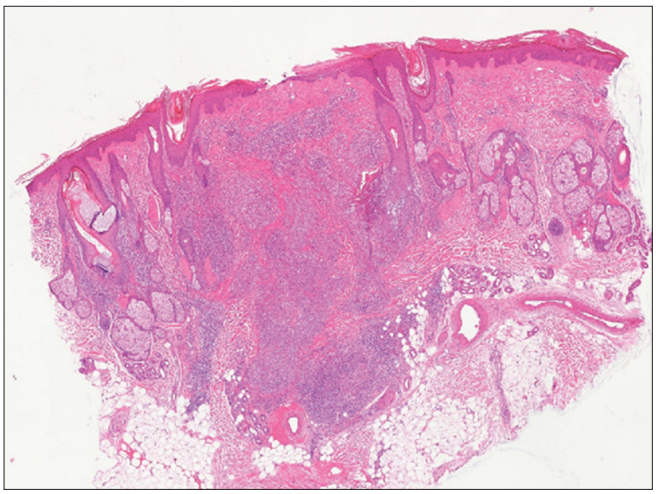

Figure 1b: The skin biopsy of a papular lesion of the scalp revealed a marked dermal, epidermotropic infiltrate made of medium-sized mononuclear cells admixed with macrophages, eosinophils and lymphocytes (H & E, ×20)

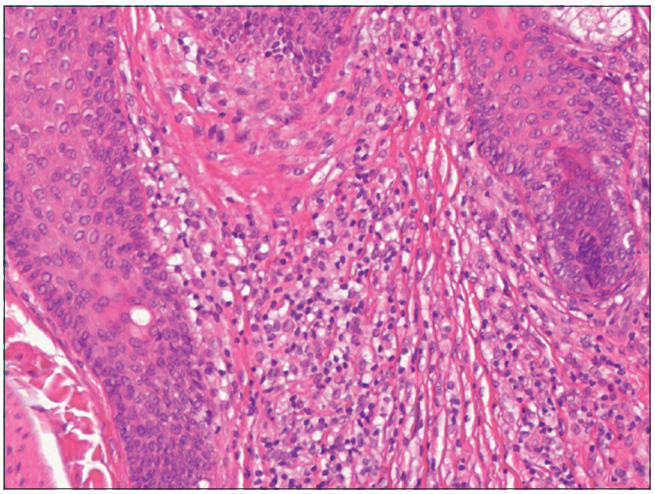

Figure 1c: A marked dermal, epidermotropic infiltrate made of medium-sized mononuclear cells with large indented nuclei admixed with macrophages, eosinophils and lymphocytes. (H & E, ×200)

Table 1: Epidemiological and clinical data of 39 LCH patients with nails involvement gathered from the literature, including the present report of year of publication

