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Research Article

Observation of a Case of Autoimmune Anti-rach Myasthenia Gravis: Clinical Aspect and Management at the West Guyanese General Pediatrics Department

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Abstract

The objectives of this observation were to describe the elements of the positive diagnosis and to evaluate the evolution under treatment of a case of myasthenia gravis antis rach autoimmune in a 17-year-old girl who had made several visits to the emergency room for walking disorder on background. weight loss and physical asthenia.

Myasthenia gravis is an autoimmune disease of the neuromuscular junction which preferentially affects young women and the elderly and whose incidence is tending to increase. Fluctuating oculo-facio-bulbar paresis of varying severity is common. Remissions and exacerbations are typical. The disease is caused by autoantibodies directed against acetylcholine receptors or more rarely against a specific muscle kinase. The therapeutic objective, mainly based on observational studies, is that of a remission which is obtained by continuous collaborative work between the attending physician and the specialized center, by the combination of symptomatic drugs (anticholinesterases) and immunomodulators/suppressants (prednisone and azathioprine), or even other alternative treatments.

Complementary examinations aim to confirm the diagnosis and to look for associated pathologies (1/10 to a thymoma or an associated autoimmune disease). The assessment includes immunological assays for autoantibodies, mainly anti-RACh or anti-MuSK antibodies, electromyography and repeated nerve simulations, thoracic imaging (75% of patients have thymic hyperplasia and 15% thymoma). A Tensilon pharmacological test, performed in a hospital setting, can confirm the diagnosis.

Keywords: Myasthenia Gravis; Antis Rach; Autoimmune Child

Introduction

Myasthenia gravis is a disorder of the neuromuscular junction characterized by fatigability, muscle weakness affecting the oculomotor, bulbar, skeletal muscles worsening with effort and yielding to rest [1]. It is an autoimmune neurological disease that can be life-threatening by affecting the respiratory muscles [2]. It begins at any age, from 6 months to over 80 years old. Myasthenia gravis affects 60% of cases, especially young adults under 40 years old, mostly women.

The management of myasthenia gravis can be divided schematically into symptomatic treatment, basic treatment and crisis treatment of the disease, treatment of associated pathologies and general measures. [3-7].

Observation

17-year-old patient, since she was 9 years old, has been overweight, correctly vaccinated, consults for gait disorder evolving for 1 month. On clinical examination, indifferent plantar cutaneous reflex, sharp and symmetrical osteotendinous reflexes, no motor disorder. Standard assessment without particularity.

On the neurological level

Conscious and oriented patient, no genito-sphecterian disorder, complaining of cramps in the lower limbs. Examination of the cranial pairs, diplopia with fatigue, poor mimicry, does not puff out the cheeks, does not smile, the mandible sags when speaking. Trouble swallowing on exertion. In terms of motor skills, fatigability on overall effort with Barré impossible in the lower limbs, Barré possible in the upper limbs with a strength rating of 4. No hypertonia or hypotonia. Hold your head properly. No dysmetria or adiadochokinesia, sharp osteotendinous reflexes at the bicipital, patellar and achilles level. Absent abdominal reflexes. No pyramidal or extrapyramidal syndrome. No sensory disturbance.

Faced with this table, a strong suspicion of myasthenic syndrome was evoked and the myasthenic score was calculated:

- 40/100 at the end of the afternoon without treatment;
- 56/100 in the morning without treatment;
- 72/100 under treatment with MESTINON 30 mg.

Positive PROSTIGMIN test, marked improvement in symptoms 10-15 minutes after injection of 0.5 mg of PROSTIGMIN. Addition of 0.25 mg of ATROPINE to moderate hypersalivation and bradycardia at 60/minutes, infusion of IMMUNOGLOBULINE 36 grams, then treatment with MESTINON 30 mg every 6 hours.

- **Digestive:** Abdomen supple, depressible, and painless, no mass palpated. No organomegaly, no pain when shaking the lumbar fossae. Tiredness during meals, dysphagia and notion of road pits, implementation of a mixed diet.
- **On the cardiovascular level:** Peripheral pulse present, regular heart sounds, no audible murmur, no sign of heart failure.
- **On the respiratory level :** Eupneic in ambient air, clear and symmetrical pulmonary auscultation without added noises.
- **Biological assessment**: Hemoglobin level 12 g/dl; leukocytes: 5.4 G/L; PNN: 2.3 G/L; Platelets: 290 G/L; Na 140 mmol/l; K: 3.7 mmol/l; creatinine 55 micromol/L; Albumin: 38 g/l; CRP: 1.1mg/l; CPK: 26 IU/l; TSH: 2.08 mIU/L; Beta HCG: plasma: sterile; Ac anti MUSK: negative; IgA anti transglutaminase: in progress; anti-RACH antibody: positive at 65.3 nmol/L; FAN in progress; ANCA in progress.
- **Thoracic CT:** Triangular thymus, homogeneous with a normal appearance. Absence of progressive mediastinal or pulmonary parenchymal lesion.

