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Case Report

Trismus as a Presenting Symptom in a Case of Progressive Encephalopathy with Rigidity and Myoclonus

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Keywords
Progressive encephalopathy with rigidity and myoclonus · Trismus · Teratoma · Plasmapheresis

Abstract
In this report we present a clinical case of trismus. The patient in question showed symptoms of trismus for 3 days, rapidly leading to respiratory insufficiency. Afterwards she developed myoclonus and progressive encephalopathy. Neurological workup showed no relevant abnormalities. A CT of the abdomen revealed a mass in the lower abdomen, which turned out to be an ovarian teratoma. Progressive encephalopathy with rigidity and myoclonus (PERM) was diagnosed clinically. Treatment with corticosteroids, benzodiazepines, and levetiracetam did not ameliorate the patient's condition. Only after the introduction of plasmapheresis was there a spectacular improvement in her clinical state. In this case we could not detect associated antibodies. The most likely cause of PERM is paraneoplastic disease secondary to ovarian teratoma. This type of tumor has been associated with multiple paraneoplastic neurological conditions, but this is the first case associated with PERM. To date there is only one publication on trismus as a sole presenting sign, with a quite similar disease course.

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Introduction

Progressive encephalopathy with rigidity and myoclonus (PERM) is a rare condition and is considered to be a form of stiff person syndrome (SPS) spectrum, although, in contrast to SPS, most of the cases of PERM are paraneoplastic. Multiple antibodies have been described of which anti-GAD and anti-GlyR are most common in SPS and PERM [1, 2]. We describe a case of seronegative PERM with underlying ovarian teratoma.

Case Presentation

A 73-year-old woman presents to the emergency department, showing symptoms of trismus leading to sudden respiratory distress and an episode of cyanosis. Anamnestic symptoms of trismus had shown up 3 days before hospitalization. Initially there had been no subjective signs of respiratory failure. The patient has no relevant history. Her chronic medication consisted of macrogol, escitalopram, mometasone, indapamide, and lorazepam. There was no notion of any use of antipsychotic or antiemetic agents. The patient's vaccination history was unknown. She did not recall any vaccination in the past 10 years. There was no history of alcohol, nicotine, or drug abuse. The patient was socially active and a recreative gardener.

On arrival of the medical team, there was no safe airway. After a Mayo tube had been placed, oxygen saturation stabilized rapidly. Neurological examination reveals trismus and mild rigidity of the neck muscles. The patient was alert. Her motor function, sensibility, and reflexes were normal. General physical examination did not reveal any abnormalities, except for small wounds in the oral mucosa due to an ill-fitting dental prosthesis. Also, the lab tests as well as brain and neck CT were all normal. CSV analysis showed normal biochemistry and cultures remained sterile.

Treatment for tetanus was started, including antibodies, vaccinations, and metronidazole. During the initial 12 h of hospitalization the patient's condition remained stable with persistent trismus (mouth opening limited to a few millimeters). Twenty-four hours after hospitalization, the patient has a sudden respiratory collapse with a hypoxic cardiac arrest of 2 min. After sedation had been stopped, the initial evaluation showed persistent trismus with need of ventilation. Further clinical evaluation, however, was unchanged compared with her general condition before cardiac arrest. In the following days there was a deterioration with the development of non-stimulus-induced myoclonus in all limbs. EEG did not show an epileptic correlate but revealed slowed background waves. The patient's consciousness declined progressively. The medical therapy was switched to diazepam and levetiracetam.

The patient was clinically diagnosed with PERM. She was started on a high dose of methylprednisolone. Further workup revealed a mass in the lower abdomen. Resection showed an ovarian teratoma. Paraneoplastic and autoimmune antibodies (including anti-GAD, anti-NMDA, anti-Ri, anti-GlyR, and anti-amphiphysin) remained negative; DPPX antibodies were not tested due to logistic reasons. MRI of the brain showed age-related atrophy. There was no evidence of hypoxic damage.

