

QUIZ

CORRECT ANSWER TO THE QUIZ. CHECK YOUR DIAGNOSIS

SUBCUTANEOUS FAT NECROSIS OF THE NEWBORN – A CASE REPORT AND REVIEW OF LITERATURE

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Subcutaneous fat necrosis of the newborn is a rare, benign, self-limited hypodermatitis that affects full-term or postmature newborn with history of perinatal stress such as hypoxia, hypothermia or local pressure trauma. The main lesions appear as subcutaneous nodules in adipose tissue.

We present a case of a three-week old newborn born in spontaneous delivery in the 40Hbd in poor general condition (inborn pneumonia and perinatal hypoxia) which was admitted to the hospital due to subcutaneous tissue induration and skin discoloration above the lesion. The skin ultrasound examination showed foci of homogeneously hyperechogenic subcutaneous tissue thickened up to 6 mm. Further examinations did not reveal any abnormalities besides the slightly increased calcium concentration (1,69 mmol/l with normal range of 1,2 mmol/l). In order to diagnose the condition a tissue sample was collected. The histological examination revealed panniculitis with infiltration with mononuclear cells, e.g. macrophages as well as multinucleated giant cells with radial arrangement of needle-shaped clefts in cytoplasm. After treatment with corticosteroids resolution of all the lesions was noted.

Key words: subcutaneous fat necrosis, perinatal stress, hypodermatitis.

Introduction

Subcutaneous fat necrosis (SFN or SCFN) is an uncommon, transient, self-limited benign disease affecting adipose tissue of full-term or postmature newborn usually with a history of perinatal stress. This condition usually appears within the first 6 weeks of life. Characteristic skin lesions comprise subcutaneous, mobile painless nodules or plaques. Typically they are located on the buttocks, cheeks, posterior trunk, arms and legs. The skin over the lesions may be violaceous, erythematous or normal in appearance. Prognosis is generally good and in the majority of cases the lesions resolve spontaneously without scarring. Hypercalcemia is the main acute

complication that is accompanied by SFN and may be life threatening.

The pathogenesis of SFN remains unknown. However neonatal hypoxia or hypothermia for various reasons and local pressure trauma could play some role in promoting the process.

Case report

Three-week old newborn was admitted to the No1 University Hospital in Bydgoszcz, the Chair and Department of Paediatric Surgery. The child's general condition at the admission was good. The main finding in this patient was a skin lesion on the

back in the form of subcutaneous tissue induration with diameter of 3×5 cm (Fig. 1). The lesion appeared in the second week of the newborn's life. The size of the eruption was gradually increasing. When the newborn was being admitted to the hospital it was discovered that the skin of the back, right arm and right buttock was discoloured. The child was also diagnosed as subcutaneous tissue induration. Further examinations did not reveal any abnormalities besides the slightly increased serum calcium concentration (e.g. 1,69 mmol/l with normal range of 1,2 mmol/l). The ultrasound scan showed a homogeneously hyperechogenic subcutaneous tissue thickened up to 6 mm (Fig. 2). The patient was the first child of young and healthy parents. The medical history revealed there were pregnancy complications resulting from the mother's accidental fall in the 38Hbd which caused premature placental ablation. The girl was born in spontaneous delivery in the 40 Hbd with body weight of 3480g in poor general



Fig. 1. A three-week old newborn with subcutaneous mobile and erythematous lesions on the back with diameter of 3×5 cm

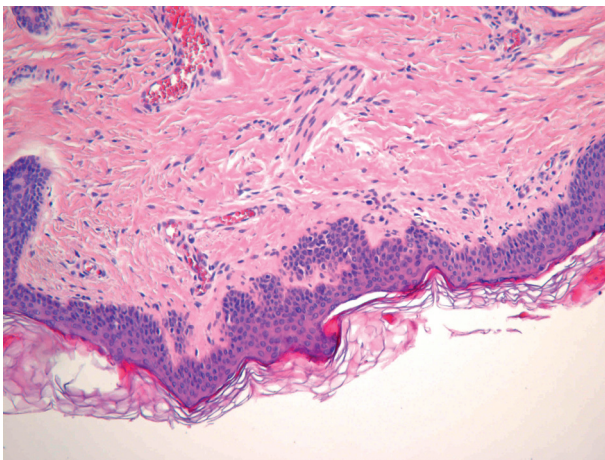


Fig. 3. Skin biopsy reveals normal structure of epidermis, dermis and upper layers of hypodermis. HE, objective magnification $4\times$

condition. The newborn Apgar score was 3 points in the first minute and 6 points in the fifth minute of postnatal life. Additionally inborn pneumonia and perinatal oxygen deficiency in tissues were diagnosed.