Transfer to pediatric intensive care at Raymond Poincaré hospital for further care.

Good evolution On the neurological level under polyvalent immunoglobin IV and MESTINON (initial dose at 30 mg times 6/day, then increased to 60 mg alternating with 40 mg every 6 hours. The myasthenic score is between 79-86/100. A first course of RITUXIMAB (375 mg/m^2) was started with clinical improvement, without particularity during the infusion.Favorable evolution: myasthenic score increased by 100/100. Subsequently, a course of polyvalent immunoglobulin at 1 g/kg every 15 days Implementation of antibiotic therapy with BACTRIM to avoid bacterial infections after RITUXIMAB treatment.

- **On the immune level:** Protein electrophoresis finds a significant hypergamma globunemia at 30.7 (VN: 7.1-20); pre-treatment lymphocyte immunophenotyping of immunoglobulins found B lymphopenia at 15%; Ig doses: G: 18 g/l, A: 3 g/l, M: 2.26 g/l; Anti-nuclear factors at 1/160 speckled; presence of ANCA atypical appearance without identified MPO/PR3 antigenic specificity. The presence of this auto-antibody does not justify a biological argument in favor of ANCA vasculitis to be compared to the clinical context.
- **Anti-ag DNA:** Soluble negative; Ac anti hepatopathy endows: negative; Ac anti IFI tissues: negative; Anti-tissue Ac: negative; Ac anti transglutaminase: negative.
- **On the endocrine level:** No hyperandrogenism, no digestive disorder and is regulated on a regular basis with painful menstruation. Height and weight growth curve shows an increase in weight gain from 5 years to 9 years, going from -2 DS to + 3 DS then at the age of 11 years a weight loss from + 2DS to – 2DS. The decay kinetics from age 16 to 17 could be related to his symptoms of autoimmune myasthenia gravis.
- **Thyroid assessment:** Is normal : FSH : 2.7 IU/l and LH : 6.7 IU/l; prolactin: 17.1 micro g/l; GH: 32 IU/l (VN: 32 IU/l (VN: 0-10); cortisol: at 8 a.m.: 343 nmol/l and at 9 a.m. 127 nmol/l; IGF1: 203 ng/ml (VN: 155- 421 ng/ml); ACTH: 1.9 pomol/l (VN: < 12 pomol/l).

- **Brain MRI:** Showing the increased anterior pituitary (Height: 9.3 mm, Thickness: 8.4 mm and Width: 13 mm) with slightly heterogeneous enhancement. No nodular formation within it. The posterior pituitary is of normal morphology and signal, in spontaneous hypersignal T1. Bulging appearance of the sellar diaphragm. The pituitary stalk showed pseudo-nodular thickening, intense enhancement. Normal optic chiasmus. Normal cavernous lodges. In addition, presence of a left temporo-polar arachnoid cyst, 40x16x16 mm, without mass effect or associated edema. No signal anomaly on the broadcast sequence.
- **In terms of infection:** PCR SARS COV: negative, HHV6 blood: positive: 55 virus copies/million cells very low; HHV8: undetectable; blood adenovirus: negative; CMV blood: negative; EBV blood: negative; Blood enterovirus: negative; hepatitis A blood: negative; VZV serology: positive at 1771 IU/L (VN: 135-165); HIV serology: negative; hepatitis B serology shows a profile compatible with vaccination; hepatitis C serology: negative; hepatitis A serology: negative; Quantify: negative; BMR and BHRe research: negative.

Weight on arrival 36 kg 9, BMI 14. A readjustment of the doses of MESTINON was made initially to be closer to 2 mg/kg/dose four times (60 mg times four/day). Treatment with RITUXIMAB was prescribed with IVIG (1g/kg) every two weeks. She gained some weight and normalized in respiratory, bulbar and motor functions (clinical examination and normal strength). Good endurance, was able to go out and did not show fatigue or weakness. Initially, a care project in a Medico educational or similar establishment had been planned.

Overall

Management of a generalized autoimmune anti-RACH myasthenia gravis, good evolution under MESTINON, IGIV and RITUXIMAB with suspicion of precocious puberty being explored.

