

Neutrophil-rich subcutaneous fat necrosis of the newborn: A potential mimic of infection



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Background: The inflammatory infiltrate seen in biopsy specimens obtained from patients with subcutaneous fat necrosis of the newborn (SCFN) has classically been described as consisting mostly of histiocytes. However, we encountered patients with SCFN whose biopsy specimens revealed mostly neutrophils, prompting infection to be an initial consideration.

Objectives: We sought to describe cases of SCFN in which neutrophils formed the majority of the infiltrate at our institution and in the literature.

Methods: We performed a retrospective analysis of patients with SCFN reported at our institution and a literature review of SCFN.

Results: Thirteen cases of SCFN were identified at our institution. In 2 of 13 cases, neutrophils composed >75% of the inflammatory infiltrate, and both lesions were 1 day old. From the literature review, neutrophils were mentioned as a component of the infiltrate in 10 of 124 cases, but in none were neutrophils described as forming the majority of the infiltrate.

Limitations: This study is limited by its retrospective nature and small sample size.

Conclusions: Neutrophils can comprise most of the inflammatory cells in patients with SCFN, especially early in the course of the disease. This variant of SCFN can be easily mistaken for infection. (J Am Acad Dermatol 2016;75:177-85.)

Key words: neutrophils; panniculitis; subcutaneous fat necrosis of the newborn.

INTRODUCTION

Subcutaneous fat necrosis of the newborn (SCFN) is a form of panniculitis affecting premature and full-term infants. It is commonly associated with a perinatal insult, particularly hypothermia.¹ This panniculitis is characterized clinically by indurated plaques and subcutaneous nodules that commonly occur on the cheeks, shoulders, buttocks, thighs, and calves. On occasion, the nodules and plaques can ulcerate and express purulent material, thereby raising a soft tissue infection as a potential clinical consideration.^{2,3}

Histopathologically, SCFN has historically been reported to be characterized by a lobular panniculitis consisting mostly of histiocytes, including multinucleated cells, with admixed lymphocytes and occasionally a few eosinophils, along with needle-shaped clefts and fat necrosis.⁴ We encountered a case of SCFN in which neutrophils formed the majority of the inflammatory infiltrate. This case initially was thought to represent an infection by the clinical team. We sought to characterize this case and to review all cases at our institution and in the literature of SCFN to assess for the presence of neutrophils.

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METHODS

We conducted a database query of all the cases of SCFN submitted to the University of California, San Francisco (UCSF) Dermatopathology service between January 1, 1995 and August 31, 2014. The study was approved by the UCSF institutional review board (15-17896). We searched for all cases coded as SCFN in which the patient was ≤ 2 months of age. Clinical data were extracted from the pathology reports and from UCSF medical records and included the following: sex, age of the patient at the onset of skin lesions, age of the patient at the time the biopsy specimen was obtained, and the site and the age of the lesion at the time the biopsy specimen was obtained. Slides for all cases were rereviewed by 2 dermatopathologists (L.B.P. and T.H.M.) and scored on a scale of 0 to 4 for the presence and density of histiocytes/lymphocytes, eosinophils, and neutrophils (0 = $<5\%$; 1 = 5-25%; 2 = 25-50%; 3 = 50-75%; and 4 = $>75\%$ of inflammatory infiltrate). In addition, the presence or absence of needle-shaped clefts was assessed and scored as either present or absent.

We also conducted a literature review of all the cases of SCFN at pubmed.gov using the search terms “subcutaneous fat necrosis of the newborn” and “fat necrosis of the newborn.” We included in our analysis reports in which either a skin biopsy specimen was obtained or a fine-needle aspiration (FNA) had been performed for ≥ 1 of the cases reported in the article. Papers were excluded if diagnoses were based on clinical grounds or imaging in the absence of confirmatory microscopic evaluation. Information from the papers was extracted and tabulated, including year of publication, number of patients in the study, sex, age of the patient at the onset of lesions, whether a biopsy specimen was obtained, the duration of involvement at the time the biopsy specimen was obtained, site of involvement, maternal age, gestational age at birth, delivery method, birth weight, perinatal course, calcium level, phosphorous level, and clinical course. The description of the histopathologic results of the biopsy specimens was reviewed, and information regarding whether neutrophils were present was recorded. In the cases in which neutrophils were present, the entire composition of the inflammatory

infiltrate was recorded. The composition of the infiltrate was also recorded in all cases <1 day old in which neutrophils were not reported to be a component of the infiltrate.

RESULTS

University of California, San Francisco patients

We identified 14 patients within the database of the UCSF Dermatopathology Service who were coded with a diagnosis of SCFN. One case consisted of slides that were sent to UCSF in consultation, and the slides could not be retrieved. Therefore, this case was excluded from further analysis. We were able to review and confirm the diagnoses in 13 patients, 1 of which was the index patient.

Index case

Our index patient (patient 13; [Table 1](#)) was a well-appearing, afebrile, 4-day-old, full-term girl born via cesarean section for failure to progress and fetal distress who developed erythematous, firm subcutaneous nodules with central fluctuance on the bilateral aspects of her upper arms and back on her third day of life (DOL 3; [Fig 1, A and B](#)). A punch biopsy specimen of a representative nodule was obtained on DOL 4, and it revealed purulent material clinically, which raised concern for infection. A microscopic examination revealed lobular panniculitis with a neutrophil-rich infiltrate and fat necrosis. In addition, there were needle-shaped clefts within adipocytes ([Fig 2, A and B](#)). Given the predominance of neutrophils and clinical concern for an infectious process, special stains for microorganisms—including Brown–Brenn, periodic acid–Schiff–diastase, and Fite—were obtained. All of these stains were negative. Culture of the expressed fluctuant material and blood cultures drawn on DOL 4 were negative. Therefore, an infection was excluded, and a neutrophil-rich variant of SCFN was thought to represent the best diagnosis. The nodules self-resolved over 6 months, leaving small and firm subcutaneous nodules. The patient had transient hypercalcemia (maximum, 11.4 mg/dL [normal range, 8.4-10.6 mg/dL]) but had no other associated abnormalities.

Clinical information from all UCSF patients

A review of the clinical charts from all patients at UCSF diagnosed with SCFN (including the index

CAPSULE SUMMARY

- The inflammatory infiltrate in subcutaneous fat necrosis of the newborn (SCFN) has classically been described as consisting mostly of histiocytes.
- We encountered patients with SCFN from whom biopsy specimens revealed inflammatory infiltrates consisting mostly of neutrophils.
- Recognition of this variant of SCFN is important because such cases can be mistaken for infection.

Table I. Clinical features tabulated from the University of California, San Francisco dermatopathology database

Case no.	Sex	Patient age at time of onset (days)	Patient age at time of biopsy (days)	Age of lesion at time of biopsy (days)	Biopsy site
1	M	NK	29	NK	Arm
2	M	NK	36	NK	Shoulder
3	F	NK	38	NK	Back
4	F	NK	40	NK	Back
5	F	8	9	1	Back
6	M	NK	19	NK	Scalp
7	F	NK	16	NK	Forearm
8	F	3	5	2	Back
9	F	9	10	1	Hip
10	M	13	17	4	Back
11	F	2	15	13	Thigh
12	M	NK	27	NK	Thigh
13	F	3	4	1	Arm

F, Female; M, male; NK, not known.