In order to diagnose the condition a tissue sample was taken and sent to the our Chair and Department of Clinical Pathology. We received formalin fixed specimen taken from the back that was composed of dermis and hypodermis. The diameter of the skin sample was 3×5 cm. The surface of the skin didn't reveal any changes but white and grey colour of the cut surface was noted. After macroscopic examination paraffin blocks were prepared. Hematoxylin-eosin staining was made on deparaffinized and rehydrated paraffin tissue section ($5 \mu\text{m}$). The microscopic examination demonstrated that there wasn't any changes in epidermis, dermis and upper layers of hypodermis (Fig. 3, 4), but patchy areas of fat necrosis and panniculitis in lower part of hypodermis were indicated. A high-pow-

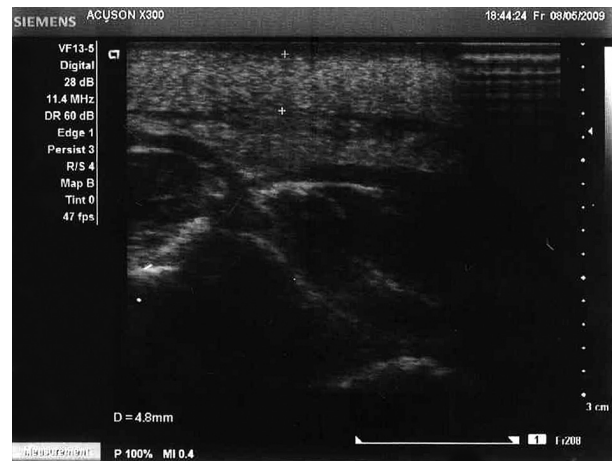


Fig. 2. The ultrasound scan demonstrates a homogeneously hyperechogenic subcutaneous tissue thickened up to 6 mm

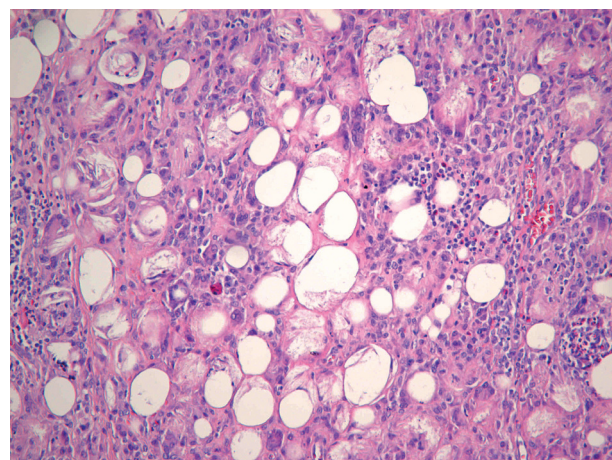


Fig. 4. Within lower part of hypodermis areas of necrosis with inflammatory infiltrate composed mainly by mononuclear cells as well as some multinucleated cells. HE, objective magnification $10\times$

er view showed that the inflammatory infiltrate contained mononuclear cells mainly macrophages and multinucleated giant cells. The characteristic histological findings of SFN showed needle-shaped crystals (Fig. 5). Needle-shaped clefts were arranged radially in cytoplasm of the macrophages, multinucleated giant cells and adipocytes. The foci of calcium and fibrosis weren't observed.

After the diagnosis the child was transferred to the Children's Hospital in Bydgoszcz and treated with steroids. A gradual complete resolution of all the lesions was noted.

