Life-Threatening Laryngeal Involvement in Isaacs Syndrome

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Introduction. Isaacs Syndrome [1] is an extremely rare disease characterized by diffuse peripheral nerve hyperexcitability provoking continuous involuntary muscle activity, cramps, fasciculations and myokimia. In most cases Isaacs syndrome ascribed to an autoimmune process targeting potassium channels in the proximal nerve membrane and in about 50% of the patient serum antibodies against potassium channels may be found. Autoimmune Isaacs syndrome may be either primary or secondary, the latter usually related to a neoplasm, constituting thus a paraneoplastic syndrome. Isaacs symptoms hyperexcitability symptoms are in most instances only annoying for the patient without constituting an hazardous condition, moreover the clinical picture often exhibits a good response to immunomodulatory and antiepileptic treatment. We present the case of a patient with a progressive and life-threatening laryngeal spasm related to an unusual form of aggressive Isaacs refractory to medical treatment.

Case Description. A 65-years-old man presented continuous unexplained diffuse sweating followed after some months by diffuse and continuous muscle twitching. Patient’s relatives also reported to have noticed in the last year the presence of whistling and wheezing during normal breathing in certain position or during prolonged talking. Neurological examination at the admission disclosed diffuse myokimia, unilateral horizontal gaze paralysis and slight weakness localized only to the deltoid muscles, without any further neurological sign. Electromyography confirmed the diagnosis of Isaacs syndrome, without any evidence of further peripheral neurological diseases. Since the presence of a pacemaker for vasovagal syncopes, MRI scans couldn’t be performed. Cerebrospinal fluid analysis was unremarkable and chest-abdomen CT scan disclosed only pleural deposits ascribed by our pneumologist to the results of previous professional exposures. Anti-potassium channels antibodies were negative. Laryngoscopy disclosed an adduction spasm of both vocal cords with a subtotal occlusion of the laryngeal space. Plasmapheresis was performed with improvement of all symptoms, including the laryngeal ones since whistling and wheezing totally disappeared. However after one moth all the symptoms relapsed and exhibited progressive worsening; a second trial of plasmapheresis was ineffective so steroid therapy (up to 1 mg/kg/die of prednisone) and carbamazepine (up to 800 mg/die) was initiated as suggested by the literature [1]. The patient experienced a strong improvent but after a further month all the symptoms rapidly worsened again with the appearance of subacute severe respiratory insufficiency so it was necessary to practice an urgent laser cordotomy. In the following months also a diffuse axonal sensormotor neuropathy appeared. Screening for heavy metals intoxication (mercury and manganese) disclosed only a slight increase of manganese level with normal mercury level. Follow-up is still ongoing.

Discussion. We described the case of a patient with Isaacs syndrome presenting an unusual resistance to all the therapies and with a life-threatening evolution which is extremely rare for this disease. So far indeed only one case of laryngeal involvement in Isaacs syndrome has been reported [2]. Even if our patient had negativity for anti-potassium channels antibodies, the autoimmune etiology is suggested by the response, even if temporary and scarce, to all the immunomodulating treatments which have been practised. Mercury intoxication have recently been claimed as mimicking autoimmune Isaacs syndrome [3], but in our case mercury levels were within the normal limits. Even if the final diagnosis is still partially open, we think that the atypical features of the patients, associated with the appearance of a sensorimotor unexplained axonal polyneuropathy, suggests the paraneoplastic etiology probably related to an occult cancer. Neurological and oncological follow-up are still ongoing.

Conclusions. Even if Isaacs syndrome is usually considered a bening disease, our case suggests to clinicians that this disease can be also life-threatening when laryngeal muscles are involved. We highlight that our patient, despite an almost complete laryngeal occlusion, was almost asymptomatic in the early course of the disease and that the respiratory insufficiency which required urgent cordotomy appeared rapidly with a fast progressive course. We therefore suggest clinicians to investigate laryngeal functions and motility in patients with Isaacs syndrome at the time of the diagnosis and periodically during the course of the disease.

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