Disclosure Statement
Nothing to disclose

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Metamorphic thyroid autoimmunity in Down Syndrome: from Hashimoto's thyroiditis to Graves' disease and beyond

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Purpose: To shed further light on the specific relationships between Down syndrome (DS) and metamorphic thyroid autoimmunity.

Design: We have reconstructed the conversion process from Hashimoto's thyroiditis (HT) to Graves' disease (GD) in a selected population consisting of 12 DS individuals aged between 3.0 and 13.5 years at HT diagnosis and between 4.1 and 19.9 years at GD diagnosis.
All the patients underwent a treatment with methimazole (MMI), at a dose that was periodically adjusted on the basis of clinical findings and thyroid function tests.

Results: After MMI treatment onset all patients exhibited, at varying time intervals, a prolonged clinical and biochemical remission of hyperthyroidism. In 8/12 patients this treatment is still being continued 2-7 years after its initiation. The mean MMI dosage needed to maintain euthyroidism in these 8 patients was 0.12 ± 0.02 mg/kg/day.
In the remaining 4 patients MMI was withdrawn from 1.9 to 7 years after its initiation and no relapses were recorded 2.0 – 2.1 years after its withdrawal. All these 4 patients developed, from 0.1 to 0.3 years after MMI withdrawal, a biochemical picture of overt hypothyroidism and needed treatment with L-T4, that is now being continued since 2.0 - 2.1 years.
No patients needed non-pharmacological therapies, such as surgery or radioiodine ablation.

Patients	Age (years)	TSH° (mU/l)	FT4°° (pmol/l)	TPOAbs* (IU/ml)	TGAbs** (IU/ml)	Therapy duration (years)
1	3.0	7.10	12.6	95	60	-
2	3.0	19.56	9.9	1310	182	2.5
3	3.3	0.07	24.6	57	187	-
4	4.0	8.80	16.8	180	120	4.0
5	4.0	5.30	12.1	26	28	-
6	5.0	0.05	50.0	284	35	1.0
7	5.9	5.10	17.4	75	302	-
8	6.0	8.20	10.5	144	104	1.0
9	8.0	0.01	38.0	278	199	-
10	9.7	9.10	11.0	37	2	6.5
11	10.0	5.10	10.5	22	119	3.0
12	13.5	4.30	18.0	23	109	1.0

Table 1
Age, TSH, FT4 and thyroid autoantobody serum levels at Hashimoto's thyroiditis diagnosis in the 12 patients of this series and duration of L-thyroxine treatment in the 7 patients who were treated.

Patients	Time interval (years)	Age (years)	Exophthalmos	Other hyperthyroid symptoms	TSH° (mU/l)	FT4°° (pmol/l	TPOAbs* (IU/ml)	TGAbs** (IU/ml)	TRABs# (IU/l)
1	2.5	5.5	-	+	0.0500	45.1	796	150	23.4
2	6.0	9.0	-	+	0.0500	36.8	1300	79	19.0
3	0.7	4.0	-	+	0.0060	47.8	44	148	85.0
4	5.9	9.9	+	+	0.0500	66.1	278	199	32.7
5	4.8	8.8	-	+	0.0001	41.9	149	758	25.2
6	1.0	6.1	-	+	0.0500	41.6	189	170	22.0
7	5.2	11.1	+	+	0.0100	31.6	248	55	28.0
8	3.0	9.0	-	+	0.0500	26.0	39	3	21.0
9	2.0	10.0	+	+	0.0050	58.7	278	199	32.7
10	3.5	13.2	-	-	0.0200	29.4	200	200	23.0
11	5.0	15.0	-	+	0.0010	34.4	45	220	16.0
12	6.5	20.0	-	-	0.0060	25.0	61	117	31.4

Table 2
Time interval between Hashimoto's thyroiditis and Graves' disease (GD), age and clinical and biochemical findings at GD diagnosis in the 12 patients of this series.

Conclusions

1) DS children may be incline to manifest over time a phenotypic metamorphosis from HT to GD.
2) A share of GD children with DS may subsequently fluctuate from hyperthyroidism to hypothyroidism.
3) In DS HT presentation is absolutely peculiar.
4) in DS GD is characterized by a mild biochemical and clinical course.

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