#	Author	Year	Age/sex/ ethnicity	Clinical presentation	Skin/ mucosae	n. nails involved	Nail biopsy	Bone	Lung	RO+	CNS	Outcome	Follow-up (mo)
	Author	TEs											
1	Bender B	1958	43/F/Cauca	MS RO+	x	>1			x	x	x	PD	48
2	Kahn	1969	3/F/Caucasi	MS RO+	x	10		x		x		PR	18
3	Civatte	1977	40/M/Cauc	MS RO+	x	>1		x		x	x	DOD	108
4	Diestelmeier	1982	2/M	MS RO-	x	>1		x			x	CR	4
5	Harper	1983	1/M	MS RO-	x	>1		x	x			DOD	5
6	Timpatanapong (4)	1984	2/M/Asian	MS RO+	x	10		x		x		DOD	30
7	Timpatanapong (6)	1984	1/M/Asian	MS RO+	x	20		x	x	x		DOD	10
8	Timpatanapong (7)	1984	2/M/Asian	MS RO+	x	20		x	x	x		DOD	12
9	Ellis	1985	12/M	SS	x	1						CR	21
10	Holzberg	1985	0/M	MS RO+	x	>1	x			x		DOD	19
11	Pareek	1985	20/M/Causi	MS RO-	x	10			x			DOD	48
12	Munro	1988	45/M	MS RO-	x	>1	x				x	SD	4
13	Satriano (1)	1988	30/M	MS RO-	x	>1		x			x		
14	Satriano (2)	1988	35/F	MS RO-	x	>1					x		
15	Alsina	1991	31/M	MS RO-	x	2	x	x			x	PR	5
16	De Berker	1994	0/M/Caucas	MS RO-	x	>1		x				SD	4
17	Jain	2000	30/M/Cauc	MS RO-	x	>1			x				2
18	Mendes	2006	3/M	MS RO-	x	10		x			x	CR	24
19	Moravvej	2006	20/M/Cauc	SS	x	20						SD	6
20	Querings	2006	1/F	MS RO-	x	10			x			SD	120
21	Ashena	2007	0/F	MS RO-	x	20		x	x			DOD	22
22	Mataix	2008	2/F	MS RO-	x	>10	x	x				PR	3
23	Chander	2008	1/M	MS RO+	x	20			x	x		DOD	4
24	Yazc	2008	3/M	MS RO-	x	>1		x	x			SD	130
25	Sabui	2009	3/F	MS RO+		20				x			
26	Ottink	2013	2/M	MS RO-		>1			x			SD	
27	De Jesus Semblano Bittencourt	2016	2/M	MS RO+	x	>10			x	x		LFU	1
28	Figueras-Nart	2016	10/M	MS RO-	x	>1	x		x			CR	17
29	Hocazade	2016	24/F	MS RO+	x	10			x		x	LFU	108
30	Calderòn-Castrat	2017	36/F/Cauca	MS RO-	x	10			x		x	SD	180
31	Ishikawa	2017	43/F	MS RO-	x	7					x		
32	Kumar	2017	1/M	MS RO+	x	20	x		x	x			
33	Mahajan (1)	2017	22/M	MS RO+	x	20				x	x	CR	11
34	Mahajan (2)	2017	43/M	MS RO-	x	20					x		60
35	Fu	2018	19/M	MS RO+	x	>1			x	x			
36	Bender NR	2018	10/M/Afrod	SS	x	20	x					PD	36
37	Narayanasamy	2019	1/F	MS RO+	x	20			x	x		PR	
38	Prayogo	2019	0/M	MS RO-	x	20	x		x			DOD	3
39	Present case	2020	41/M/Cauc	SS	x	1	x					SD	10

a third of cases each. Risk organ involvement had similar incidence in children and adults.

Two papers investigated the BRAF mutational status (including present case) and both were wild-type.[4]

Most patients were treated with polychemotherapy including prednisone, vinca alkaloids, 6-mercaptopurine, methotrexate, cyclophosphamide, etoposide, and/or cytosine arabinoside. 5/31 (16.1%) patients with follow-up data, achieved complete remission, while 9/31 (29.0%) died of disease after a median of 15.5 months.

Among the patients who died of the disease, most were males (7/8, 87.5%) with all fingernails involved, had a median age at diagnosis of two years (range 0–40) and all displayed multisystem involvement.

According to our review of literature, nail involvement in Langerhans cell histiocytosis is rare; it occurs more

Table 2: Epidemiological and clinical analysis on Langerhans cell histiocytosis patients with nails involvement gathered from the literature, including the present report

