Prevalence of Skin Cancer and Hearing Loss in Rothmund-Thomson Syndrome Cohort

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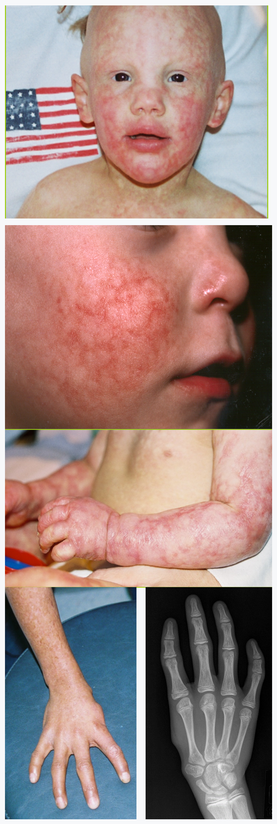
INTRODUCTION AND BACKGROUND

Rothmund-Thomson Syndrome (RTS) is a rare autosomal recessive genodermatosis that is characterized by a skin rash known as **poikiloderma** that lasts throughout life. Other features of this syndrome include **sparse/absent hair**, **abnormal nails and teeth**, **small stature**, **skeletal dysplasias, cataracts and increased risk of cancer**. RTS is classified into two types: **Type 1** is associated with juvenile cataracts and mutations in the *ANAPC1* gene, while **Type 2** is defined by presence of mutations in the *RECQL4* gene and is associated with the development of bone cancer (osteosarcoma).

While there are anecdotal and case reports describing skin cancer and hearing loss in RTS, there has been no formal study to determine the actual prevalence of these conditions among individuals with RTS.

Therefore the goal of this project is to determine the prevalence of skin cancer and hearing loss and to better characterize the specific types and collect information about treatment. This information will inform future counseling and management of these conditions in the RTS population.



PROJECT GOALS

Our goal is to determine the prevalence of skin cancer and hearing loss in a cohort of RTS patients and to gather information about the specific types of cancer (e.g., squamous vs. basal cell carcinoma vs. melanoma) and hearing loss (conductive vs. sensorineural, etc).

METHODOLOGY

To determine the prevalence of skin cancer and hearing loss, we queried data from an existing RTS database developed out of the RTS Patient Registry at Baylor College of Medicine. 93 of the 155 patients enrolled in the RTS Registry who we had contact information for were surveyed via email and/or mail. The survey was designed to gather information regarding whether or not the patient ever had skin cancer or hearing loss, specific types of either condition, details of diagnosis and treatment, and physician contact information to allow us to collect medical records/source documentation. Returned survey data were entered into an existing RTS database, and the combined data are presented here.

RESULTS

RTS Probands with Skin Cancer

Subject #	DOB	Current Age	Sex	RTS Type	Skin Cancer Type	Age of Onset	Source
TYPE 1							
1	7/11/81	Deceased	M	1	SCC	24	Database
2	2/18/86	Deceased	M	1	SCC	23	Database
3	11/17/67	55	M	1	SCC	27	Database
4	10/27/42	Deceased	F	1	SCC	77	Database
5	11/1/72	50	F	1	BCC	Adult	Database
6	5/21/70	52	M	1	BCC	Adult	Database
TYPE 2							
7	7/14/77	45	M	2	SCC, BCC	32, 34	Database
8	3/17/98	25	F	2	SCC	18	Database
9	2/25/83	Deceased	F	2	Melanoma	23	Database
10	6/15/63	59	M	2	Unknown (Not melanoma)	58	Survey
Unknown Mutation Status							
11	7/23/58	64	F	Unknown	Unknown	Unknown	Database
12	3/7/40	83	M	Unknown	SCC, BCC	69, 71	Survey

Summary of RTS and Skin Cancer

- 12 out of 47 subjects with available data reported skin cancer resulting in a prevalence of **25.5%**.
- Of the 12 cases of skin cancer, 5 (42%) were squamous cell carcinomas, 2 (17%) were basal cell carcinomas (16.67%), 1 (8%) was a melanoma, and 2 (17%) were combined basal and squamous cell carcinomas. 2 cases (17%) were of unknown type.
- Of the 12 cases of skin cancer, 6 (50%) had Type 1 RTS, 4 (33%) had Type 2 RTS, and 2 (17%) had unknown mutation status.

