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Rothmund-thomson syndrome and cutan T-cell lymphoma in childhood

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ABSTRACT

We report a 3-year-old girl suffering from Rothmund-Thomson Syndrome (RTS). The patient at birth had multiplex anomalies: poikilodermatous rash, sceletal abnormalities: palatoschisis, micrognathi, aplasia radii, hypoplastic right and left thenar and thumbs, pesequinus on both site, ectopy renis. The patient in the later ages was detected dental malformation, facial dysmorfism. At the age 3, she had lasion in her muscle. After biopsy, histological examination showed cutan T-cell lymphoma. The patient is the first case who had cutan T-cell lymphoma associated with RTS in this young age.

Keywords: Rothmond Thomson Syndrome; Genetic Disorder; Cutan T-Cell Lymphoma

1. INTRODUCTION

The RTS was described firstly in 1868 by Rothmund. Up to nowadays approximately 400 cases have been reported in the literature. Cells from patients with RTS demonstrate genomic instability, mutations in RECQL4 gene [1-3].

RTS patients are particularly prone to developing osteosarcoma as well as nonmelanoma skin cancers [4-15]. RTS has been grouped with other genetic cancer predisposition disorders that fall into the class of DNA repair or chromosomal instability disorders. Patients with other disorders have well-known increased sensitivity to DNA-damaging agents including ionizing radiation and ultraviolet radiation [16]. Usually the disease tends to progress during the first year of life, but becomes static so that patients may have a normal lifespan with a good quality of life.

The mortality from neoplastic disease during the second or third decade is very significantly increased [17-23]. Patients generally present: skin rash, small stature, and skeletal dysplasias.

Cutaneous symptoms: photosensitivity, poikiloderma, hyperkeratosis, alopecia.

Other abnormalities: dystrophic teeth, nails, juvenile cataract, short stature, hypogonadysm, congenital bone defects, soft tissue contractures, mental retardation. More than 90% of patients develop the initial skin manifestations during the first year of life, usually from age 3 - 6 months. The acute phase begins in early infancy as red patches or edematous plaques, sometimes with blistering. The cheeks are usually first involved, later spread to other areas of the face, the extremities, and the buttocks. Over months to years, the rash enters a chronic stage characterized by poikiloderma (atrophy, telangiectasias, and pigmentary changes). Photosensitivity is a feature in more than 30% of cases. The characteristic skin findings are the most consistent feature of the syndrome. Irregular erythema and edema of the skin are replaced by reticulated red-brown patches associated with punctate atrophy and telangiectasias (poikiloderma). These characteristic skin changes are typically seen on the face, extensor extremities, and buttocks with sparing of the chest, abdomen, and back.

Acral hyperkeratotic lesions on the elbows, knees, hands, and feet can be seen at puberty. Palmar keratoderma has been reported [24]. Patients may have sparse hair, premature canities, and dystrophic or atrophic nails.

Dental abnormalities include malformation: microdontia, failure of eruption.

Juvenile cataracts have been reported in as many as 40% - 50% of patients aged 4 - 7 years. Patients usually have short stature, which ranges from dwarfism to a small build.

About one half of patients have skeletal abnormalities, most frequently a characteristic facies with frontal bossing, saddle nose, and micrognathia. Small hands and feet disproportionate to the patient's body size are observed in 20% of patients. Approximately 10% of patients have

absent or malformed radii, and 5% of patients have absent or partially formed thumbs (**Figure 1**).

2. CASE REPORT

Our patient was born in 40 gestation weeks, with 2430 gr. At birth had multiplex anomalies: poikilodermatous rash, palatoschisis, skeletal abnormalities (aplasia radii, hypoplastic right and left thenar and thumbs, pes equinus on both side), ectopy renis. Chromosome examination showed: 46(XX), normal kariotype. Further dental malformations, growth retardation, cranial dysostosis with saddle nose and facial dysmorfism, sparse scalp hair, eyebrows and eyelashes, teleangiectasia, dystrophic nails and photosensitivity, mild mental retardation (**Figure 2**).

At the age of 3 years old, she had lesions in her muscle (nose and shanks) (**Figures 3** and **4**).