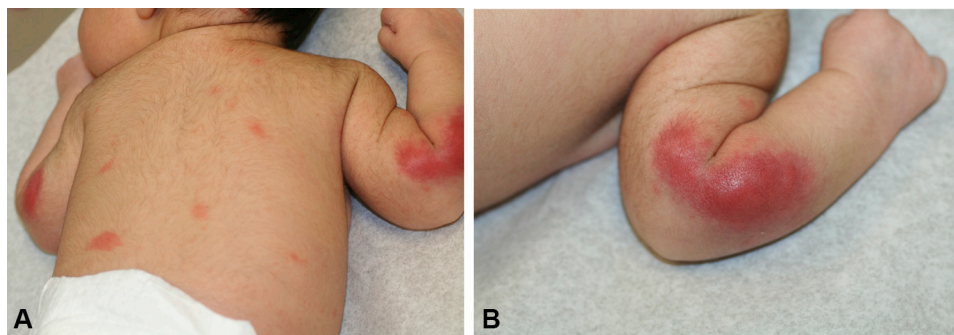


Fig 1. Subcutaneous fat necrosis of the newborn. Clinical presentation of patient 13. **A**, Erythematous to violaceous nodules and plaques on arms and back. **B**, Biopsy site.

patient discussed above, patient 13) revealed that the age at the time of biopsy ranged from 5 to 40 days, and 8 of 13 (62%) patients were female (Table I). For cases in which the time of onset and time of biopsy were available, the age of the lesions at the time the biopsy specimen was obtained ranged from 1 to 13 days. In the patients in whom the clinical information was obtainable, all presented with erythematous subcutaneous nodules. Similar to patient 13, infection was the initial concern for patient 9, in part because purulent material was identified at the time the biopsy specimen was obtained (Fig 3, A and B). Therefore, concurrent biopsies for bacterial, mycobacterial, and fungal culture were performed and were negative. In addition, special stains for microorganisms including Brown–Brenn, periodic acid–Schiff–diastase, and Fite were performed on the hematoxylin–eosin-stained slide and were negative. Based on these negative studies, an infectious cause of the eruption was excluded.

Histopathologic features

All biopsy specimens (13/13) had needle-shaped clefts in the subcutis. In 2 of 13, there was a dense neutrophil-rich infiltrate in which >75% of the cells were neutrophils (patients 9 and 13; Table II; Figs 2 and 4). In 4 of 13 cases, 25% to 50% of the infiltrate was composed of neutrophils (patients 5–8; Fig 5, A–D). One case had 5% to 25% of the infiltrate composed of eosinophils (patient 6). Six biopsy specimens had <5% of neutrophils, and concurrently >75% of the cellular infiltrate for each of those specimens consisted of histiocytes, including multinucleated cells and lymphocytes (patients 2–4 and 10–12; Table II).

Literature review

The literature review identified 92 unique reports comprising 158 individual patients; FNA was used on or biopsy specimens were obtained from 124 of these patients (Supplemental Table I; available online at www.jaad.org).^{1–92} Of these, 10 of 124

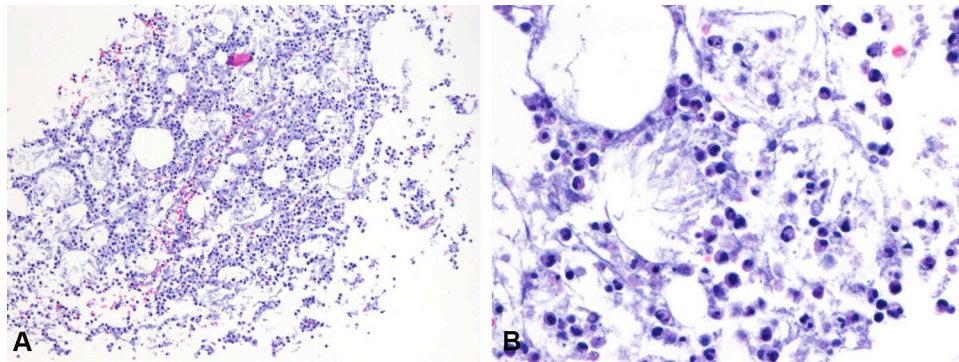


Fig 2. Subcutaneous fat necrosis of the newborn. Histopathologic findings of patient 13. **A**, Lobular panniculitis composed mostly of neutrophils with needle-shaped clefts (original magnification: $\times 100$). **B**, High magnification ($\times 400$).

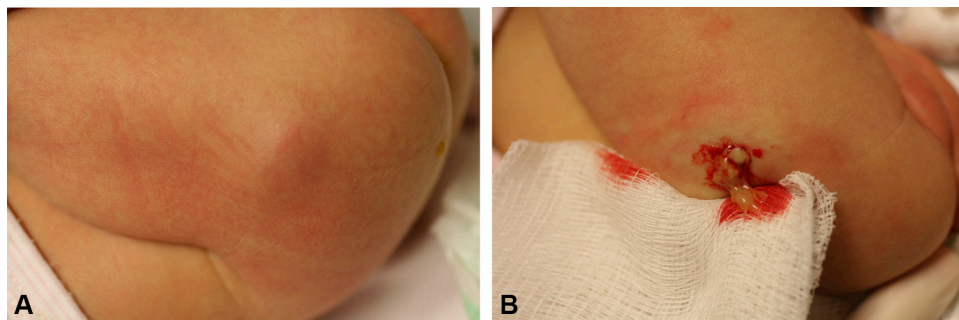


Fig 3. Subcutaneous fat necrosis of the newborn. Clinical presentation of patient 9. **A**, Erythematous nodule on the right hip. **B**, Significant purulent material at the time the biopsy specimen was obtained.

Table II. Histopathologic features tabulated from University of California, San Francisco biopsy specimens

Case no.	Histiocytes/ lymphocytes	Eosinophils	Neutrophils	Clefts
1	4	1	1	Present
2	4	0	0	Present
3	4	1	0	Present
4	4	0	0	Present
5	2	0	2	Present
6	2	2	2	Present
7	2	1	2	Present
8	3	1	2	Present
9	1	0	4	Present
10	4	0	0	Present
11	4	1	0	Present
12	4	0	0	Present
13	1	0	4	Present

0 = <5% of the infiltrate; 1 = 5-25% of the infiltrate; 2 = 25-50% of the infiltrate; 3 = 50-75% of the infiltrate; 4 = >75% of the infiltrate.

biopsy specimens were described as having a neutrophilic or neutrophil-enriched infiltrate as part of the inflammation.^{2,3,18,22,35,50,54,66,73,76} In at least 2 instances, there was frank purulent material at

the time the biopsy specimen was obtained, which prompted obtaining tissue for microbiologic culture and blood cultures, and empiric treatment of the children with systemic antibiotics until the culture results were available.^{2,3} In both patients, the biopsy specimens for culture and blood cultures did not reveal the presence of any microorganisms.

In 3 of 10 patients, the duration of involvement at the time the biopsy specimen was obtained was reported.^{35,66,73} In 1 of those reports, the biopsy was 16 days old, and most of the cells were reported to be large with poorly defined cytoplasm that probably represented histiocytes (the paper was written in 1951 and therefore many cell types had not yet been defined), with only a small number of admixed neutrophils.³⁵ In another of those reports, the lesion from which the biopsy specimen was obtained was at least 12 days old—the paper⁶⁶ reported 4 patients in aggregate, and the ages of the lesions were between 12 and 40 days old. In the paper, the bulk of the infiltrate was also reported to be composed of histiocytes with only occasional neutrophils. In the third report, the lesion that was biopsied was 1 day old and the cellular infiltrate was composed of histiocytes, neutrophils, lymphocytes,

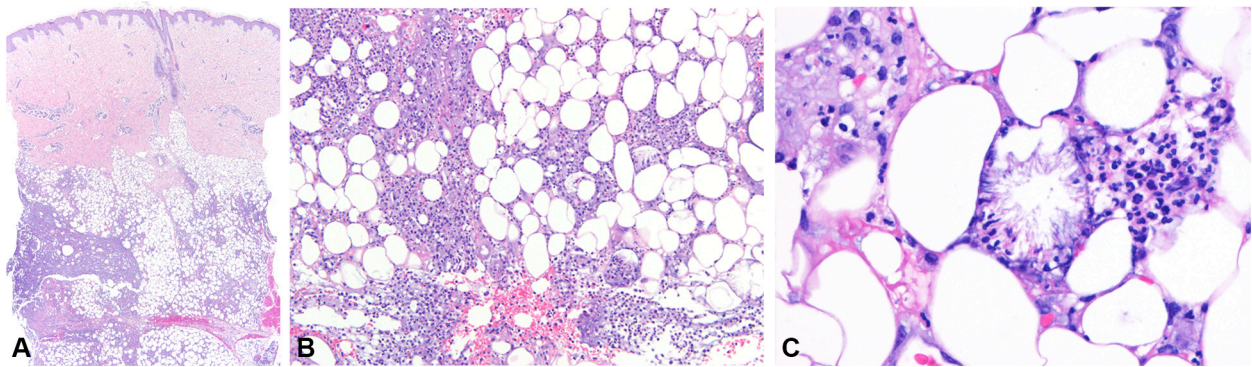


Fig 4. Subcutaneous fat necrosis of the newborn. Histopathologic findings of patient 9. **A**, Lobular panniculitis (original magnification: $\times 40$). **B**, Neutrophils comprise $>75\%$ of the infiltrate (original magnification: $\times 100$). **C**, Needle-shaped clefts are present (original magnification: $\times 400$).