	All pts.	Pediatric pts.	Adult pts.
n. of patients	39/39 (100)	23/39 (61.5)	16/39 (41)
M/Tot (%)	28/39 (71.8)	17/23 (73.9)	11/16 (68.8)
Median age at presentation (y) (range)	3 (0–45)	2 (0–12)	33 (19–45)
Clinical picture			
Single-system *n* (%)	4/39 (10.3)	2/23 (8.7)	2/16 (12.5)
MS Tot *n* (%)	35/39 (89.7)	22/23 (95.7)	14/16 (87.5)
MS RO+ (%)	15/39 (38.5)	10/23 (43.5)	5/16 (31.3)
Skin involvement *n* (%)	37/39 (94.9)	22/23 (95.7)	16/16 (100)
Bone involvement *n* (%)	14/39 (35.9)	11/23 (47.8)	3/16 (18.8)
Lung involvement *n* (%)	19/39 (48.7)	13/23 (56.5)	6/16 (37.5)
CNS-ND *n* (%)	3/39 (7.7)	1/23 (4.3)	2/16 (12.5)
CNS-DI *n* (%)	12/39 (30.8)	1/24 (4.3)	11/16 (68.8)
Outcome Tot *n*=31 (Pediatric=21, Adults=10)			
CR	5/31 (16.1)	4/21 (19)	1/10 (10)
PR	4/31 (12.9)	3/21 (14.3)	1/10 (10)
SD	8/31 (25.8)	4/21 (19)	4/10 (40)
PD	2/31 (6.5)	1/21 (4.8)	1/10 (10)
DOD	10/31 (32.3)	8/21 (8.1)	2/10 (20)
Median time to death for DOD (mo) (range)	15.5 (3–108)	11 (3–30)	78 (48–108)
Median FU (mo) (range)	18 (1–180)	18 (1–130)	29.5 (4–180)

CNS-DI: Diabetes insipidus, CNS-ND: Neurodegeneration, CR: Complete remission, DOC: Dead for other cause, DOD: Dead of disease, FU: Follow-up, LFU: Lost at follow-up, M: Male, mo: Months, MS: Multisystem, PD: Progressive disease, PR: Partial remission, pts.: Patients, Rel: Relapse, RO: Risk-organs involvement, SD: Stable disease, SS: Single-system, Tot: Total, y: Years

frequently in male children and is often associated with skin lesions.

Clinically, the major differential diagnosis of nail changes in Langerhans cell histiocytosis includes onychomycosis, psoriasis, chronic mucocutaneous candidiasis, Darier disease, pachyonychia and dyskeratosis congenita. Clinical, histopathological and laboratory findings are needed to confirm the diagnosis.

Nail involvement in Langerhans cell histiocytosis associates with a multisystem presentation and with an unusually high incidence of lung involvement in children. While pulmonary involvement is observed in around 25% of children with Langerhans cell histiocytosis, in our review, lung involvement occurred in 13/23, (56.5%) of pediatric patients with Langerhans cell histiocytosis with nail changes. The opposite was observed for adults, with 6/16 (37.5%) having lung involvement in patients with nail involvement, compared with 62% in the general adult Langerhans cell histiocytosis population, respectively.

Interestingly, both patients showing the involvement of a single nail (including ours), presented with single-system cutaneous involvement and displayed a favorable outcome, while most patients who had a fatal outcome showed involvement of all fingernails.

Despite BRAF mutation in Langerhans cell histiocytosis is associated with a worse prognosis in both low and high-risk patients; data are lacking concerning Langerhans cell histiocytosis patients with nail involvement. Therefore, we could not analyze this aspect in our work.[5]

Our review highlights an association between nail involvement in Langerhans cell histiocytosis and multisystem presentation with lung involvement in pediatric patients. This is of special interest given the rarity of the lungs involvement in Langerhans cell histiocytosis children and may be a useful and inexpensive dermatological marker of disease extent and perhaps of prognosis.

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Authors' contributions

Study concept, design and supervision: AB. AB wrote the first draft. Acquisition, analysis and interpretation of data: AB, EB. EP, SF and EB provided the data and performed clinicopathological correlations. Histological and immunohistochemical reviews were performed by AB and EB. All authors edited and approved the final draft.

Ethics approval

The study was conducted following local ethical guidelines (Fondazione IRCCS Ca′ Granda Institutional review board approval #179/13).

Consent to participate and for publication

The patient's informed consent was gathered and the study was conducted following the Helsinki declaration.

Availability of data and material

All presented data are available and accessible from international literature.

Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent.

Financial support and sponsorship

Nil.

Conflicts of interest

There are no conflicts of interest.

