DOI: 10.4274/tpa.1183

A newborn with subcutaneous nodules

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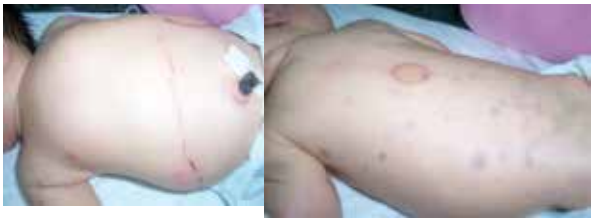
Case

Our patient who was born in another center with a birth weight of 3920 g as from the first pregnancy and as the first living child of a 38-year-old mother and a 42-year old father who had no consanguinity. No problem occured during the prenatal follow-up. The APGAR scores for the first and 5th minutes postnatally were assessed to be 9/10. No pathological finding was observed on physical examination. There was no ABO or Rh incompatibility between the mother and the baby. No additional test was performed in the patient who had a normal birth weight and gestational week. The newborn was compliant with the mother and his nutrition was adequate. After a 24-hour follow-up period the patient was discharged following heel blood sampling for metabolic screening tests. Three days after discharge the patient was brought to our emergency outpatient clinic on the fourth postnatal day with complaints of decreased feeding, malaise and skin eruption which occured in the last one day. The newborn reflexes were decreased at presentation. The axillary temperature was found to be 38.2^{0}C, the upper extremity arterial blood pressure was found to be 80/40 mm Hg and the pulse rate was found to be 162/min. Examination of the respiratory system was found to be normal. There was no pathological finding on examination of the cardiovascular system except for tachycardia. Widespread petechiae and ecchymoses which were prominent on the anterior part of the trunk, marked subcutaneous nodules on the back and hepatosplenomagaly (the liver was palpable 5 cm below the costal margin in the midclavicular line and the spleen was palpable 4 cm below the costal margin in the midclavicular line) were found on physical examination. Complete blood count, biochemical tests and coagulation tests were performed. No pathology was found in the biochemical and coagulation tests. Complete blood count was as follows: WBC: 51 600/mm^3 Hb: 12.5 g/dL, Hct: % 37 Plt: 16 000/mm^3. LDH was found to be 1313 IU/L.



Picture 1. Appearance of the subcutaneous nodules of the patient

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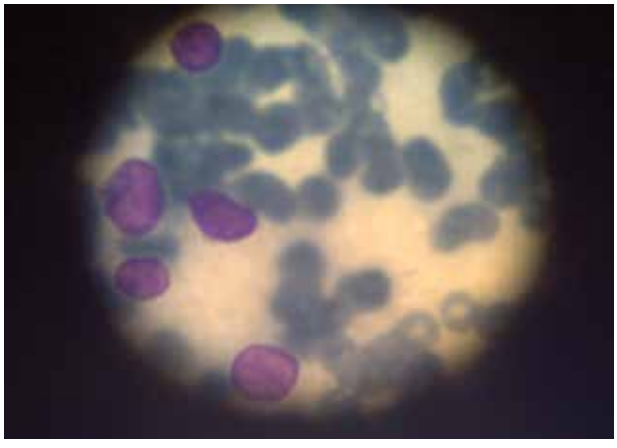
Turkish Archives of Pediatrics, published by Galenos Publishing

Diagnosis: Congenital leukemia

A peripheral blood smear was performed and blasts were observed with a rate of 58%. On bone marrow examination, blasts which were compatible with ALL-L1 in the FAB classification were found with a rate of 70%. High CD 19, CD 22, CD 34, HLA-DR, CD 45 expressions were found in the blast area in the immunophenotyping of the bone marrow.The CD 10 value was low. A diagnosis of Pro-B ALL was made in the patient as a result of immunophenotyping and cytochemical examination. ALL-specific translocations were found to be negative in the bone marrow. The pathological examinations of the cerebrospinal fluid obtained by lumbar puncture and skin biopsy samples obtained from the back were evaluated to be compatible with ALL involvement. The "infant leukemia protocol" which is used for ALL patients below the age of one in our clinic was started in the patient. Chemotherapy was discontinued because of sepsis on the 15th day of treatment, but the patient was lost on the 29th day of hospitalization despite supportive treatment.

