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CASE REPORT

Guillain-Barré syndrome as an atypical manifestation of an esophageal carcinoma

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Abstract Guillain-Barré syndrome (GBS) is an acute demyelinating polyradiculoneuropathy normally associated with a preceding infection, but sometimes it can be linked to a subjacent malignancy. We report an unusual case of GBS occurring as the first clinical manifestation of an esophageal adenocarcinoma in a 65-year-old patient. A GBS neuropathy of undetermined origin may be associated with an underlying tumor and esophageal cancer has to be considered in the differential diagnosis.

Keywords Guillain-Barré syndrome · Esophageal carcinoma · Paraneoplastic syndrome

Introduction

Guillain-Barré syndrome (GBS) is an acute inflammatory, demyelinating peripheral polyneuropathy characterized by a rapidly ascending muscle weakness or paralysis accompanied by absent or depressed deep tendon reflexes and, in some cases, by respiratory distress. Abnormal immune response through both humoral and cell-mediated mechanisms is the proposed etiopathogenesis to explain GBS [1]. Most cases of GBS, are preceded by respiratory or gastrointestinal infections or immunization, but GBS has also been linked to malignancies as a possible paraneoplastic complication. Lymphomas [2], breast [3], small cell lung [3, 4], and renal carcinomas [5], are the most frequent tumors associated with GBS. On the other hand, the link between GBS and esophageal carcinoma is less commonly found and only few cases are reported in literature. We describe here the case of a 65-year-old man presenting a GBS 2 months before the diagnosis of an esophageal adenocarcinoma.

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Case report

A 65-year-old man with history of alcohol and smoke abuse, presented with an initial numbness of the feet, followed by a progressive lower limbs weakness, difficulty to walk, and impossibility to remain fully ambulant. The patient had no back pain, headaches or preceding history of infection or illness. Physical examination revealed a symmetrical bilateral weakness in knee flexion and extension, associated with a deficit in the plantar and dorsal flexion of the feet. Pallesthesia alteration and pinprick sensation loss were found below the T-11 dermatome. Reflexes were absent in the lower limbs, without sphincterial muscles involvement. Cranial nerves, cerebellar and higher functions examinations were normal. A tendency to postural hypotension was found.

A lumbar puncture performed 2 days later demonstrated a raised cerebrospinal fluid (CSF) protein concentration of 1.79 g/L. CSF biochemistry, cytology, cell counts, and culture as well as the routine hematology, the electrolytes and the liver function tests were normal. Spinal compression or acute transverse myelitis was excluded by a magnetic resonance imaging of the whole spinal cord. Clinical neurophysiological studies showed evidence of an acute polyradiculopathy with reduced motor conduction velocities and prolonged distal latencies. On the basis of the clinical presentation, CSF and neurophysiological studies findings, the diagnosis of GBS was evoked. A treatment of human intravenous immunoglobulin at standard doses was,

therefore, administered permitting a partial improvement in the motor function of the lower limbs without recovery in the ability to walk.

Negative history for a previous gastrointestinal or respiratory infection or another triggering event such as immunization, surgery, trauma or bone-marrow transplantation, suggested the differential diagnosis of a possible paraneoplastic syndrome. First radiological assessments with the total body computed tomography did not show any tumoral lesion explaining the GBS. 2 months later, the patient started to develop a progressive dysphagia for solids. Esophagogastroduodenoscopy revealed an obstructive, circumferential lesion in the lower third of the esophagus, positive at biopsy for an adenocarcinoma. [18F]-Fluorodeoxyglucose-positron emission tomography (FDG-PET/CT) showed a local disease with sub-diaphragmatic extension to the cardia without distant metastasis and esophageal endoscopic ultrasonography permitted ultimately to stage the lesion as T3N1. A preoperative treatment of induction chemotherapy followed by chemoradiation as proposed in the Swiss multicenter SAKK 75/02 protocol was, therefore started [6]. After the induction chemotherapy consisting of docetaxel (75 mg/m^2) and cisplatin (75 mg/m^2) on days 1 and 22, the patient presented a good metabolic response at the FDG-PET/CT with a standardized uptake value (SUV) that diminished from 14.5 at the diagnosis to 5.6. This treatment was followed by a radiotherapy to 45 Gy (25 $\times$ 1.8 Gy) and by a concurrent weekly chemotherapy comprising docetaxel (20 mg/m^2) and cisplatin (25 mg/m^2) that was administered only two times and successively interrupted as a consequence of the important hemato-toxicity. Due to the surgical inoperability of the lesion and to the high comorbidities of the patient, the decision to deliver an exclusive radiotherapy treatment to a total dose of 61 Gy was taken.