Discussion

Subcutaneous fat necrosis of newborn is a rare condition in healthy babies born as full-term or prolonged pregnancy [1]. The real frequency of this condition has not been established yet. Predilection for gender and race has not been established either [2]. Skin lesions appear in the first few weeks of a newborn's life, usually between 1st and 6th week after the delivery. They are indurations described as subcutaneous tissue in the form of nodules or more extensive plaques [1]. The lesions are usually painless during palpation, mobile and well-defined. The skin over the lesions is either red or red and purple in colour, although it is also possible that the skin over the lesions remains its natural colour [3]. Most often the lesions appear on the trunk, especially the back and than in decreasing incidence on buttocks, arms, thighs, chin, and cheeks [2].

In most cases spontaneous resolution of the subcutaneous nodules leave any lesions. Eruption softening, liquefaction and oozing with subsequent healing process with scar formation or with atrophical lesions have been recorded and described also. Calcification of the eruptions can occur with diverse intensity and can be revealed in the ultrasonographic techniques [3, 4].

One of the rare complication of subcutaneous fat necrosis of newborn is hypercalcemia. It occurs within 1-4th month after appearing the first lesions. The clinical symptoms of hypercalcemia expressed in laboratory findings as high calcium concentration in the blood serum. They include such phenomena as irritability, convulsions, failure to thrive or nephrocalcinosis [2, 4, 5]. Hypercalcaemia can become the cause of death and, therefore, even after the lesions resolution it is necessary to monitor calcium concentration in the blood serum in the first six months of the child's life [6]. Other rare complications, e.g. thrombocytopenia, hypoglycaemia or hypertriglyceridaemia have also been described [3-5].

Calcium concentration increase is believed to be caused by active vitamin D₃ (1,25 dihydroxycholecalciferol), produced by active macrophages in gran-

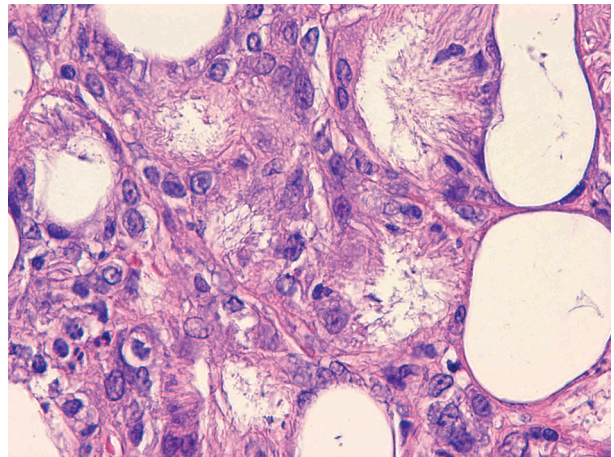


Fig. 5. The most characteristic feature of SFN are needle-shaped clefts arranged radially in cytoplasm of the macrophages, multinucleated giant cells and adipocytes. HE. Prim. obj. magnification 40×

ulation, analogically to sarcoidosis. The active form of vitamin D₃ causes increased absorption of calcium in kidneys and the gastrointestinal tract [4, 7, 8].

In majority cases the patient is diagnosed based on the clinical picture. In some cases might be helpful to perform histopathological study of the skin sample collected from the patient. As an alternative, the sample can be collected in fine-needle biopsy [3]. In this presented patient the histopathological examination showed steatonecrosis foci with foci of calcification, as well as granulomatous inflammation with mononuclear cells, macrophages and multinucleated giant cells. One of the characteristic feature is the presence of radially arranged, needle-shaped clefts within cytoplasm of macrophages or multinucleated giant cells and lipocytes [2, 3, 9, 10].

The etiopathogenesis of this condition has not been entirely clarified. To cover as much as possible risk factors it is necessary to take into consideration a wide range of the perinatal stress conditions such as: meconium aspiration, placenta praevia, pre-eclampsia, surgeries in hypothermia, Rh factor incompatibility, mother's addiction to cocaine [2, 4, 6, 8, 11]. There even was described a case of subcutaneous fat necrosis of newborn, in whom the mother of the newborn had suffered from antiphospholipid syndrome and protein C deficiency. Another rather interesting description covers a case of a newborn who had been exposed to a low temperature procedure according to stimulate the pneumogastric nerve in order to treat supraventricular tachycardia. It is highly probable that oxygen deficiency in tissues alone and/or hypothermia are the main factors that initiate the subcutaneous fat damage and than followed by its necrosis [2]. Traumatic and physical factors may also be relevant, as frequency of subcutaneous fat necrosis of newborn babies born in