Because of lack of improvement on methylprednisolone, she was started on plasmapheresis (five sessions). This led to an obvious neurological improvement of conscience: the patient was able to follow instructions and to answer questions correctly in a nonverbal way. The myoclonic movements disappeared completely. Rigidity was less pronounced and remained only in the legs. Trismus was less pronounced and there was no longer any need for

breathing assistance. During the days following this improvement there were multiple complications with medical-toxic bone marrow suppression, spontaneous retroperitoneal bleeding, sepsis, and spontaneous intestinal perforations. Due to those complications, further plasmaphereses were no longer possible. The patient died of multi organ failure. No autopsy was performed.

Discussion

There are multiple considerations in this case report. We will focus on the rare presentation with trismus as the most prominent feature, seronegativity, and potential differential diagnoses in this case.

Trismus as a clinical sign can have many different causes. These are mostly obvious, for example local irritation of the temporomandibular joint (e.g., after radiation, infectious and oncological causes) or medicinal side effects (e.g., dystonia on antipsychotics, antiemetics). After considering the patient's medical history and analyzing the head and neck CT, these causes could be excluded quite easily. Furthermore, trismus is the most common presentation of tetanus infection (in 50–75% of cases), but in present times this infection has become rare in developed countries [3, 4].

We searched PubMed for other cases of PERM or SPS and trismus; we found only one case report in which trismus as a primary presentation of PERM was described. Similar to our case, the condition of the patient in question deteriorated rapidly, but improved after plasmapheresis [5]. However, there are other cases of very focal bulbar onset as presentation of PERM, as is shown by a case report of PERM presenting with stiff tongue [6]. In a cohort of 45 GlyR antibody-positive patients, 47% had symptoms in the bulbar, facial, or trigeminal area at presentation. In most cases these were combined with other symptoms [1].

Recent research on antibodies of patients with SPS and related conditions such as PERM shows that anti-GAD is the most common causal antibody in cases of autoimmune SPS. In research in paraneoplastic cases, multiple antibodies have been described (e.g., anti-GAD, anti-amphiphysin, anti-GlyR). Seronegativity was not rare, however; it was diagnosed in 5 of the 19 cases of paraneoplastic SPS spectrum disease. Breast cancer was the most common underlying malignancy (8 out of 19 cases), but lung, colon, thymus, melanoma, and other malignancies occurred as well [1, 2]. Ovarian teratoma has been linked to different paraneoplastic neurological diseases. Moreover, it is the most frequent underlying malignancy in NMDA encephalitis. Although other conditions such as ataxia, demyelization, and encephalitis caused by other antibodies such as AMPA are also linked to ovarian teratoma [7–10], there are no other publications on cases of PERM in association with teratoma. In cases of suspected neurological paraneoplastic phenomena, thorough screening for underlying malignancies might significantly improve life expectancy [11].

In our case, we are aware of the fact that it is difficult to make a definite diagnosis of PERM because no antibodies were found and no autopsy was performed. As myoclonus was present after a short cardiac arrest, hypoxic myoclonus is a possible differential diagnosis. Acute hypoxic myoclonus can be ruled out because the patient only became symptomatic after regaining consciousness. It could be part of Lance-Adams spectrum, but this seems less likely in the absence of hypoxic damage on cerebral MRI. Also, the absence of effect of levetiracetam and diazepam is unusual in Lance-Adams myoclonus, and the spectacular effect of plasmapheresis would not be expected [12, 13].

Conclusion

We would like to conclude this case report with the following recommendations. The diagnosis of PERM should be included in the differential diagnosis when patients present with trismus or other focal bulbar signs such as stiff tongue. Also, we recommend oncological workup and analysis of paraneoplastic antibodies when there is a high suspicion of PERM, although the diagnosis cannot be ruled out in the absence of primary tumor or antibodies. There are no reasons to assume that other treatments should be initiated with patients with focal onset of PERM in comparison with classic presentation of PERM. The primary intervention should include treatment of the underlying oncological problem if present and immunosuppressive medication (e.g., corticosteroids and plasmapheresis), in combination with symptomatic treatment.

Statement of Ethics

This article does not contain any studies with human participants performed by any of the authors. Informed consent was given to publish this case.

Disclosure Statement

The authors have no conflicts of interest to declare.

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Author Contributions

L. Blomme: clinical follow-up of the patient, writing of the first draft, final approval. K. Van de Velde: clinical follow-up of the patient, adjustment of the first draft, final approval.

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