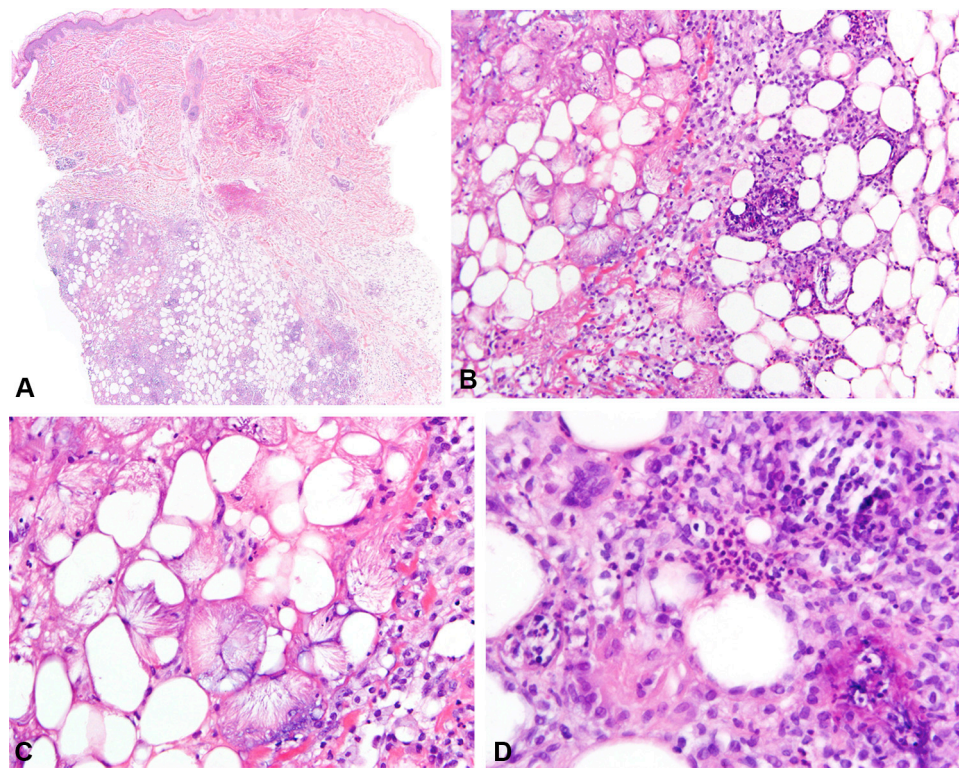


Fig 5. Subcutaneous fat necrosis of the newborn. Histopathologic findings of patient 5. **A**, Lobular panniculitis without involvement of the dermis or epidermis (original magnification: $\times 40$). **B**, The infiltrate is composed of mixture of histiocytes and neutrophils in roughly equal proportions (original magnification: $\times 100$). **C**, Needle-shaped clefts are well-developed (original magnification: $\times 200$). **D**, Neutrophils are admixed with histiocytes (original magnification: $\times 400$).

and eosinophils. The percentages of each cell type were not reported in the paper.⁷³

In 5 of 124 patients, biopsy specimens were obtained from lesions of ≤ 1 day duration, but neutrophils were not mentioned as a component of the infiltrate in these specimens.^{1,15,72,74,89} In 3 of these

5 patients, no information regarding the composition of the infiltrate was reported.^{1,74,89} In 1 of 5, the sampling was performed via FNA, and this sample was reported to be paucicellular with a few histiocytes and lymphocytes and crystalline in cytoplasm in adipocytes.⁷² In 1 of these 5 patients, the infiltrate was

reported to be composed of histiocytes infiltrating between adipocytes with eosinophilic cytoplasm.¹⁵

DISCUSSION

SCFN is a relatively common form of panniculitis in newborns that is typically characterized by fat necrosis, needle-shaped clefts in the fat cells, and an inflammatory infiltrate consisting predominantly of histiocytes, lymphocytes, and foreign body giant cells. We describe that a neutrophil-rich infiltrate can be found as part of the histopathologic spectrum of SCFN.

From our database, we identified 2 patients having a remarkably prominent neutrophil-rich infiltrate (>75%). In both patients, there was a report of purulence observed at the time the biopsy specimen was obtained; concurrent tissue was obtained for cultures and proved to be negative for microorganisms. In addition, special stains for microorganisms were negative from the hematoxylin–eosin-stained slides. Because the biopsies contained an infiltrate composed mostly of neutrophils, an infectious process was thought to be possible based on histopathologic examination. However, there were no other systemic signs or symptoms reported to suggest a disseminated infection, and all cultures and special stains were negative. Two cases in the literature also reported that an infection was an initial consideration, and those patients were initially treated with antibiotics because of this concern.^{2,3} The involvement in our 2 patients self-resolved over time, and this corroborates that the eruption represented a neutrophil-rich form of SCFN rather than an infectious process.

Interestingly, in the 2 cases from our database in which neutrophils formed >75% of the infiltrate, the duration of involvement was 1 day. In an additional patient in which the neutrophils formed 50% to 75% of the infiltrate (patient 8), the duration of involvement was 2 days. This suggests that neutrophils predominate at the time of the initial insult and that histiocytes follow, which is a sequence of inflammation that is commonly seen in other inflammatory processes, particularly wound healing.⁹³ It is understood that neutrophils are often the major cell type in an acute inflammatory reaction, a setting in which they are chemotactically attracted to damaged tissue. Once at the site of the damaged tissue, neutrophils play a key role in the phagocytosis and elimination of organisms and immune complex formation. In the setting of neutrophil-rich SCFN, we suspect that the damaged tissue from focal fat necrosis served as the stimulus to attract neutrophils.

We analyzed the cases in the literature to assess whether the biopsy specimens that reported neutrophils were also from young lesions, which would support the idea that neutrophils can predominate in the initial stage of SCNF. Unfortunately, in only 3 of 10 was the duration of involvement reported.^{35,66,73} In 2 biopsy specimens that were 16 and 12 days old, respectively, neutrophils formed only a small component of the infiltrate. This finding corroborates our observation by inference, because neutrophils would have mostly been replaced by histiocytes in older involvement. In the single paper with duration of involvement of 1 day, the composition of the infiltrate was not mentioned. Therefore, it is not possible to fully extract from these data whether neutrophils were prominent in “younger” areas of involvement.

We also reviewed all reported “young” lesions (ie, 0 or 1 days old) in the literature for information regarding the biopsy results; there were 5 such lesions.^{1,15,19,72,74} Unfortunately, in 3 of 5 cases, no information regarding the composition of the infiltrate was reported.^{1,74,89} It is possible that neutrophils were present. In 1 of these 5 cases, the sampling was performed with FNA, and the sample was reported to be relatively paucicellular, although neutrophils were not mentioned.⁷² In 1 report, the infiltrate was documented to be composed of histiocytes infiltrating between adipocytes with eosinophilic cytoplasm, and neutrophils were not specifically mentioned.¹⁵ These data suggest that neutrophils are not present in all early lesions of SCNF, although the data are not particularly robust given that 3 of the reports did not document the composition of the infiltrate. It is possible that neutrophils were present.