spontaneous delivery is much higher than in case of babies born by caesarean section. Such influence of physical factors seems to be proved by the fact that subcutaneous fat necrosis of newborn occurs much more often in cases of a complicated or protracted labour, as well as in an instrumental delivery. Distinctive features visible in the histological examination result from the fatty acids crystallization. Newborn's fatty tissue consists mainly of saturated fatty acids (palmitic and stearic acids). Fatty acids are dominant most likely because of the immaturity of the newborn's enzyme systems or metabolic disorders hindering the reduction in subcutaneous fat. Their melting temperature is relatively high and reaches 64°C. In cases of subcutaneous fat necrosis of newborn with hypothermia, saturated fatty acids crystallize to create radially arranged needles-shaped clefts [2, 4, 8, 12].

In differential diagnosis it is necessary to distinguish between subcutaneous fat necrosis of newborn and sclerema neonatorum. The later is another very rare condition with not entirely clear pathogenesis. In premature infants and newborns in a poor general condition (with congenital heart disease, septic state, respiratory failure), lesions can be diagnosed earlier, in the first week of the newborn's life (most often between postnatal 2-4 day). In sclerema neonatorum the subcutaneous tissue induration appears at first on the shin and thigh and then it spreads in the proximal direction to reach the whole body, with the exception of palms, feet and the urogenital area. The skin over the induration is pale, waxy or pale-yellow. In the histological examination sclerema neonatorum, fat necrosis and/or foci of calcification do not occur. However, it does involve fibrous septa thickening and oedema. The inflammatory infiltration consists of lymphocytes, macrophages and multinucleated giant cells, as it is in case of subcutaneous fat necrosis of newborn. In sclerema neonatorum, however, the inflammatory infiltration is not that much intensified and it does not include granulomatous inflammation. Furthermore, in SFN there are much more common needles-shaped clefts in macrophages and multinucleated giant cells [2, 9, 10].

Another condition that must be taken into consideration in SFN differential diagnosis is cold panniculitis. Clinically, a red-and-purple induration appears within 72 hours from the exposure of the spot to low temperature. The histological examination shows inflammatory infiltrations. Prognosis in both cold panniculitis and subcutaneous fat necrosis of newborn is promising. In the differentiation diagnostics serious cases of dermatitis and panniculitis, such as cellulitis or erysipelas, should also be taken into consideration [2]. These conditions are accompanied by intensive systemic symptoms, such as fever, shiver and bad physical and mental state. The lesion

is an erythematous inflammation, with increased temperature and tenderness during palpation. In erysipelas the inflammatory focus is well-defined, with a smooth, glossy and taut surface. In erysipelas the inflammatory infiltration affects the dermis, epidermis and the outer layer of the subcutaneous tissue. In newborns, it occurs most often around the umbilical stump. In the case of cellulitis the lesion is not as well-defined as in the previous mentioned disease. One can see that it is in red and purple lesion and it is usually placed on the cheek. The histological examination shows an abundant inflammatory infiltration of neutrophils and the dilation of blood vessels. In cellulitis neutrophils occur mostly in the inner layer of the dermis and in the subcutaneous tissue [13, 14].

As subcutaneous fat necrosis of newborn manifests itself as hard and palpable nodules under the dermis, another conditions that should be taken are such conditions as angioma and neurofibroma. They are examples of easily palpable lesions, too [2]. Capillary hemangioma and cavernous hemangioma are soft, red, lobuliform nodules and they can appear on the body at the moment of birth (cavernous hemangioma) or in the first few months of the newborn's life (capillary hemangioma). Histological examination is crucial in the diagnosis, as it shows many capillary canals or larger spaces with endothelium. Neurofibromas, especially plexiform neurofibroma can occur as single or multiple lesions. They are spread on a wide range and create not well-defined, soft areas, which in the histological examination will be show as proliferating perineurium cells, with the extracellular matrix [15-17].