Discussion

Multiple cutaneous and subcutaneous nodules may be observed in the newborn period. The majority of these nodules are self-limiting lesions with benign sizes. The differential diagnosis of benign conditions which cause to subcutaneous nodules in the newborn period is shown in Table 1. Nodular lesions in the newborn period may rarely be related with malign diseases. In infancy, nodular involvement related with "infantile myosarcoma" may be observed in the head-neck region and lower extremities (5). The treatment consists of chemotherapy or removal of the lesion totally by surgery. The nodular primary cutaneous form of rhabdomyosarcoma which shows a substantially malign prognosis may mimic hemangioma by adhering to the skin superficially and the subcutaneous tissue (6). The treatment consists of surgery and chemotherapy. Skin involvement of neuroblastoma which is the most common congenital malign tumor is found in approximately 1/3 of the patients. Skin involvement include solid, painless, nodular, blue-purple colored lesions which can be found widespread in the whole body. Although the prognosis varies according to the stage of the disease, the mainstay of therapy consists of chemotherapy and surgery.



Picture 2. Blasts on the peripheral blood smear of the patient

Neonatal or congenital leukemia is defined as leukemia which occurs prenatally (7). It is the second most common malignancy in infants. Depending on the growth rate of the leukemic cells the disease occurs at birth or in the first 4 weeks after delivery (8). It is a very rare disease and constitutes less than 1% of all childhood leukemias. Its prevalence is 1 per 1-5 millions live births (9). 200 cases have been reported in the literature until the present time. 80% of congenital leukemias are myeloid leukemias in contrast to the other childhood leukemias (10). Acute lymphoblastic leukemia constitutes only 20% of the cases. Most patients with ALL in the newborn period have pro-B ALL and its prognosis is the worst prognosis among all childhood ALLs. The patients present with signs and symptoms including petechiae, purpura, hepatosplenomegaly, lethargy, poor feeding, fever and pallor which are not specific for the newborn period. In 30-50% of the patients with congenital leukemia, leukemia cutis related with skin infiltration of the immature malign hematopoetic cells is observed in addition to these findings. Skin involvement is the first presentation complaint in 50% of the patients. Skin involvement may include nodular lesions which are named 'blue berry-muffin' (widespread lesions with varying size which progress from eryhtema to blu-purple nodules) or macules, vesiculopustules and purpura less commonly. Skin involvemetnis mostly observed in AML M-4 and M-5 (11). Congenital leukemia has a poor prognosis (12). In clinics, it should be differentiated especially from bacterial infection with leukomoid reaction, severe hemolysis and severe hypoxia. In addition, it may be confused with congential infection, transient abnormal myelopoesis in Down syndrome and neonatal neuroblastoma because of similar skin findings.

In this article, we presented a patient who presented with subcutaneous nodules in the newborn period and diagnosed with congenital leukemia. Our patient was diagnosed with pro-B ALL which is observed less commonly among congential leukemias. He was lost in the early period because of treatment-related complications. In this article, the differential diagnosis of neonatal subcutaneous nodules and congenital leukemia were discussed.