For some of our specimens, a neutrophilic panniculitis, such as subcutaneous Sweet syndrome (SS), was an initial consideration based on the histopathologic results.^{94,95} However, SS is rare in newborns, and because patients with SS usually have fever and systemic symptoms, it was relatively easy to make this distinction despite the overlapping histopathologic results. Microscopically, the presence of needle-shaped clefts was also a discriminating feature, because such clefts are not present in patients with subcutaneous SS. While there are other forms of neutrophilic panniculitis, such as α -1 antitrypsin deficiency, pancreatic panniculitis, and erythema nodosum, these conditions were not considered as diagnostic possibilities for the cases seen at our institution because these diseases typically affect adults.⁹⁶

In conclusion, this report raises awareness that newborns with subcutaneous fat necrosis can present with a neutrophil-rich variant, and our cases

suggest that it is a more likely occurrence in newly developed rather than older lesions. However, data from the literature suggest that not all new lesions contain neutrophils. The neutrophil-rich variant of SCFN can be difficult to distinguish from an infection. However, in a neonate without systemic symptoms and with negative cultures, SCFN should be considered as an explanation for a neutrophilic panniculitis, in particular if there are hints of needle-shaped clefts. Therefore, recognition of this variant can be pivotal in rendering a correct diagnosis during the neonatal period.

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Supplemental Table I. Literature review of all cases of subcutaneous fat necrosis of the newborn found in PubMed in which either a skin biopsy or a fine needle aspiration was performed

Year of publication	Investigators	No. of patients in study	Patient no.	Sex	Age of patient at onset, days	Biopsy done?	Age of lesion at time biopsy specimen obtained, days	Site	Maternal age, y	Gestational age, wks	Delivery method	Birth weight, g	Perinatal course	Ca levels* (8.7-10.1 mg/dL)	Maximum Ca (2.20-2.65 mmol/L)	Phosphorus (2.5-7.1 mg/dL)	Clinical course	Neutrophils reported	If neutrophils present, infiltrate composition	If neutrophils not mentioned but lesion <1 day old, composition of the infiltrate
2005	Acun et al	1		F	6	Yes	NK	Buttocks, back	NK	Full term	CS	3500	Fever, vomiting	Normal		NK	Resolution of lesions (time course not specified)	No		
2013	Akcay et al	1		F	13	Yes	NK	Back, legs	32	41	CS	3020	Asphyxia, meconium aspiration	15.3		6.9	NK	No		
2011	Akin et al	1		F	4	Yes	3	Thighs, arms, back	NK	Term	Vaginal	NK	Tachypnea, omphalocele	Normal		Normal	Resolution of lesions in 4 wks	No		
1961	Anbari	6	Anbari - 1	F	NK	No	NK	Face, neck, shoulders, back	NK	NK	Vaginal	NK	Difficult labor	NK		NK	NK	NK		
			Anbari - 2	F	7	No	NK	Cheek, thigh	NK	NK	Vaginal (forceps)	NK	Difficult labor	NK		NK	NK	NK		
			Anbari - 3	F	1	No	NK	Periauricular	NK	NK	Vaginal (forceps)	NK	Difficult labor	NK		NK	NK	NK		
			Anbari - 4	M	1	No	NK	Cheek	NK	NK	Vaginal (forceps)	NK	Forceps delivery	NK		NK	NK	NK		
			Anbari - 5	F	1	Yes	NK	Trunk, thigh, neck	NK	NK	Vaginal (forceps)	NK	Difficult labor	NK		NK	Resolved in 6 months	No		
			Anbari - 6	M	30	Yes	NK	Arm, back, thigh, abdomen	NK	NK	Vaginal	NK	Wrapped cord twice around neck	NK		NK	NK	No		
1999	Anderson et al	1		F	15	Yes	NK	Back, shoulders	NK	Term	Vaginal	2125	Asphyxia	NK		NK	NK	Unknown (no details of biopsy given)		
1987	Balazs et al	1		F	11	Yes	5	Dorsal aspect of hand, scalp, back	NK	NK	NK	4250	Erb—Duchene	Normal		NK	Improved by 6 wks	No		
1963	Bartrop	1		M	NK	Yes	NK	Chest, legs	NK	NK	CS	4563	Toxemia	12.1		NK	All lesions resolved (time course not specified)	No		
2006	Borgia et al	1		M	28	Yes	NK	Back, shoulders, arms, buttocks, thighs	NK	Term	CS	NK	Asphyxia, acidosis	16.2		NK	Near complete resolution by 2 months	No		
1958	Browne et al	2	Browne - 1	F	3	Yes	5	Back	39	41	Vaginal	4000	Febrile	NK		NK	Resolved by 21 wks	No		
			Browne - 2	M	1	Yes	15	Arms	25	Term	Vaginal (forceps)	4110	Erb—Duchene	NK		NK	Resolved by 16 wks	No		
1999	Burden et al	11	Burden - 1	F	7	Yes	NK	Bilateral buccal	NK	40	CS	2940	Well	Normal		NK	Resolved by 3 months	No		

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Supplemental Table I. Cont'd

Year of publication	Investigators	No. of patients in study	Patient no.	Sex	Age of patient at onset, days	Biopsy done?	Age of lesion at time biopsy specimen obtained, days	Site	Maternal age, y	Gestational age, wks	Delivery method	Birth weight, g	Perinatal course	Ca levels* (8.7-10.1 mg/dL)	Maximum Ca (2.20-2.65 mmol/L)	Phosphorus (2.5-7.1 mg/dL)	Clinical course	Neutrophils reported	If neutrophils present, infiltrate composition	If neutrophils not mentioned but lesion <1 day old, composition of the infiltrate
			Burden - 2	M	21	Yes	NK	Trunk, thighs	33	40	CS	4800	Asphyxia, sepsis, meconium aspiration		Normal	NK	Resolved by 3 months	No		
			Burden - 3	F	4	Yes	NK	Back	31	38	CS	3590	Asphyxia, acidosis		3.7	NK	Resolved by 3 months	No		
			Burden - 4	M	28	Yes	NK	Arms	39	40	CS	4100	Asphyxia, meconium aspiration		Normal	NK	Resolved by 3 months	No		
			Burden - 5	M	30	Yes	NK	Cheeks, trunk, arms	33	37	CS	2600	Asphyxia, septicemia, meconium aspiration		3.3	NK	Resolved by 3 months	No		
			Burden - 6	F	4	No	NK	Thighs, trunk, arms	NK	40	CS	NK	Asphyxia, uremia, meconium aspiration		3.8	NK	Resolved by 3 months	NK		
			Burden - 7	F	2	No	NK	Trunk	26	41	Vaginal (forceps)	4190	Asphyxia, uremia, meconium aspiration		Normal	NK	Resolved by 3 months	NK		
			Burden - 8	F	5	No	NK	Buttocks, trunk, arms	35	41	CS	3750	Asphyxia, meconium aspiration		Normal	NK	Resolved by 3 months	NK		
			Burden - 9	M	7	No	NK	Back, arms	29	35	CS	3160	Asphyxia, volvulus, meconium aspiration		Normal	NK	Resolved by 3 months	NK		
			Burden - 10	M	3	No	NK	Back, thighs	22	40	CS	4300	Asphyxia, meconium aspiration		4.9	NK	Resolved by 3 months	NK		
			Burden - 11	F	10	No	NK	Forearms	36	40	CS	3300	Asphyxia, seizures, meconium aspiration		Normal	NK	Resolved by 3 months	NK		
2013	Calisici et al	1		F	3	Yes	0	Back, arms	30	40	CS	2500	Meconium, Apgar 2/3	6.8		Normal	Gradual resolution	No		Histiocytes infiltrating between adipocytes with eosinophilic cytoplasm
1994	Carraccio et al	1		M	5	Yes	10	Thigh, trunk, arm	NK	36	Vaginal	2100	Hypotension, hyperbilirubinemia	NK		NK	NK	No		
1981	Chen et al	1		M	3	Yes	NK	Buttocks, upper back, shoulder, thighs	NK	43	CS	4500	Asphyxia, seizure, acidosis, hypercoagulability	NK		NK	80% resolution by 2 weeks	No		

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Supplemental Table I. Cont'd