Yet another condition is Farber's disease, a rare genetically determined, autosomally regressive inherited condition. This condition should also be taken into consideration under discussion on SFN as it often affects the dermis. Due to ceramidosis deficiency, ceramides concentrate in macrophages. Clinical examination reveals nodules concentrated around joints (elbows and knees) and in the subcutaneous tissue, especially on auricle, neck and fingers. Such lesions are accompanied by pain and limited mobility of the joints. Mental disability is clinically clearly recognized. Additionally hoarseness might be found, as the larynx is also affected. The histological examination shows macrophages with ceramides but with lack of radially arranged, needles-shaped clefts, lymphocytes and multinucleated giant cells. In older lesions fibrous connective tissue can also occur [18].

Conclusions

Subcutaneous fat necrosis of newborn is a rare condition diagnosed usually based on the clinical picture. However, in the described case it was necessary to collect a skin sample in order to make proper

diagnosis. The histological examination does not usually leave any doubts. In the differentiation diagnostics sclerema neonatorum is the first condition taken into consideration, with its first lesions, but clinical data should help the proper differential diagnosis. The differences are also visible in the histological examination of skin biopsy. Then, one should take into consideration other conditions with symptoms such as indurated nodules in the subcutaneous tissue. In these cases the histological examination is decisive. Skin lesions usually regress spontaneously without treatment. In this case lesions regressed after steroid therapy. Subcutaneous fat necrosis of newborn usually runs a mild course. One of rare complications described in literature is hypercalcaemia. In the case described the concentration of calcium in the blood serum was increased. It was proposed by some authors that the history of perinatal stress might initiate skin lesions.

Reference

1. Wiatrowski T, Marshman G. Subcutaneous FAT necrosis of the newborn following hypothermia and complicated by pain and hypercalcemia. *Australasian Journal of Dermatology* 2001; 42: 207-210.
2. <http://emedicine.medscape.com/article/1081910-overview>
3. Fenniche S, Daound L. Subcutaneous FAT necrosis: Raport of two casus. *Dermatol Online J* 2004; 10: 12.
4. Tran JT, Sheth AP. Complications of subcutaneous FAT necrosis of the newborn: a case report and review of literature. *Pediatric Dermatology* 2003; 20: 257-261.
5. Vijayakumar M, Prahlad N. Subcutaneous Fat Necrosis with Hiperkalcemia. *Indian Pediatrics* 2006; 43: 360-363.
6. Burden AD, Krafchik BR. Subcutaneous FAT Necrosis of the Newborn: A Review of 11 Cases. *Pediatric Dermatology* 1999;16: 384-387.
7. Bonnemains L, Rouleau S. Severe neonatal hypercalcemia caused by subcutaneous FAT necrosis with any apparent cutaneous lesion. *Eur J Pediatr* 2008; 167: 1459-1461.
8. Kerachristou K, Siahianidou T. Subcutaneous FAT necrosis associated with severe hypocalcemia. *Journal of Perinatology* 2006; 26: 64-66.
9. Aljaser F, Einstein M. A 1-week-old newborn with hypercalcemia and palpable nodules: subcutaneous FAT necrosis. *The Canadian Journal of Medical Association* 2008; 178: 1653-1654.
10. Zeb A, Darmstadt GL. Sclerema neonatorum: a review of nomenclature, clinical presentation, histological findings, differential diagnosis and management. *J Perinatol* 2008; 28: 453-460.
11. Mahe E, Girszyn N. Subcutaneous fat necrosis of the newborn: a systematic evaluation of risk factor, clinical manifestations, complications and outcome of 16 children. *Pediatric Dermatology* 2007; 156: 709-715.
12. Hicks M, Moise L. Subcutaneous fat necrosis of the newborn and hypercalcemia: case report and review of the literature. *Pediatric Dermatology* 2008;10: 271-276.
13. <http://emedicine.medscape.com/article/1052445-diagnosis>.
14. <http://emedicine.medscape.com/article/1053686-diagnosis>.
15. <http://pathologyoutlines.com/softtissue3.html>.
16. <http://pathologyoutlines.com/topic//softtissue3neurofibromaplexiform.html>.
17. Rosai J. *Rosai and Ackerman's Surgical Pathology* 9th edition, Mosby 2004; 2266-69, 2285-2287.
18. Yager AM, Armfield U. Bone marrow transplantation for infant ile ceramidase deficiency (Farber disease). *Bone marrow transplantation* 2000; 26: 357-363.

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