Sleep apneas in Silver Russell syndrome : A constant finding

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Background

Silver-Russell syndrome (SRS) is an imprinting disease resulting in intrauterine growth restriction (IUGR), poor postnatal growth with feeding difficulties (often requiring early nutritional support) and facial dysmorphosis (relative macrocephaly at birth, protruding forehead, body asymmetry - see photo below). Molecular abnormalities are identified in about 60 % of the patients and can be either chromosome 7 maternal uniparental disomy or impaired methylation in 11p15 region. Imprinting disease such as Prader-Willi syndrome are associated with sleep disordered breathing (SDB) but no data are available SRS although many patients describe excessive daytime sleepiness, nocturnal sweat and snoring. Our objective was to characterize sleep in SRS patients and to evaluate growth hormone (GH) therapy impact on it.

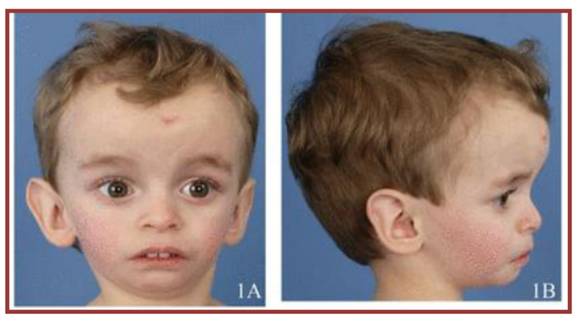


Fig. 1

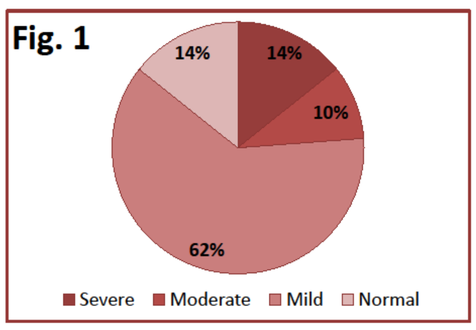
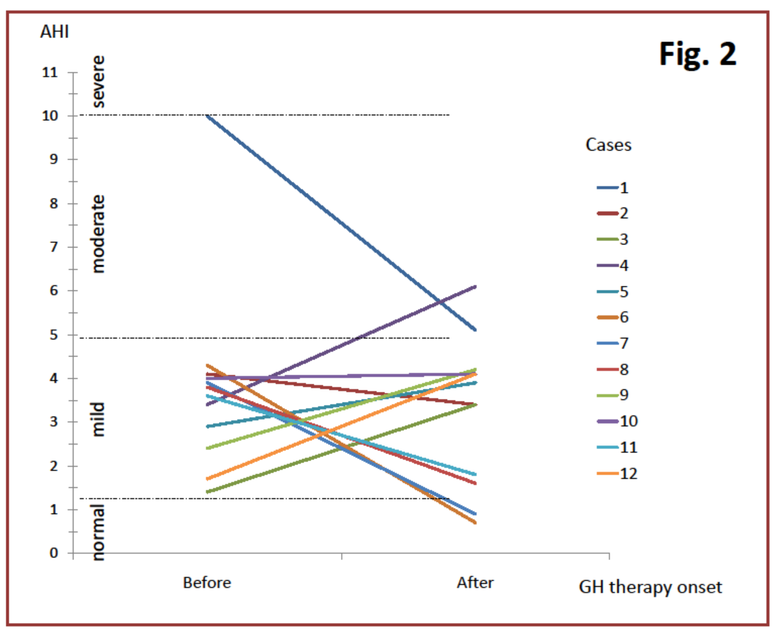


Fig. 2



Patients and methods

We restrospectively analyzed 61 sleep polygraphies and polysomnographies in 40 patients with proven SRS (32 with anomalies in 11p15 region and 8 with uniparental disomy in chromosome 7). Twenty-one recording were performed prior to GH therapy, 39 during GH therapy and 1 after GH therapy. Twelve patients had sleep evaluation prior and after GH therapy initiation.

Results

Mean apnea-hypopnea index (AHI) was 3.4 (0-12.4), with a mean central AHI of 0.5 (0-2.4). SDB was identified in 73.8% (n=45) of the recordings and was severe in 4.9%. SDB was present in 86.4% of patients before GH therapy and was severe in 13.6% (fig.1).

In 12 patients with sleep recording before and after GH therapy initiation, SDB was present in all but one patient at baseline and we found one relevant worsening of AHI in case 4 after 13 months of GH therapy, going from mild to moderate SDB. Two patients normalized their mild SDB after 21 and 22 months (cases 7 and 12), whereas case 1 showed an important improvement of is severe SDB to a moderate form after 9 months of treatment (fig.2).

Eight patients (25%) had hypoxemia and 4 had hypercapnia (12.5%). Minimal oxymetry was under 90% in 21 recordings (34.4%) and minimal transcutaneous oxygen pressure was under 85mmHg in 14 patients (43.8%).

Mean GH dose was 0.23mg/kg/week (0.09-0.37), with mean IGF1 1.7SDS (-1.9-6.6) and IGFBP3 1.93SDS (-1.3-11.4) (table 1).

Table 1

	Prior GH therapy			During GH therapy		
	Mean	Minimum	Maximum	Mean	Minimum	Maximum
IGF1 (SDS)	1,3	-1,9	4,5	2,0	-0,6	6,6
IGFBP3 (SDS)	1,1	-1,3	3,3	2,4	-0,7	11,4
Awaken SpO2 (%)	98	98	99	98,0	95,0	99,0
Mean sleeping SpO2 (%)	97	96	98	97,0	93,0	99,0
Minimum sleeping SpO2 (%)	90	80	96	91,0	82,0	96,0
Percentage of time with sleeping SpO2<90% (%)	0,1	0,0	1,0	0,05	0,0	1,0
Snoring index	105,6	0,0	1582,0	60,4	0,0	545,0
TcPO2 difference between sleep and arousal (mmHg)	-6,4	-14,0	0,0	-4,9	-17,0	7,0
TcPCO2 difference between sleep and arousal (mmHg)	5,8	2,0	10,0	7,2	3,0	12,0
AHI	4,1	0,3	12,4	3,1	0,1	11,5
Obstructive AHI	3,4	0,0	10,2	2,7	0,0	10,6
Central AHI	0,7	0,0	2,4	0,4	0,0	1,9
Age at onset (years)				3,7	1,0	9.3
Dose (mg/kg/week)				0,23	0,09	0,37

Conclusion

Most patients with SRS present SDB with obstructive main feature. Maxillo-facial abnormalities and tonsil hypertrophy could be implicated in such sleep pattern and we recommend systematic Ear-Nose-Throat evaluation in SRS patients and polysomnography in case of clinical anomaly, preferably before GH therapy initiation. High microwakennings index could contribute to day asthenia sometimes described in SRS patients. Caution should be given to central apnea presence even if not predominant they could testify of hypothalamic involvement as in PWS patients.

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