Year of publication	Investigators	No. of patients in study	Patient no.	Sex	Age of patient at onset, days	Biopsy done?	Age of lesion at time biopsy specimen obtained, days	Site	Maternal age, y	Gestational age, wks	Delivery method	Birth weight, g	Perinatal course	Ca levels* (8.7-10.1 mg/dL)	Maximum Ca (2.20-2.65 mmol/L)	Phosphorus (2.5-7.1 mg/dL)	Clinical course	Neutrophils reported	If neutrophils present, infiltrate composition	If neutrophils not mentioned but lesion <1 day old, composition of the infiltrate
1995	Chuang et al	1		M	21	Yes	NK	Hand, leg	24	37	CS	3050	Asphyxia, sepsis, PDA, VSD	Normal	Normal	Normal	Gradual resolution	Yes	Histiocytes, lymphocytes and neutrophils (percentage of each cell type not mentioned)	
1992	Cook et al	1		F	1	Yes	NK	Back, arm	22	41	CS	4369	Asphyxia, meconium aspiration	High	Normal	Normal	Near complete resolution by 2 months	No		
2013	Coondoo et al	1		M	9	Yes	NK	Back, buttock, thighs	NK	Full term	CS	NK	Birth asphyxia	12.4	NK	NK	Resolution (time course no specified)	No		
1994	Darmstadt et al	1		M	4	Yes	NK	Cheeks, arms, upper chest, back, buttocks	NK	Full term	CS	3967	Asphyxia, acidosis, neutropenia, hypotension	High	NK	NK	Resolved in 4 months	No		
2006	Diamantis et al	1		F	2	Yes	NK	Cheek, shoulder	NK	38	Vaginal	4361	Supraventricular tachycardia	Normal	NK	NK	Resolution by 10 weeks	Yes	Histiocytes, neutrophils, lymphocytes and eosinophils (percentage of each cell type not mentioned)	
1968	Duhn et al	2	Duhn - 1	M	14	No	NK	Lower back, trunk, arms, thighs, legs	20	Full term	Vaginal	3970	Asphyxia, acidosis	9.7	6.2	6.2	NK	No		
			Duhn - 2	F	35	Yes	NK	Trunk, extremities	23	43	Vaginal (forceps)	3180	Asphyxia, bradycardia	9.8	6.8	6.8	Resolution by 4 months	No		
1907	Fabyan	1		M	3	Yes	11	Cheeks, forearms, head, buttocks, lower leg	22	Full term	NK	2970	Asphyxia	NK	NK	NK	All lesions resolved except facial plaque. DOL 14 died of accidental suffocation	No		
2008	Farinelli et al	1		NK	1	Yes	NK	Neck, back	NK	NK	NK	NK	Transient brain ischemia	Normal	NK	NK	Resolution by 6 months	No		
2002	Fernandez-Lopez et al	1		M	14	Yes	4	Buttocks, thighs	NK	41	Vaginal (vacuum)	3300	Seizure, cerebral hemorrhage	10.74	Normal	Normal	Resolution by 6 weeks	No		

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Supplemental Table I. Cont'd

Year of publication	Investigators	No. of patients in study	Patient no.	Sex	Age of patient at onset, days	Biopsy done?	Age of lesion at time biopsy specimen obtained, days	Site	Maternal age, y	Gestational age, wks	Delivery method	Birth weight, g	Perinatal course	Ca levels* (8.7-10.1 mg/dL)	Maximum Ca (2.20-2.65 mmol/L)	Phosphorus (2.5-7.1 mg/dL)	Clinical course	Neutrophils reported	If neutrophils present, infiltrate composition	If neutrophils not mentioned but lesion <1 day old, composition of the infiltrate	
1988	Finne et al	1		F	6	Yes	29	Back, upper arms	NK	41.5	CS	4510	Asphyxia	High		Normal	NK	No			
1948	Flory et al	1		M	1	Yes	64	Neck, back	38	40	Vaginal	3650	Acidosis, nasopharyngitis	NK		NK	FTT, death at 66 days	No			
1933	Fox	5	Fox 1	F	17	Yes	45.5	Back, buttocks, legs, vulva	29	Full term	Vaginal (forceps)	3400	Asphyxia	NK		NK	All lesions resolved over approximately 3 months	No			
			Fox 2	F	25	Yes	9	Back and arms	NK	NK	NK	3300	Normal	NK		NK	All lesions resolved over approximately 2 months	No			
			Fox 3	M	0	No	NK	Back, arms, cheeks, chest	NK	full term	NK	NK	Normal	NK		NK	All lesions resolved over approximately 2 months	NK			
			Fox 4	F	10	Yes	35	Back, buttocks, legs, face	23		NK	Vaginal - forceps	3750	NK	NK		NK	NK	No		
			Fox 5	F	0	No	NK	Buttocks, vulva, back, legs	45		NK	NK	4310	NK	NK		NK	All lesions resolved over approximately 5 wks	NK		
1989	Friedman et al	1		M	9	Yes	NK	Back, shoulders, thigh, buttocks	36	43	CS	3950	Hypoglycemia, oliguria with hyponatremia (SIADH), left leg paresis	High		Normal	Resolution by 2 months	No			
1991	Glover et al	2	Glover - 1	M	134	Yes	NK	Elbows, forearm	NK	NK	NK	NK	2 wks post VSD closure		2.77	Normal	Resolution in 3 wks	No			
			Glover - 2	F	35	No	NK	Arms, back	NK	NK	NK	NK	Correction of transposition of great arteries at 7 days of life	NK		NK	Resolution in 4 wks	NK			
2013	Gomes et al	2	Gomez-1	M	1	Yes	NK	Back and upper limbs	NK	Term	CS	3480	Nuchal cord, sepsis, respiratory compromise	Slightly increased		NK	Resolution by 40 wks	No			
			Gomez-2	F	30	Yes	NK	L buttock, submandible, arms	NK	Term	CS	3240	Meconium, thrombosis of caval, iliac veins	Normal		NK	Resolution by 4 months	No			

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Supplemental Table I. Cont'd

Year of publication	Investigators	No. of patients in study	Patient no.	Sex	Age of patient at onset, days	Biopsy done?	Age of lesion at time biopsy specimen obtained, days	Site	Maternal age, y	Gestational age, wks	Delivery method	Birth weight, g	Perinatal course	Ca levels* (8.7-10.1 mg/dL)	Maximum Ca (2.20-2.65 mmol/L)	Phosphorus (2.5-7.1 mg/dL)	Clinical course	Neutrophils reported	If neutrophils present, infiltrate composition	If neutrophils not mentioned but lesion <1 day old, composition of the infiltrate
1995	Gupta et al	1		NK	3	FNA	NK	"All over infant's body"	NK	0	K	4180	Asphyxia		2.96-3.62	NK	Lesions regressed on follow up, at age 40 weeks child in good health	No		
1998	Hernandez-Martin et al	1		M	7	Yes	NK	Leg, popliteal fold, toes	NK	38	Vaginal	2900	Uncomplicated	NK		NK	NK	No		
1993	Hicks et al	1		F	28	Yes	NK	Malar, upper back, shoulder, chest	35	NK	CS	3950	Meconium aspiration and hypoxia	High		Normal	Resolution (time course no specified)	No		
2012	Hogeling et al	3	Hogeling-1	M	9	Yes	15	Scalp, neck, back	NK	Full term	Vaginal	4200	Cardiac arrest, Apgar 0 at birth, cooling	NK		NK	Resolution by age 10 weeks	NK		
			Hogeling-2	M	11	Yes	3	Back	NK	Full term	CS	3500	Fetal distress, meconium, resuscitation	11.5		NK	Resolution within a few weeks	NK		
			Hogeling-3	F	5	Yes	0	Back, arms, shoulders	NK	37	CS	3560	Meconium	NK		NK	NK	NK		No details of biopsy findings provided
1951	Holzel et al	3	Holzel - 1	M	14	Yes	~16	Thighs, back, scapula	NK	NK	Vaginal	4082	Asphyxia	NK		NK	Resolution ~1 month after appearance of the lesions	Yes	Mostly large cells with ill- defined cytoplasm (probably histiocytes) and a few polymorphonuclear cells	
			Holzel - 2	M	7	No	NK	Buttocks	NK	NK	Vaginal	3175	Severe cyanosis	NK		NK	Resolved by 2 months	NK		
			Holzel - 3	F	12	No	NK	Upper arm, neck, mastoid	NK	NK	Vaginal (forceps)		Severe asphyxia	NK		NK	Resolved after 2 months	NK		
2003	Hung et al	1		F	1	Yes	4	Back buttocks, extremities	36	Term	CS	3758	Acidosis, elevated liver enzymes		2.8	7.1	Plaques started to improve during 4th week of life	No		
2011	Ichimiya et al	2	Ichimiya-1	F	13	Yes	16	Left upper back	NK	Term	NK	3238	Arrhythmia	NK		NK	NK	No		