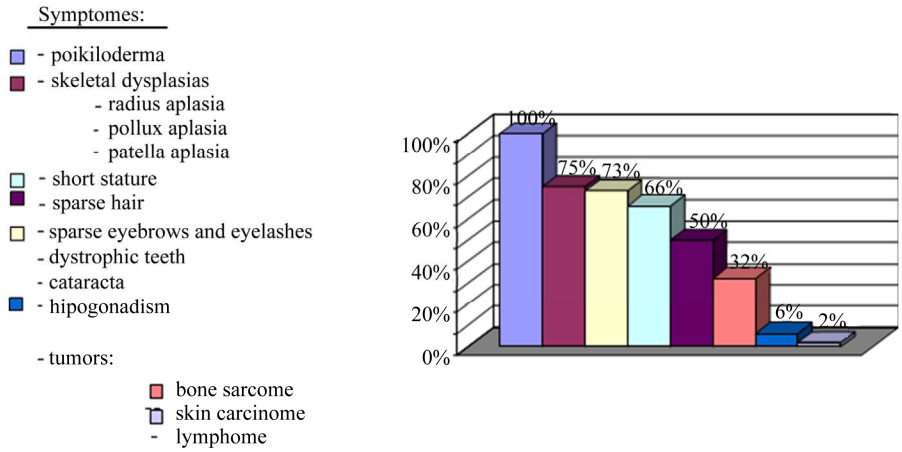

Figure 1. Frequency of symptomes.

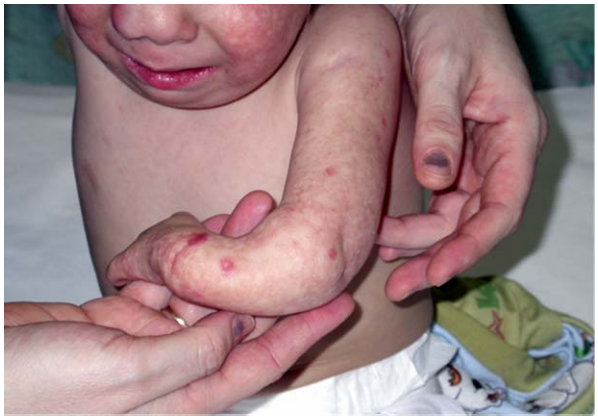

Figure 2. Skin poikiloderma.

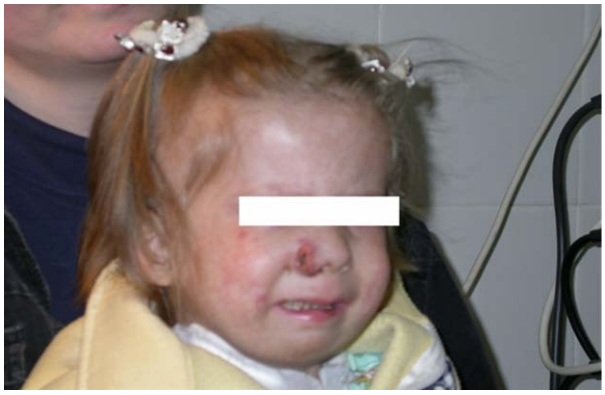

Figure 3. Nasal destruction.

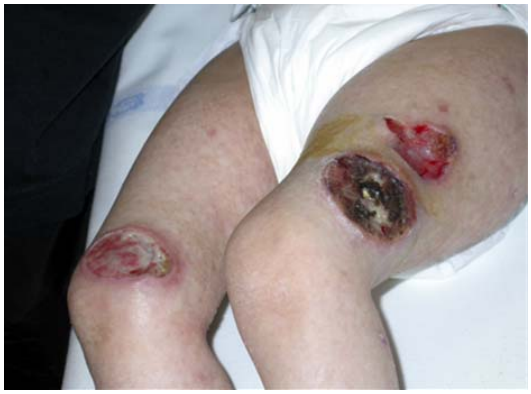

Figure 4. Shank destruction.

