

## Severe Course of Juvenile Grave's Disease accompanied by Myasthenia Gravis

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### Abstract

Grave's disease is the most common cause of hyperthyroidism in children. Symptoms of hyperthyroidism associated with Grave's disease include goiter, tachycardia, tremor or diplopia caused by exophthalmos. Marked fatigue and weight loss may be observed due to hypermetabolic state. Myasthenia Gravis is far less frequent, with juvenile onset in fewer than 10% of the patients. Ocular symptoms: ptosis or diplopia, and weakness and fatigability of limb and bulbar muscles are hallmarks of myasthenia. In some of the patients Grave's disease and myasthenia may mimic each other though coincidence of both diseases can be also observed. We report the case of a girl with abrupt onset of hyperthyroidism with severe dysphagia and weight loss. Family history positive for Grave's disease and laboratory results confirming hyperthyroidism delayed diagnosis and treatment of her severe myasthenia.

**Keywords:** Hyperthyroid; Bulbar; Neuromuscular myasthenia; Graves; Acetylcholine receptor antibody

### Introduction

Grave's disease is the most common cause of hyperthyroidism in children, with a peak incidence of 3.01 cases per 100,000 persons for girls, aged 10-14 years [1]. There is strong genetic susceptibility to autoimmune thyroid disease [2]. Grave's disease patients have antibodies against TSHR, often also antibodies against thyroid peroxidase (anti-TPO) or thyroglobulin (anti-TG). Symptoms of hyperthyroidism associated with Grave's disease include goiter, tachycardia, and exophthalmos with diplopia, tremor, and increased sweating, fatigue and weight loss. Myasthenia Gravis is less frequent, with estimated incidence of 5 -10 cases per million population, with juvenile onset in fewer than 10% of the patients [3]. The majority of myasthenia gravis patients present with ptosis or diplopia, and approximately 70% of them progress to generalized disease with

dysphagia, dysarthria or generalized muscle weakness and fatigability [3,4]. We present the case of a child whose symptoms were caused by both myasthenia gravis and Grave's disease, but family history and laboratory results confirming Grave's disease, delayed diagnosis and treatment of her severe myasthenia.

### Case Report

A 14-year-old Caucasian girl with a three months history of generalized fatigue and weight loss of 10% of her body weight was admitted to Neurology Department. She had family history of Grave's disease in her mother and maternal grandmother. A month after onset of symptoms TSH and TSHR antibodies were tested confirming diagnosis of Grave's disease. Despite treatment with methimazole her symptoms exacerbated: she complained of severe fatigue, had marked difficulties with swallowing and nasal speech. There was neither exophthalmos nor diplopia.

	On admission	Three weeks later	Six months later	Reference value
Total TSH	0.01	<0.005	2.476	0.270-4.200
FT3	43.1	10.79	4.76	3.1-6.8 pmol/l
FT4	75.3	20.68	17.51	12.0-22.0 pmol/l
Anti-TSHR	10.84	7.96	1.45	<1.75 IU/l
Anti-TPO	82	72.24	10.45	<34.0 IU/l
Anti-TG	Not done	2193	214.0	<115.0 IU/l

Table 1: Laboratory thyroid function tests and antithyroid antibody results during the course of the disease.

Pharmacological test with pilydostygmine bromide was positive with improvement of speech and temporary alleviation of her swallowing difficulties, and the girl was referred to our Department with preliminary diagnosis of Myasthenia Gravis. On admission she had marked weakness of facial muscles with mild ptosis, and weakness

of eyelid closure. Dysphagia was severe she could not handle her saliva and required feeding with nasal tube for four days. Upper and lower extremity muscles had normal tone and strength deep tendon reflexes were preserved. Her HR was 74/min, temperature was normal. Arterial blood O<sub>2</sub> and CO<sub>2</sub> were normal. Repetitive nerve stimulation test with

stimulation of her facial nerve with recording from orbicularis oris muscle revealed significant decrement of the amplitude of compound muscle action potential of 30%. Acetylcholine receptor antibodies were positive (19.0 nmol/l, normal <0.4 nmol/l), confirming diagnosis of seropositive myasthenia gravis. CT of her chest showed enlarged thymus. Thyroid tests results are presented in Table 1. She only partially responded to Piryostygmine bromide in a dose of 300 mg/day. Therefore IVIG, 2 g/kg bw over five days was administered, and she was started on prednisone 1mg/kg/day. Her condition stabilized, but one more course of IVIG was necessary four weeks later for dysphagia worsening. Her neurological condition gradually improved over the next months. She was treated with thymectomy and two months later became symptom free reaching pharmacological remission.

## Discussion

Autoimmune thyroid diseases accompany MG in approximately 5-10% of cases. MG associated with AITD is considered a mild disease, with predominantly ocular symptoms [5,6]. Ophthalmoplegia and diplopia in MG with autoimmune thyroid diseases, or caused by Grave's diseases alone may lead to diagnostic difficulties in children [7,8]. Our case highlights a different course of both MG and thyroid disease, with dysphagia and no ocular symptoms at presentation. Generalized fatigue presented by our patient could have been attributed to the girl's hyperthyroid state. Yet, severity of dysphagia that led to over 10% loss of her body weight prompted search for alternative diagnosis. Dysphagia is a very rare manifestation of hyperthyroidism, but can be seen in most of the patients with generalized MG, and is severe in almost 40% of them [4,9]. Other potential causes of painless dysphagia of acute or sub acute onset in a previously healthy child include Guillain-Barre syndrome or polymyositis. If local pathology of the throat is suspected a thorough otolaryngology consultation with appropriate instrumental examination of swallowing is indicated [10,11]. Video fluoroscopy is also valuable in the differential diagnosis between central and peripheral nervous system etiology of swallowing difficulties [12].

Muscular weakness with fatigue, dyspnoe, and dramatic weight loss, as seen in our patients, may also herald the thyroid storm. Yet, on admission, she was lacking other symptoms of hyper metabolic state. If no other explanation could be found for her significant weight loss, anorexia nervosa should also be included in the differential diagnosis.

Treatment of the girl's severe MG with piryostygmine bromide and immunosuppression led to marked improvement [12]. Resolution of the thyroid state possibly also facilitated favorable outcome of MG [7].

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