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Supplemental Table I. Cont'd

Year of publication	Investigators	No. of patients in study	Patient no.	Sex	Age of patient at onset, days	Biopsy done?	Age of lesion at time biopsy specimen obtained, days	Site	Maternal age, y	Gestational age, wks	Delivery method	Birth weight, g	Perinatal course	Ca levels* (8.7-10.1 mg/dL)	Maximum Ca (2.20-2.65 mmol/L)	Phosphorus (2.5-7.1 mg/dL)	Clinical course	Neutrophils reported	If neutrophils present, infiltrate composition	If neutrophils not mentioned but lesion <1 day old, composition of the infiltrate
			Ichimiya-2	F	23	Yes	7	Upper back, buttocks, posterior thighs	29	42 5/7	NK	NK	NK	NK	NK	NK	NK	No		
2007	Isaiah et al	1		M	42	Yes	NK	"Many areas of his body"	NK	35	NK	NK	Asphyxia	20		NK	Resolution starting at 13 wks	No		
1953	Ivy et al	1		M	1	Yes	16	Upper arm, shoulder, back, buttocks, thigh	24	NK	CS	4200	Respiratory difficulty	NK		NK	Minimal residual induration at age 27 days	No		
1993	Janssens et al	1		M	5	Yes	4	Trunks, buttocks	NK	Term	NK	NK	Asphyxia	Normal		NK	Skin abnormality pronounced between 3-13 wks after birth then gradually resolved	No		
1984	Katz et al	1		M	11	Yes	7	Nipple	NK	43	Vaginal (forceps)	3860	Asphyxia, sepsis	Normal		NK	Lesion gradually resolved, discharged from hospital at 29 days of age	No		
2007	Kenani et al	2	Kenani - 1	F	3	Yes	NK	Back, shoulder, arms, thigh, buttocks	NK	Post term	CS	NK	Respiratory distress	High		NK	Regression by 45 days, resolution by 3 months of age	No		
			Kenani - 2	M	4	Yes	NK	Back, neck, arms	NK	Full term	Vaginal	NK	NK	NK		NK	Regression by 15 days, resolution by 3 months of age	No		
2009	Kim et al	1		F	5	Yes	NK	Neck, back, shoulders	NK	Full term	CS	2875	VSD, PDA	12.1		8.5	Discharged at 61 days, succumbed to SIDS	No		

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Supplemental Table I. Cont'd

Year of publication	Investigators	No. of patients in study	Patient no.	Sex	Age of patient at onset, days	Biopsy done?	Age of lesion at time biopsy specimen obtained, days	Site	Maternal age, y	Gestational age, wks	Delivery method	Birth weight, g	Perinatal course	Ca levels* (8.7-10.1 mg/dL)	Maximum Ca (2.20-2.65 mmol/L)	Phosphorus (2.5-7.1 mg/dL)	Clinical course	Neutrophils reported	If neutrophils present, infiltrate composition	If neutrophils not mentioned but lesion <1 day old, composition of the infiltrate
1993	Kruse et al	2	Kruse - 1	F	14	No	NK	Neck, back, cheeks	NK	38	CS	4600	Well	14		6.3	Resolution by 9 weeks of age, Ca and Phosphorous normal	No		
			Kruse - 2	F	19	Yes	37	Arms, back, buttocks	NK	At term	CS	3400	Meconium aspiration, septicemia	11.6		5.7	Gradual resolution	No		
2009	Ladoyanni et al	1		F	2	Yes	10	Back, arm	NK	NK	CS	NK	NK		2.92	High	Improved by 1 month after appearance of lesions	No		
2001	Lee et al	1		M	22	FNA	NK	Left cheek, extremities	NK	NK	NK	NK	NK	NK		NK	Resolved after 3 months	No		
1994	Lewis et al	1		M	4	Yes	NK	Back, buttocks	NK	38	CS	4520	"Poor Apgar scores"		2.57	NK	Prednisolone treated, plaques barely palpable by age 4.5 months	No		
1951	Lightwood et al	2	Lightwood - 1	M	1	Yes	39	Arm	NK	NK	Vaginal	3666	Radial nerve palsy	NK		NK	Lesion was excised; indurated area disappeared 12 days after excision	No		
			Lightwood - 2	F	3	No	NK	Arm	NK	Term	Vaginal	NK	Radial nerve palsy	NK		NK	Lesion shrunk to size of "pea" by 2 months	No		
1993	Liu et al	1		M	32	Yes	3	Shoulder, back, thigh, cheek	NK	NK	Vaginal	LGA	Asphyxia, meconium aspiration	NK	3.3 (day 35)	Normal	Free of lesions at 2 month follow up	No		
2010	Lopez et al	1		F	4	FNA	NK	Arm, back	NK	Term	CS	NK	NK	Normal		Normal	Resolution over 4 wks	Yes	Histiocytes and neutrophils, percentage of each cell type not mentioned	

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Supplemental Table I. Cont'd

Year of publication	Investigators	No. of patients in study	Patient no.	Sex	Age of patient at onset, days	Biopsy done?	Age of lesion at time biopsy specimen obtained, days	Site	Maternal age, y	Gestational age, wks	Delivery method	Birth weight, g	Perinatal course	Ca levels* (8.7-10.1 mg/dL)	Maximum Ca (2.20-2.65 mmol/L)	Phosphorus (2.5-7.1 mg/dL)	Clinical course	Neutrophils reported	If neutrophils present, infiltrate composition	If neutrophils not mentioned but lesion <1 day old, composition of the infiltrate
2009	Lund et al	1		M	1	Yes	NK	Arm	NK	38	NK	NK	Well	Hypocalcemia		NK	NK	No		
1988	Lusk et al	1		F	28	Yes	NK	Left cheek	16	NK	CS	NK	Cyanosis, bradycardia, hypoglycemia			NK	NK	No		
2007	Mahe et al	16	Mahe - 1	F	NK	7/16	NK	Diffuse, ≥ 4 nodules	Range 21-42 years old	Term	NK	NK	Infection, meconium amniotic fluid, macrosomia	Hypercalcemia in 9/13 children evaluated		Not reported in any of the cases	Reported as an aggregate; mean time to recovery 86 days (range, 25-180 days)	Biopsies on 7/16 cases		
			Mahe - 2	M			NK	Localized, <4 nodules	Average age 33	Term	NK	NK	Infection, meconium amniotic fluid, hypoxemia					No mention of neutrophils on the 7 biopsies		
			Mahe - 3	F			NK	Diffuse, ≥ 4 nodules		Term	Vaginal (forceps)	NK	Well							
			Mahe - 4	M			NK	Diffuse, ≥ 4 nodules		Term	NK	NK	Infection, meconium amniotic fluid, hypoxemia, macrosomia							
			Mahe - 5	F			NK	Diffuse, ≥ 4 nodules		Term	NK	NK	Infection, meconium amniotic fluid, hypoxemia, coma, hypoglycemia, macrosomia							
			Mahe - 6	M			NK	Diffuse, ≥ 4 nodules		Term	Vaginal (forceps)	NK	Well							
			Mahe - 7	M			NK	Localized, <4 nodules		Term	Vaginal (forceps)	NK	Infection, macrosomia							
			Mahe - 8	F			NK	Diffuse, ≥ 4 nodules		Term	Vaginal (forceps)	NK	Well							
			Mahe - 9	M			NK	Diffuse, ≥ 4 nodules		Term	NK	NK	Hypoglycemia, macrosomia							
			Mahe - 10	M			NK	Diffuse, ≥ 4 nodules		Term	Vaginal (forceps)	NK	Infection, hypoxemia, coma, seizure, macrosomia							
			Mahe - 11	F			NK	Diffuse, ≥ 4 nodules		Term	Vaginal (forceps)	NK	Infection							