RTS Probands with Hearing Loss

Subject #	DOB	Current Age	Sex	RTS Type	Age of Onset	Hearing Loss Type	Which Ear	Hearing Aids	Source
TYPE 1									
1	3/10/80	Deceased	M	1	Unknown	Unknown	Unknown	Unknown	Database
2	3/29/91	32	M	1	8	Does not know	Bilateral	No	Survey
3	5/17/99	23	F	1	7	Conductive	Bilateral	Yes	Survey
4	7/18/10	12	M	1	Unknown	Unknown	Unknown	Unknown	Database
TYPE 2									
5	5/20/89	33	F	2	10	Unknown	Unknown	Yes	Database
6	3/11/96	27	M	2	Toddler	Unknown	Unknown	Unknown	Survey
7	7/14/77	45	M	2	2	Conductive	Left	Unknown	Database
8	12/6/90	32	F	2	Unknown	Unknown	Unknown	Yes	Database
9	11/13/91	31	M	2	Unknown	Unknown	Unknown	Unknown	Database
10	4/11/74	49	F	2	Birth	Unknown	Left	No	Survey
11	1/2/80	Deceased	M	2	Unknown	Sensorineural	Unknown	Unknown	Database
12	2/28/90	33	F	2	Unknown	Unknown	Unknown	Unknown	Database
13	4/20/71	51	M	2	Childhood	Conductive	Right	Yes-sometimes	Survey
14	7/1/80	42	F	2	4	Unknown	Bilateral	Unknown	Database
15	9/7/04	18	F	2	1 month	Sensorineural	Bilateral	Yes	Survey
16	11/16/79	43	F	2	Unknown	Unknown	Unknown	Unknown	Database
17	6/15/63	59	M	2	59	Unknown	Bilateral	No	Survey
18	2/23/02	21	M	2	18	Sensorineural w/mixed high frequency	Bilateral	Yes	Survey
19	5/13/03	19	M	2	9	Unknown	Unknown	Unknown	Database
20	12/17/04	18	F	2	Unknown	Unknown	Unknown	Unknown	Database
21	11/4/06	16	F	2	6	Sensorineural	Bilateral	Yes	Survey
22	3/16/05	18	M	2	12	Unknown	Unknown	Yes	Database
23	10/8/09	13	F	2	Unknown	Unknown	Unknown	Unknown	Database
24	4/4/96	27	M	2	Childhood	Sensorineural	Bilateral	No	Survey
25	7/25/14	8	M	2	Unknown	Unknown	Unknown	Unknown	Database
Unknown Mutation Status									
26	9/7/05	17	M	Unknown	9	High frequency, chemo induced	Bilateral	Yes	Survey
27	7/9/92	30	M	Unknown	Unknown	Unknown	Unknown	Unknown	Database
28	11/22/50	72	F	Unknown	Unknown	Unknown	Unknown	Unknown	Database
29	6/5/98	24	M	Unknown	Unknown	Unknown	Unknown	Unknown	Database
30	10/27/18	4	F	Unknown	1	Unknown	Bilateral	Unknown	Database

RTS and Hearing Loss

- 30 out of 56 subjects with available data reported hearing loss resulting in a prevalence of **53.6%**.
- Of the 12 cases of hearing loss, 3 (10%) were conductive, 5 (17%) were sensorineural , and 22 (73%) were of unknown type.
- Of the 12 cases of hearing loss, 10 (33%) were bilateral, 3 (10%) were unilateral (3%) and 17 (57%) were of unknown location.
- Of the 30 cases of hearing loss, 4 (13%) had Type 1 RTS, 21 (70%) had Type 2 RTS, and 5 (17%) had unknown mutation status.

CONCLUSIONS AND TAKEAWAYS

- Prevalence of skin cancer in this cohort is 26% which approaches what is reported in the literature (40%) although prior estimates were based on case reports and likely less accurate.
- Prevalence of hearing loss 54% is very high and has not previously been reported in the literature.
- It appears that hearing loss tends to occur early in life; therefore, early diagnosis and management may improve childhood development and quality of life.
- Skin cancer occurs in both Type 1 and Type 2 RTS, in contrast to osteosarcoma which is only seen in Type 2 RTS.

FUTURE DIRECTIONS

- Obtain medical records to fill in unknown gaps in information regarding specific types of skin cancer and hearing loss, ages of onset, etc.
- Disseminate knowledge through publication of manuscript and updating of public resources (e.g., Genereviews)

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