Table 1. Benign subcutaneous nodules observed in the newborn period

	Patients	Localization-Characteristics	Treatment
Benign subcutaneous fat necrosis	Healthy, term infant	Cheek, back, gluteal region, arms and legs Sharply-circumscribed, indurated nodules and plaques with varying diameters Painful when touched	Regresses spontaneously, no need for treatment
Sclerema neonatorum	Especially premature infants and term infants with poor general status	Widespread and regional rapidly spreading, wax-colored indurations in the skin in the first weeks of life	Disappears with improvement of the underlying disease
Panniculitis (1)	Neonatal sepsis (term-preterm)	Widespread nodular lesions	Disappears with improvement of the underlying disease
Intrauterine infections (2) (CMV, chickenpox, toxoplasma, HSV, rubella, Coxsackie B2)	Affected newborn (term-preterm)	Maculo-papular,vesicular Rarely nodular rash	Treatment directed to disease
Dermoid cyst	Term-preterm	Generally a slowly growing single lesion with a diameter of 1-4 cm and rubber stiffness having light blue color or the color of the skin	Should be removed because of risk of complication
Tyroglossal duct cyst	Term-preterm	A single nodular lesion in the middle area of the neck	Monitoring, surgery if infection or skin fistulization is present
Branchial cleft cyst	Term-preterm	A single nodular lesion anterior to the sternocleidomastoid muscle	Surgical excision
Deep hemangiomas	More frequent in preterm infants and female infants	Becomes prominent in the second month after birth Raised, blue-colored nodular lesion pale in the center It may have telengiectasies on the surface	Compression to vital organs Treatment if there is loss of function or if infection is present
Meningiomas (3)	Term-preterm	Frequent isolated cutaneous lesions in the head-neck region	Difficult to diagnose, histopathological diagnosis is needed, follow-up is recommended
Infantile myofibromatosis (4)	Term-preterm (single lesion, more frequent in male infants)	A single lesion or widespread disease Mobile, nodular, superficial lesion on an erythematous background with rubber stiffness Generally located in the extremities	Close monitoring of the lesion if there is no involvement of internal organs Excision if there is involvement of internal organs
Cutaneous mastocytosis	Term-preterm	Flushing with scratching and rarely hypotension Single nodule or multiple nodules	İmproves spontaneously as the patient gets older

References

1. Güneş T, Büyükkayhan D, Öztürk F. Yenidoğanda pseudomonas aeruginosa sepsisine bağlı subkutan nodüller. Türkiye Klinikleri 2006; 15: 169-171.
2. Ukşal Ü. Yenidoğanın sık görülen dermatozları. Klinik Gelişim Dergisi 2009; 22: 1-5.
3. Hussein MR, Abdelwahed AR. Primary cutaneous meningioma of the scalp: a case report and review of literature. J Cutan Pathol 2007; 34: 26-28.
4. Wyatt AJ, Hansen RC. Pediatric skin tumors. Pediatr Clin North Am 2000; 47: 937-963.
5. Russell H, Hicks MJ, Bertuch AA, Chintagumpala M. Infantile fibrosarcoma: clinical and histologic responses to cytotoxic chemotherapy. Pediatr Blood Cancer 2009; 53: 23-27.
6. Megarbane H, Doz F, Manach Y, Fletcher C, Jaubert F, de Prost Y, Hamel-Teillac D. Neonatal rhabdomyosarcoma misdiagnosed as a congenital hemangioma. Pediatr Dermatol 2011; 28: 299-301.
7. Badhe PB, Sane SY. Congenital leukemia-organ involvement in six autopsy cases. J Postgrad Med 1992; 38: 127-129.
8. Weinstein HJ. Congenital leukemia and the neonatal myeloproliferative disorders associated with Down's syndrome. Clin Hematol 1978; 7: 147-154.
9. Weitzman S, Grant R. Neonatal oncology: diagnostic and therapeutic dilemmas. Semin Perinatol 1997; 21: 102-111.
10. David GN, Frank AO. Hematology of infancy and childhood. In: acute and chronic myeloproliferative disorders and myelodysplasia. 4th edition. New York: Saunders, 1993: 1288-1218.
11. Torrelo A, Madero L, Mediero IG, Baño A, Zambrano A. Aleukemic congenital leukemia cutis. Pediatr Dermatol 2004; 21: 458–461.
12. Heerema NA, Arthur DC, Sather H, Albo V, Feusner J, Lange BJ, Steinherz PG, Zeltzer P, Hammond D, Reaman GH. Cytogenetic features of infants less than 12 months of age at diagnosis of acute lympho-blastic leukemia: impact of the 11q 23 break-point on outcome: a report of the Childrens Cancer Group. Blood 1994; 83: 2274-2284.