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			Mahe - 12	M			NK	Localized, <4 nodules		Term	NK	NK	Infection, hypoxemia, coma, seizure, hypoglycemia							
			Mahe - 13	M			NK	Diffuse, ≥4 nodules		Term	Vaginal (forceps)	NK	Infection, red cell alloimmunization, macrosomia							
			Mahe - 14	F			NK	Diffuse, ≥4 nodules		Term		NK	Infection, hypoxemia							
			Mahe - 15	M			NK	Diffuse, ≥4 nodules		Term	Vaginal (forceps)	NK	Infection, meconium amniotic fluid, hypoxemia							
			Mahe - 16	F			NK	Diffuse, ≥4 nodules		Term	NK	NK	Cardiac surgery					No		
1957	Martin et al	1		F	5	Yes	NK	Back, shoulder, thigh	38	NK	Vaginal	3500	Petechial hemorrhages, subconjunctival hemorrhages	12		NK	Fevers and FTT, discharged at 2.5 months of age	Yes	Mostly histiocytes, including multinucleated giant cells with a small area with neutrophils	
1997	Mather et al	1		M	10	Yes	8	Back	NK	33	CS	NK	NK	NK		NK	NK	No		
2011	Mitra et al	1		M	3	Yes	NK	Chest, abdomen, arm, neck, scalp	NK	33	CS	2300	Asphyxia, acidosis, hypoxic ischemic encephalopathy	High		NK	Renal calcifications on ultrasonography	No		
1981	Mogilner et al	1		F	4	Yes	10	Upper thighs, inner arms	40	Post-term	CS	4260	Meconium aspiration, resuscitation, intubation	Normal		NK	Lesions resolved by age 4 months	No		
1983	Moreno-Gimenez et al	1		NK	NK	Yes	NK	Cheek, arm, buttocks	NK	Term	CS	NK	Normal pregnancy	NK		NK	Nodules regressed spontaneously and gradually during 5 months	No		
1949	Noojin et al	1		M	1	Yes	NK	Trunk, shoulder	NK	NK	NK	NK	NK	NK		NK	NK	No		

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1997	Norton et al	2	Norton - 1	M	14	FNA	14	Cheek, neck	NK	Full term	Vaginal	NK	Transposition of great vessels	Normal		NK	Disappearance of masses by 6 month of life	No		
			Norton - 2	M	7	No	NK	Cheek	NK	Full term	Vaginal (forceps)	NK	Well	Normal		NK	Resolution by 2 months	NK		
1987	Norwood-Galloway et al	1		M	1	Yes	NK	Thigh, back	29	NK	CS	4720	Meconium aspiration, seizures, cerebellar hemorrhage and infarction	17		Normal	Episode of hypercalcemia; nodules resolving by 2 months of age	No		
2011	Oliveira	2	Oliveira-1	F	13	Yes	NK	Back, bilateral cervical region	NK	Term	Vaginal (vacuum)	4850	Gestational diabetes, macrosomia, shoulder dystocia	Normal		NK	Gradual regression of lesions	No		
			Oliveira-2	M	28	Yes	NK	Left parieto-temporal region	NK	35	NK	1840	Light for gestational age	Normal		NK	Regressed spontaneously over months leaving atrophic scarring			
1978	Oswalt et al	1		M	10	Yes	NK	Trunk	43	NK	CS	3140	Asphyxia, meconium aspiration, pneumonia	NK		NK	Poor sucking/feeding, metabolic acidosis; died at 3 wks of age; biopsy at time of autopsy	No		
2010	Oza et al	1		M	6	Yes	NK	Upper back, buttocks, arms	32	Term	CS	NK	Decelerations, placental abruption	11.2		NK	Peak calcium day 22; no comment about resolution of lesions	Yes	Mostly histiocytes, with scattered neutrophils and lymphocytes	

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2007	Pai et al	1		M	10	Yes	NK	Neck, axilla, inguinal	NK	34	CS	NK	Hypoxia, seizure, unconjugated hyperbilirubinemia	NK	NK	NK	Patient lost to follow-up	No		
2005	Parvathidevi et al	1		NK	NK	Yes	NK	Back, arms	NK	40	Vaginal	3600	Asphyxia, meconium aspiration		2.76-2.98	NK	Lesions regressed, in good health at 7 wks of age	No		
1978	Pasyk et al	4	Pasyk-1	F	2	Yes	12	Back	NK	41	NK	3150	Anoxemia	NK		NK	NK	Yes, at least in 1 case; histopathology for all cases reported in aggregate	Mostly histiocytes, occasional single neutrophils and eosinophils	
			Pasyk-2	M	12	Yes	30	Trunk, extremities, face	NK	Term	Vaginal	4200	NK	NK		NK	NK			
			Pasyk-3	M	2	Yes	40	Back, abdomen, buttock, cheek	NK	NK	CS	4550	NK	NK		NK	NK			
			Pasyk-4	M	14	Yes	28	Back, chest	NK	NK	Vaginal	3580	CNS injury symptoms	NK		NK	NK			
2010	Perrota et al	1		M	3	Yes	NK	Forearm	NK	Term	CS	2950	Full thickness ulcers; local flaps and graft of autologous keratinocytes	NK		NK	Persisted for over 6 months; left permanent scars of grafted site	No		
1999	Repiso-Jimenez et al	1		F	10	Yes	NK	Back, scalp	NK	36	Vaginal	2760	Hypertonia, cyanosis, hyperthermia	Normal		NK	All nodules disappeared without scarring by 3 months	No		

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Supplemental Table I. Cont'd

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1998	Rosbotham et al	1		F	1	Yes	NK	Face, buttock, back, shoulder, arms	38	39	Vaginal	3970	Asphyxia, meconium staining, pneumothorax, seizure	Normal	NK	NK	Plaque persisted beyond age 6 months and was associated with pain; both resolved by 9 months	No		
1990	Salas Valien et al	1		M	9	Yes	NK	Back, shoulders	NK	Full term	CS	3250	Distressed	NK	NK	NK	Lesions resolved (time course not specified)	No		
2012	Savic et al	1		F	3	Yes	NK	Back, arm, thighs	NK	Term	CS	2800	Tachypnea	Low	NK	NK	Observed regularly for 6 wks; lesions resolved by 3rd month	Yes	Histiocytes, lymphocytes, plasma cells and neutrophils (percentage of each cell type not mentioned)	
1998	Scales et al	1		F	10	Yes	32	Back and buttocks	NK	NK	CS	4290	Respiratory distress and cyanosis; FTT	14.9 mg/dL	3.6 mg/dL	3.6 mg/dL	Plaque improved at 6 months, nephrocalcinosis	No		
2012	Schubert et al	2	Schubert-1	M	2	FNA	1	Cheek	NK	33	CS	2100	Respiratory distress	NK	NK	NK	NK	No		A few histiocytes and lymphocytes; crystalline in cytoplasm in adipocytes
			Schubert-2	F	1	FNA	29	Right postauricular	NK	NK	NK	NK	Mass initially clinically diagnosed as hemangioma	NK	NK	NK	Mass soft, nontender after 2 weeks	No		