Discussion

The observation of our case, at the beginning, reveals a diagnostic wandering after several consultations in the emergency room for the same symptoms, especially when it comes to a priori non-neurological cases. In our case, the diagnosis of suspicion was made after tests carried out and confirmed by the etiological assessments. According to data in the literature, myasthenia can begin at any age from 6 months to 80 years old but mainly affects adults under 40 years old, mostly women [8-10] and our patient was 17 years old.

The clinical manifestations were dominated by fatigability when walking and at mealtimes with a slight sign of respiratory distress. In our case, the neuromuscular manifestations were not overly represented at the onset of the disease, but which gradually became apparent during the hospital stay. This confirmed our diagnosis. Black subjects are more likely than whites to develop ophthalmia and complete ptosis according to Heckman., *et al*. [11] while our patient was of Native American origin.

After one year of evolution, in 80 to 90% of patients, other areas are affected such as the pharyngolaryngeal muscles, the muscles of the limbs. However, respiratory muscle involvement and severe swallowing disorders characterizing severe forms (20 to 30% of patients in the literature) were observed in two of our patients [12,13]. Indeed, the dosage of anti-RAch Ab was positive in our patient at 65.3 nmol/L and anti MUSK Ab: negative, its positivity reveals seropositive myasthenia. But cases of seronegative myasthenia gravis are also reported in the literature [14-16]. The negativity of anti-RAch Abs often induces the search for anti-MUSK Abs [9,10].

In generalized myasthenia gravis, anti-Rach antibodies are present in 80% of cases and absent in 20% of cases [8,17]. A thymoma may be associated with it in 20 to 30% of cases. In our case there was no associated thymoma after the result of the chest MRI. The role of the thymus and the T cell immune system in initiating and modulating the production of anti-RACH antibodies is still debated but seems important [11].

Myasthenia gravis in patients with thymoma is, according to several authors, more severe than in patients without thymoma [18-21]. The association of myasthenia gravis with other autoimmune pathologies has been found in the literature [11].

Thus, we noted the association with precocious puberty which was being explored. Thyroid balance T4 and T SH was normal. Anticholinesterases are the first-line treatment for myasthenia gravis. They increase the amount of acetylcholine at the motor endplate and are effective in all forms of myasthenia gravis [24]. According to many studies, immunosuppressant treatment is used to decrease pathogenic antibodies [22-24].

Some authors have found that the addition of an immunosuppressant is essential in order to prevent the rapid rise of anti-RACH Abs, others however suggest that plasma exchanges make the lymphocytes more sensitive to the action of immunosuppressants. Thus, there could be a synergy between plasma exchange and immunosuppressants. After three plasmapheresis sessions, the total body burden of IgG is reduced by 70%, IgM by 80% and it will take about five sessions to eliminate 95% of the immunoglobulins [2,24-26].

Plasmapheresis has a great rapidity of action and makes it possible to reduce the sequestration of anti-RACH antibodies with a delay of action of 12 days [12,22]. In terms of infection, the HHV-6 virus was positive and HHV-8 undetectable, Covid PCR negative twice. Herpes virus 6 (HHV-6 for Human herpes virus 6) infects 90% of the population in a latent state, the primary infection occurring in childhood, associated with a mild eruption. But in some individuals (about 1% of the population), the viral genome integrates into the genome of all germ and somatic cells. It is then found in all the samples taken from these individuals in an equivalent quantity, around one copy of the viral genome per cell. This integrated form is a priori not pathogenic and does not require any particular treatment.

Varicella zozter virus (VZV), positive in our patient, is a double-stranded DNA neurotropic virus from the Herpesviridae family and the alpha-herpesvirinae subfamily, whose only reservoir is the human being. After infection of the nasopharyngeal lymphoid tissue, the virus spreads to the regional lymph nodes and causes viraemia before infecting the skin and causing the typical rash [27]. There follows a lag phase in the sensory neurons located in the posterior horn of the spinal cord, with opportunities for reactivation, favored by a decrease in immunity, stress, a febrile state or another infection.

Conclusion

The evolution of myasthenia gravis is capricious, usually characterized by the occurrence of flare-ups sometimes following remissions and a tendency to aggravation in the first years. The severity of myasthenia gravis varies widely from patient to patient and, in the same patient, from time to time.

Involvement of the respiratory muscles and severe swallowing disorders characterize the severe forms (20 to 30% of patients) whose management in intensive care has considerably reduced mortality. Monitoring and treatment are made difficult by the inherent and unpredictable fluctuations of the disease, but also by the heaviness and complications of the drugs.

From the outset, the patient must be informed that the treatment will be long, certainly several months; if it is long, it is usually effective; if it is well conducted, remission is obtained 8 times out of 10 in three to four months. Severe forms require rapid treatment, generating at least one day hospitalization (most often intravenous Ig).

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