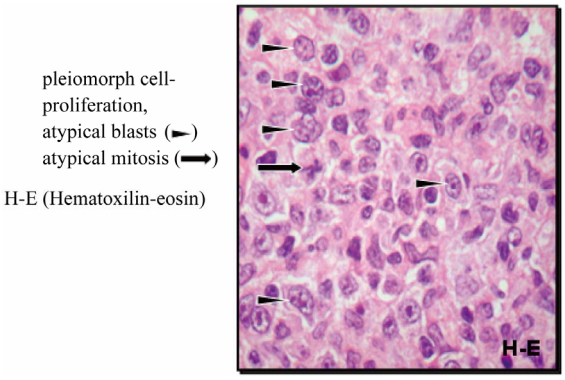

Figure 5. Histology.

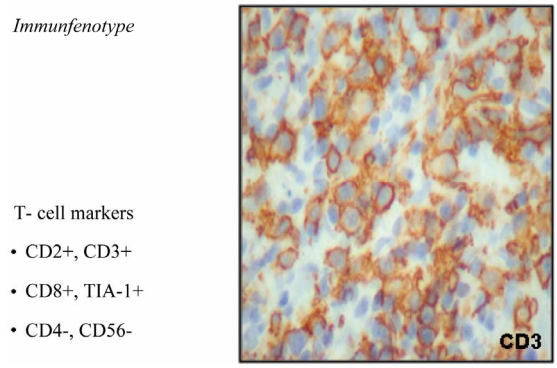

Figure 6. T-cell markers histology.

The patient was treated as the pyoderma gangrenosum by dermatologist. Inspite of adminestered antibiotics in low and mild dosis and steroid was not improvement in a muscle lesion. Progression of the symptomes biopsy was performed. Histological examination showed cutan T-cell lymphoma (**Figures 5** and **6**).

At the first admission she had negative ultrasaund and chest X-Ray results. Peripheral blood smears showed mild anaemia (Ht: 0.29, Hb: 92 g/l). Liver and kidney function was normal.

Flow cytometry of bone marrow was normal. Bacterial culture result from secretion of leison was: *Pseudomonas aeruginosa*, *Proteus vulgaris*, *Streptococcus pyogenes*. Antibiotic therapy was given (ceftriaxone, aminoglycosid, clindamycin).

We started with NHL BFM SR (low risk) protokol (induction: prednisolon (60 mg/m^2/day) Vincristin 2 mg/m^2/week, Daunorubicin 20 mg/m^2/week, Asparaginase 10,000 U/m^2 2×/week).

At the beginning of treatment, Central Vein Catheter (CVC) implantation was revealed into jugular vein. The skin necrose was improved 2 weeks later. On the 3rd week of the treatment in relatively good condition she suddenly died at home. Dissection showed thrombosis in central vein catheter and sinus sagittalis superior vein, inspite of the catheter heparinisation. It was an unexpected event.

3. DISCUSSION

We report a new case of cutan T-cell lymphoma assotiation with Rothmund-Tomson Syndrome. Our patient, who had RTS and childhood cutan T-cell lymphoma in young age, had a typical RTS, and she was the first case.

Cutan T-cell lymphoma is an extranodal, indolent non-Hodgkin lymphoma of T-cell origin that primarily develops in the skin, but can involve the lymph nodes, blood, and visceral organs. This is the adult type of lymphoma, but very rare in childhood.

The RTS association with malignancy is well known. Many osteosarcomas are described in the literature association with RTS. During the second or third decade malignancy is very significantly increased, but very rare in very young age.

Sudden death was unexpected. Maybe the cause of death outputs some thrombotic agents from damage tissue, asparaginase and RTS.

Early diagnosis is very important for the newborn baby with multiplex anomalies.

Cutaneous and extracutaneous features of cancer-predisposing syndrome should result in the early diagnosis of an underlying cancer in children.

Careful prevention and follow-up are very important, so that we can take early diagnosis of cancer. Unfortunately our patient died from unexpected event, therefore, we don't know if the therapy is successful or not.

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ABBREVIATIONS

Rothmund-Thomson Syndrome (RTS)
Central Vein Catheter (CVC)