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2005	Schulzke et al	1		F	6	Yes	1	Back, neck, arms	NK	Term	CS	3830	Fetal decelerations during labor, acidosis	Normal		NK	Complete resolution by 12 wks	Yes	Histiocytes, including multinucleated cells, neutrophils, lymphocytes and eosinophils (percentage of each cell type not mentioned)	
1995	Sharata et al	2	Sharata-1	M	4	Yes	17	Back, upper arms, buttocks, cheeks	22	40	CS, emergent	4850	Apgar 3, 6; hypoglycemia, leukocytosis, thrombocytopenia	11.4 mg/dL		Normal	Complete resolution of plaques and hypercalcemia	No		
			Sharata-2	F	5	Yes	0	Back, knees, elbow	29	40	Vaginal	2980	Apgar 9, 9; Ebstein anomaly with cyanosis	Normal		Normal	Focal seizure activity on phenobarbital; mild acrocyanosis; no comment on resolution of plaques	No	No details of biopsy findings provided	
1970	Sharlin	2	Sharlin-1	M	14	No	NK	Legs, back	NK	Full term	CS	4479	Preeclampsia, pitting edema of lower extremities	11.1		5.1	Initial nodules improved by 27 days of age. Nodular recurrences over the following months. FTT at 6 months	NK		
			Sharlin-2	M	NK	Yes	NK	Lumbosacral area, abdomen, buttocks, thighs, arms	NK	40	Vaginal	4990	Well; "stiffness of the legs" shortly after birth	12.2		NK	Subcutaneous indurations slowly resorbed over 3 months	No		

Continued

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1986	Silverman et al	1		F	20	Yes	NK	Back, buttocks, arms	25	45	CS	3900	Truncus arteriosus, VSD	NK		NK	Resolution within 1 month	Yes	Mostly histiocytes and lymphocytes, with small foci of neutrophils	
2007	Singalavanija et al	7	Singalavanija - 1	F	7	Yes	NK	Thigh, shoulder	NK	Full term	CS	3180	Meconium aspiration, pneumothorax	High		NK	Prednisolone treatment; lesions resolved in 4 months without scarring	No		
			Singalavanija - 2	M	20	Yes	NK	Arm	NK	Full term	CS	3640	Asphyxia, cardiopulmonary resuscitation	Elevated		Normal	Lesions resolved by age 5 months; cerebral palsy	No		
			Singalavanija - 3	M	3	No	NK	Back	NK	Full term	CS	3335	Hypoglycemia, hyperbilirubinemia	Elevated		NK	Resolution at age 1 month	NK		
			Singalavanija - 4	F	42	No	NK	Shoulder	NK	NK	CS	3790	Hypoglycemia, hypothyroidism, Down syndrome	Elevated		Normal	Nodules decreased in size at age 4 months and completely disappeared at age of 7 months	NK		
			Singalavanija - 5	M	5	Yes	17	Back, arm	NK	NK	CS	3330	Asphyxia, sepsis	High		NK	Lesions resolved in 2 months	No		
			Singalavanija - 6	M	4	No	NK	Neck	NK	Full term	Vaginal	NK	Meconium aspiration	High		NK	Lesions disappeared by 1 month of age	NK		
			Singalavanija - 7	F	5	No	NK	Back, buttocks	NK	Full term	CS	2900	Omphalocele, fetal distress	High		NK	Resolved by 2 months	NK		

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2006	Srinath et al	1		M	23	Yes	NK	Axilla	39	37	CS	NK	Pulmonary hypertension, PDA, anemia, thrombocytopenia	NK		NK	Lesions had resolved at the 6-month follow up	No		
1961	Steiness I	2	Steiness-1	M	11	Yes	NK	Back of neck, hips, arms	36	Term	Vaginal	4500	Placenta accreta, DM	NK		NK	Skin changes completely disappeared by 2 months of age	No		
			Steiness-2	F	10	Yes	NK	Upper arms, thighs, buttocks	36	Term	Vaginal	4100	Intracranial obstetric trauma	NK		NK	Lesions resolved around 2 months of age	No		
2007	Tajirian et al	1		F	10	Yes	NK	Back	NK	NK	CS	NK	Meconium aspiration, hypoglycemia, hypothermia, seizure	10.4		NK	No subsequent seizure activity or recurrence of nodules	No		
1980	Thomsen	1		F	16	Yes	5	Jaw, arms, thighs, back	NK	Full term	Vaginal	4143	Asphyxia	13.6		Normal	Hypercalcemia treated with low calcium diet and no vitamin D; lesions softened over weeks	No		
1976	Tsuji et al	2	Tsuji - 1	M	1	Yes	23	Buttock, thigh, forearm, leg, back	NK	38	CS	3800	Asphyxia	NK		NK	NK	No		
			Tsuji - 2	F	21	Yes	11	Back, shoulder, chest	NK	NK	Vaginal	3300	Well	NK		NK	NK	No		
1994	Urban et al	1		F	7	Yes	NK	Back, shoulders, elbows	41	Term	Vaginal	2650	Apneic episodes, peripheral cyanosis, jaundice, leukocytosis	Elevated		NK	Complete resolution of skin changes at day 34 of life	No		

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2009	Vasireddy et al	1		F	18	Yes	NK	Neck	NK	36	CS	3100	Hypoglycemia, cardiomyopathy, pulmonary hypertension	High	NK	NK	Palpable abnormalities on neck no longer apparent after 2 months	No		
1991	Vera et al	1		NK	1	Yes	NK	Buttocks	NK	NK	NK	NK	NK	NK	NK	NK	NK	No		
1993	Vonk et al	1		M	5	Yes	4	Posterior trunk, buttocks	NK	Term	Vaginal (vacuum)	4060	Intrapartum asphyxia, metabolic acidosis	Low, 6.96	NK	NK	Indurated plaques remained for about 4 months	No		
1993	Walker et al	1		M	NK	Yes	NK	Right zygoma	NK	Term	Vaginal (forceps)	NK	Cleft soft palate	NK	NK	NK	NK	No		
1966	Weary et al	5	Weary - 1	M	3	Yes	NK	Buttock, back	34	At term	Vaginal	4337	Well	NK	NK	NK	Lesions improved by the time of discharge (2 weeks old)	No		
			Weary - 2	M	56	Yes	NK	Arms, legs, back, buttocks	22	NK	NK	NK	Well	NK	NK	NK	Patient died, autopsy not performed	No		
			Weary - 3	M	1	Yes	NK	Buttock, scalp, chest, arms, legs, back	30	At term	Vaginal	3600	Prolapsed cord, marked anoxia	12.3	5.4	NK	NK	No		
			Weary - 4	M	6	Yes	NK	Thigh, buttocks, shoulder, back, arms	17	At term	Vaginal (forceps)	3480	Asphyxia, meconium aspiration, seizures	NK	NK	NK	Lesions healed with depressed scar	No		
			Weary - 5	M	4	No	NK	Buttocks, back, arm	33	At term	NK	NK	Erythroblastosis	NK	NK	NK	Some softening at the 6-week checkup	NK		

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1964	Wilkerson JA	1		M	NK	Yes	NK	Back, buttocks, scalp, thorax and extremities	NK	NK	Vaginal	3285	Prolonged labor, cord prolapse, anoxia	12.3		5.44	Hypercalcemia; patient died from cardiac arrest at 16.5 weeks of age; multiple calcifications in many organs at autopsy	No		
2001	Wiadrowski et al	1		F	6	Yes	1	Thigh, back	NK	At term	Vaginal (forceps)	4350	Asphyxia, meconium aspiration		3.74	NK	Resolution of most nodules by 6 months of age	No	Needle-shaped clefts present, but composition of infiltrate not described	
1990	Wolach et al	1		F	21	Yes	NK	Thigh, chest	36	40	Vaginal	3800	Asphyxia, meconium aspiration, acidosis, hypoglycemia, seizures	Normal		NK	Lesions resolved gradually and entirely disappeared by 3 months of age	No		
2007	Zaulyanov et al	1		F	6	Yes	NK	Buttocks	26	41	CS	NK	Thrombocytopenia, elevated ferritin (9× the upper limit)	High		NK	Ferritin decreasing and otherwise normal laboratory findings at 1 month	No		

Data from <https://www.ncbi.nlm.nih.gov/pubmed/>.

CNS, Central nervous system; CS, caesarean section; DM, diabetes mellitus; FNA, fine-needle aspiration; FTT, failure to thrive; NK, not known; PDA, patent ductus arteriosus; SIDS, sudden infant death syndrome; VSD, ventricular septal defect.

*One or more cases with abnormal calcium levels is reported as abnormal (high or low).