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References

1. Emile JF, Abla O, Fraitag S, Horne A, Haroche J, Donadieu J, *et al*. Revised classification of histiocytoses and neoplasms of the macrophage-dendritic cell lineages. Blood 2016;127:2672-81.
2. Jain S, Sehgal VN, Bajaj P. Nail changes in Langerhans cell histiocytosis J Eur Acad Dermatol Venereol 2000;14:212-5.
3. Mataix J, Betlloch I. Lucas-Costa A, Pérez-Crespo M, Moscardó-Guillem C. Nail changes in Langerhans cell histiocytosis: A possible marker of multisystem disease. Pediatr Dermatol 2008;25:247-51.
4. Bender, NR, Seline, AE, Siegel, DH, Sokumbi, O. Langerhans cell histiocytosis with prominent nail involvement. J Cutan Pathol 2019;46:1-5.
5. Héritier S, Emile JF, Barkaoui MA, Thomas C, Fraitag S, Boudjemaa S, *et al*. BRAF mutation correlates with high-risk Langerhans cell histiocytosis and increased resistance to first-line therapy. J Clin Oncol 2016;34:3023-30.

Pyogenic granuloma-like lesions due to antifungal-corticosteroid combination creams

Sir,

Three men between 40 years and 55 years of age presented with eruptions in the groins of one to two months' duration. They had suffered from repeated episodes of tinea cruris in the past one year. Topical fungicidal creams were used by all for around six weeks with clinical improvement and resolution, but the lesions would recur within one or two weeks (even after using different antifungal preparations). When the episodes lasted over many months, the physician prescribed them combination creams containing mid-potent or potent corticosteroids - beclomethasone, betamethasone and clobetasone. No oral antifungal agents were given. After early relief, they started applying the steroid-containing combination creams on their own, barely noticing the development of striae. The onset of some new eruptions along the striae made them seek advice from the dermatologist.

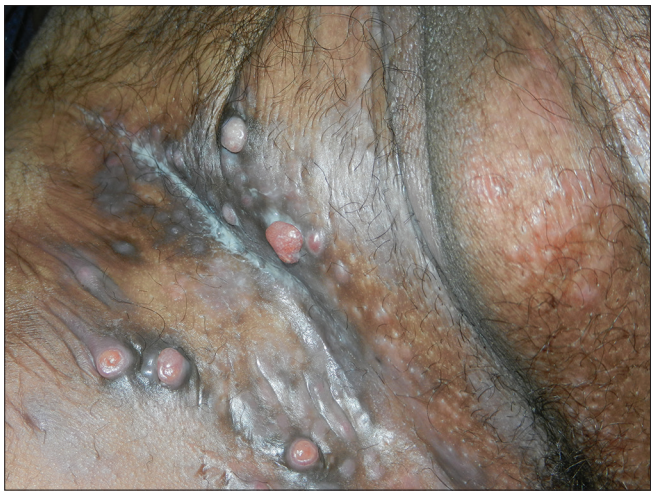

Figure 1: Tiny lesions arising along striae

On examination, circumscribed, sessile and eroded papules of varying diameter from 2-5 mm were seen in the inguinal folds, predominantly along the striae, one or more on either side or both. In one patient with a longer duration of lesions, the skin around the papules was hyperpigmented [Figure 1]. The diagnoses considered included pyogenic granuloma, iatrogenic ulcers and secondary syphilis. Biopsy was done in two patients. Histopathology showed irregular acanthosis with ulceration; the dermis revealed proliferating blood vessels of varying sizes amidst fibrotic collagen along with edema and acute and chronic inflammatory cells [Figures 2a and b]. Periodic acid–Schiff stain for fungus was negative. The histopathological features were of non-lobular capillary hemangioma simulating granulation tissue. Blood investigations including venereal disease research laboratory test was negative in all. Combination creams were strictly withheld. Oral terbinafine 250 mg daily, potassium permanganate soaks and topical betadine were advised. Four weeks later, resolution of the lesions was seen. The patients were asked to continue therapy for two more weeks after which topical fungicides were added.

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