MILLER FISHER SYNDROME, INTERNAL AND EXTERNAL OPHTHALMOPLEGIA AFTER FLU VACCINATION

SÍNDROME DE MILLER FISHER, OFTALMOPLEJÍA INTERNA Y EXTERNA TRAS VACUNACIÓN ANTIGRIPAL

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ABSTRACT

Case report: Miller Fisher Syndrome (MFS) is the most frequent variant of the Guillain-Barré Syndrome. It is characterised by the classic triad of ophthamoplegia, ataxia and areflexia. We present a case of a patient who developed these clinical findings 5 days after flu vaccination.

Discussion: Miller Fisher Syndrome is an unusual condition seen in ophthalmologic clinical practice. Although respiratory and digestive infections have been reported as antecedent infectious agents in MFS, it has not previously been described in relation to the flu vaccine (Arch Soc Esp Oftalmol 2008; 83: 433-436).

Key words: Anti-GQ1b antibody, internal ophthalmoplegia, external ophthalmoplegia, ataxia, areflexia, antiflu vaccine, Miller Fisher syndrome.

INTRODUCTION

Miller Fisher Syndrome (MSF) is a single-phase polyradiculopathy. It is characterized by the classic triad of ophthamoplegia, ataxia, and areflexia. The disease is generally associated to respiratory or digestive infections.

A case is presented of an MFS patient, whose only antecedent was flu vaccination five days earlier.

CASE REPORT

A 64 year old male patient was admitted into ophthalmic E&R due to double vision and dizziness, with apparently no other noteworthy symptoms; however, instability in bipedestation was detected, which could not be attributed only to diplopia.

The only antecedent of interest, as explained by the patient, was flu vaccination five days before.
Visual acuity was 0.7 for both eyes, with both pupils dilated and areflexic, and no previous contact with midriatic products (fig. 1). Limited abduction of both eyes was visible, larger for the left eye (fig. 2), in suprabduction of both eyes (fig. 3), and difficulties in the rest of ocular movements, with horizontal diplopia. The rest of the ophthalmic examination was normal.

Given the diagnostic suspicion of Miller Fisher Syndrome, the patient was referred to the Neurology Department, where ataxia and hyporeflexia were detected, and limb weakness was discarded. The patient was then admitted for a complete study and follow-up. Results of emergency blood tests and CT scan were normal.

A respiratory difficulty was seen 24 hours after admission, requiring oxygen and physiotherapy. New neurological symptoms developed over the following weeks, such as: facial paralysis, dysphonia, and dysphagia.

A lumbar puncture was performed during admission, and an albumina cytologic dissociation was detected. The MRI study definitely discarded a space-occupying injury, or demyelinization. The electromyographic study provided no additional information.

The immunological study was positive for anti-GQ-1b antibodies, thus finally confirming the initial diagnosis.

The patient showed improvement two weeks after admission, after two cycles of immunoglobulines. Clinical evolution was slow and polysymptomatic, with a persistent diplopia, and prolonged bilateral abduction.

DISCUSSION

Miller Fisher Syndrome is a peripheral neurological condition, mostly associated with respiratory or digestive infections (1). The average time for neurological symptoms to appear after infection is 1-2 weeks, and diagnosis is based on proving seroconversion. It is rarely associated to the acute phase of the process (2). Our case was not associated to chronic or acute infections, but it was related to flu vaccination.

MFS is considered to be initiated by a self-immune process. High counts of antiganglioside antiGQ1b antibodies in blood serum, analyzed with ELISA (3), are MFS-specific, though later studies have also associated this to Guillain-Barré syndrome with ophthalmoplegia, to Bickerstaff brain

Fig. 1: Internal ophthalmoplegia in initial examination.

Fig. 2: Extrinsic ocular motility: limited abduction of right eye.

Fig. 3: Difficulties to raise both eyes under suprabduction.
stem encephalitis (4), and to acute ophthalmoparesis with no ataxia.

The optic nerve and oculomotor nerves contain a large amount of GQ1b gangliosides. Some infectious agents share homonymous epitopes (1) with some surface gangliosides for the peripheral nerves, thus initiating production of antibodies against them, and a cross-reaction with nervous tissues. Antibodies get bound to the chains of the paranodal regions in the infranuclear portion of the oculomotor, trochlear, and abducens nerves, with weaker links to the cerebral nucleus, thus blocking the motor nerve. They would thus be responsible for ataxia and ophthalmoplegia.

Perhaps the flu vaccination shares these epitopes, thereby initiating our patient’s condition.

The typical triad for this syndrome includes ophthalmoplegia, ataxia, and areflexia. It is usually initiated by a limitation in abduction (1), and there are cases where ophthalmoplegia is not full. At the time of coming into E&R, the patient was affected by paralysis in abduction, with a limitation of the rest of ocular movements. Complete paralysis of all extraocular muscles was developed within hours, with no ptosis. Ataxia and hyporeflexia were present from the start.

Other symptoms which may also develop include dysphagia, dysphonia, facial paralysis, or respiratory insufficiency. Respiratory difficulties are more frequent in elderly patients, such as the one in this case, and they usually require mechanical respiratory support, with a worse prognosis and a higher recurrence rate. When respiratory insufficiency is present, Guillain-Barré syndrome with ophthalmoplegia must be discarded. This is difficult due to the limited specificity of tests, and the clinical essence of the diagnosis.

Internal ophthalmoplegia are infrequent (4). A differential diagnosis must be performed for a ponto-mesencephalic dorsal injury (ictus, encephalitis, expansive injury), which is most of the time discarded through clinical evidence and image tests; a differential diagnosis must also be performed with botulism, where a mild areflexic midriasis and dysphagia are present, and where the clinical history and accompanying signs suggest a diagnosis. Antiganglioside antibodies may appear in both conditions, so that they may be discarded.

In order to explain a mechanism for internal ophthalmoplegia, Radziwill (4) assumes that anti-GQ-1b antibodies may bind themselves to the ciliary ganglion, similarly to the way in which they get linked to the paranodal regions of the nerves in charge of extrinsic ocular motility, thus producing denervation of the pupillary sphincter (5). A number of different authors have used the pupillary hypersensitivity test, which suggests that sensitivity increases for the pupillary sphincter muscle after pilocarpine 0.125% instillation (4). This is a useful indicator of the presence of postganglionary parasympathetic dysfunction, so the authors suggest that this is a predominantly peripheral condition.

The lack of alterations in the MRI test, and the electroneurographic findings, which are compatible with demyelinizing poliradiculopathy support the peripheral injury location for these symptoms.

As a conclusion, a rather infrequent case of MFS is presented with involvement of extrinsic ocular motility. This occurs only for 37% of all cases of patients with no previous history of infection. The only antecedent mentioned was antiflu vaccination five days earlier. No cases were found in the literature associating this syndrome with an earlier vaccination, as opposed to Guillain-Barré Syndrome.

MFS is described as a benign condition, and is usually treated with immunoglobulines, though their effectiveness is arguable (some authors have presented cases where no treatment was required) (2), but it seems that they accelerate recovery. However, this cannot be considered a trivial condition. The patient in this case required respiratory support, and clinical evolution was slow and polysymptomatic, with a persistent dyplopia, and prolonged limitation of bilateral abduction.

REFERENCES