At the end of the treatment, we assisted at a good clinical improvement in the neurological status of the patient with a full functional recovery in the ability to mobilize independently and in a routine control after 6 months the patient presented no evidence of persistent esophageal disease. However, 21 months later, a local symptomatic recurrence was diagnosed and a palliative attitude with an esophageal stent placement was adopted. The clinical neurological status continued to be normal.

Discussion

Paraneoplastic neurological syndromes represent a clinical entity extremely rare in cancer patients with an estimated incidence rate of about 7% [7]. When a neurological disorder is reported as a paraneoplastic disease, it is mandatory to find the direct correlation between the malignancy and the neuropathy. The commonly proposed criteria used to define a paraneoplastic disease are based on the increased incidence of a specific cancer in a population affected by a particular neurological disorder, the short latency between the onset of the neuropathy and the cancer, the presence of specific onco-neural antibodies directed against antigens expressed by the tumor and the nervous system cells and the absence of other causes explaining the pathogenesis of the neuropathy [8, 9].

The association between malignancies and GBS is still controversial and the existence of a paraneoplastic GBS is not completely accepted. However, different tumor types such as Hodgkin's lymphomas, small cell lung carcinoma, breast, and renal cancer [2–5] have been linked with GBS. Rare associations are even been reported for T cell non-Hodgkin's lymphoma [10], endometrial cancer [11], gall bladder carcinoma [12] or after autologous, and allogenic bone marrow transplantations [13, 14]. In a population-based study of 435 GBS patients, Vigliani et al. [15] found that the incidence of cancers within 6 months before or after GBS was significantly greater than normally expected. These authors stated consequently that a possible pathogenetic relationship between cancer and some cases of GBS could exist, fulfilling sometimes the criteria necessary to define this association as a paraneoplastic phenomenon.

Esophageal cancer has been rarely associated with neurological syndromes and only one case describing its relationship with GBS has been reported in the literature [15]. Our case documents a GBS occurring in a patient as first clinical manifestation of an esophageal adenocarcinoma diagnosed 2 months after the onset of the neurological disorder.

In our patient, the progressive neurological symptoms onset, the increased protein concentration in CSF and the electrodiagnostic signs of demyelinization fulfill the commonly used criteria for GBS diagnosis. Exclusion of the common triggering events for GBS and the short latency between the beginning of the neuropathy and the diagnosis of the esophageal cancer, evokes a potential pathogenetic relationship between the two diseases and could suggest a possible paraneoplastic nature of the GBS. Moreover, the different timing in the clinical onset of GBS and cancer observed in our patient may contribute to eliminate supplementary bias related to the cancer therapy. In several case reports, the GBS in cancer patients was related to the oncological treatment, especially when chemotherapy agents containing platinum were used [11, 16]. The immunosuppressive status induced in these cases by the treatment could have confounded the real action of the malignancy in the development of GBS by enhancing the immunologic-mediated myelin damage catalyzed normally by the tumor epitope.

However, applying more restrictive criteria to define a paraneoplastic syndrome [8], our conclusions may become

more uncertain. Differing from other neurological syndromes, which usually are associated with cancers expressing onco-neural antibodies, in tumor associated-GBS there do not exist a specific serological profile to be used in clinical practice in order to characterize this relationship [11, 15]. Furthermore, despite a first clinical improvement, the two diseases had thereafter an independent evolution with the recurrence of esophageal cancer and the stability of the neurological disorder. Based on these more conservative considerations, in our patient the association between GBS and cancer could alternatively be considered as merely casual.

In conclusion, we document with this case report the rare association existing between an esophageal adenocarcinoma and a GBS. The nature of this relationship remains nevertheless unclear and the real existence of a paraneoplastic GBS remains still unconfirmed.

Conflict of interest statement The authors have no potential conflict of interest.

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