CASE REPORT

Guillain-Barré syndrome as a paraneoplastic manifestation of disseminated squamous cell carcinoma

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SUMMARY

We describe a 65-year-old woman who developed ascending, symmetrical paraesthesia and weakness. This was on a background of metastatic disseminated squamous cell carcinoma, with a likely recurrent mandibular primary. Serum testing for antiganglioside antibodies was strongly positive. Despite a 5-day course of intravenous immunoglobulin, the patient passed away on day 34 of admission. This is the first case, to our knowledge, of Guillain-Barré syndrome in association with squamous cell carcinoma.

BACKGROUND

To our knowledge, this was the first case that had an association between squamous cell carcinoma and Guillain-Barré syndrome.

CASE PRESENTATION

A 65-year-old woman developed a 2-week history of numbness of finger tips and toes that had progressed to the knees, with an associated weakness in the legs. This was on a background of increasing shortness of breath, non-bloody diarrhoea, daily episodes of fever with facial flushing and 15 kg of weight loss over the previous 3 months. She presented to the acute medical team following a fall secondary to her evolving neurological symptoms. There was no complaint of rigours, night sweats, cough, dysuria, rash, arthralgia or other systemic symptom. Her recent deterioration in functioning had meant that she was no longer able to perform activities of daily living. She had a medical history of primary squamous cell carcinoma of the tongue that had recurred postresection, a postirradiation gingival sarcoma and a mandibular spindle cell (sarcomatoid) squamous cell carcinoma. There was no history of alcohol misuse or a significant family history.

On examination, she was alert and orientated with a sinus tachycardia of 120 bpm and oxygen saturations of 82% on room air. Her conjunctivae were pale. Respiratory, abdominal and cardiovascular examinations were unremarkable. Neurological examination revealed a weakness of all limbs, corresponding to Medical Research Council grade 4/5 in all ranges of movement. No fasciculations were noted. Cerebellar and cranial nerve signs were absent. Light touch sensation was absent to the knees bilaterally with pain sensation absent to the level of mid-tibia bilaterally. These signs were symmetrical. There was decreased light touch and

pain sensation of both hands. There were absent deep tendon reflexes in the legs and both plantars were downgoing. Reflexes in the arms were brisk.

In the following fortnight, her neurological symptoms worsened with ascending paraesthesia to the waist and decreasing power in the lower limbs. The areflexia progressed to involve all reflexes in the upper limbs where there was also progressive sensory loss to the elbows, but with retained power. The working diagnosis was Guillain-Barré syndrome (GBS) secondary to a para-neoplastic process. The patient was too unwell to travel to the neurological unit for nerve conduction studies. Serial vital capacity measurements were undertaken twice daily and reduced over time.

INVESTIGATIONS

The patient had a normocytic anaemia (9.7 g/dl), thrombocytosis ($753 \times 10^9/l$) and a neutrophilia (neutrophil count of $11.1 \times 10^9/l$). Renal, hepatic and thyroid functions were normal. In addition laboratory tests including antinuclear antibody, serology for *Campylobacter jejuni*, HIV, cytomegalovirus and Borrelia and urinalysis (including 5-hydroxyindoleacetic-acid and catecholamines) proved negative. Cerebrospinal fluid (CSF) analysis 5 days postadmission showed no significant cellularity, normal plasma:CSF glucose ratio, no organisms on Gram staining, but a raised protein of 506.7 mg/l.

Owing to the lack of a clear focus of pathology, a whole body positron emission tomography scan was performed that showed multifocal intense fluorodeoxyglucose uptake within numerous bones (figure 1) and the right lobe of the thyroid. Ultrasound scan of the thyroid showed a heterogeneous appearance with no suitable nodules for fine needle aspiration. A left sacral alar biopsy (figure 2) was obtained under CT guidance. This showed metastatic poorly differentiated squamous cell carcinoma with some spindle/sarcomatous differentiation and areas of signet-ring-like morphology (figure 3). This was judged likely to be a metastatic recurrence of the previous neoplastic lesion in the patient's mandible given the similar histology.

Serum testing for antiganglioside antibodies was initially negative, but on day 5 of admission it became strongly positive with a titre of 1 in 3200 (0–200 normal range) by day 13. Investigations for antineuronal antibodies were negative. MRI imaging of the brain and spine was unremarkable.

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Figure 1 Total body fluorodeoxyglucose (FDG) positron emission tomography scan showing multifocal intense FDG uptake in numerous bones, in particular involving the cervical and thoracic spine, the left sacral alar and left femur.

TREATMENT

There were no curative or palliative chemotherapy or radiotherapy options for this patient and therefore the priority was symptom control.

A course of intravenous immunoglobulins at 2 g/kg was started for 5 days, but this resulted in no neurological improvement.

OUTCOME AND FOLLOW-UP

She died on day 34 of her admission from respiratory arrest.

Figure 2 Superimposed axial CT fluorodeoxyglucose (FDG) positron emission tomography scan of pelvis showing intense FDG uptake in the left sacral alar.

DISCUSSION

Here, we present a case of a lady who developed paraneoplastic GBS secondary to a disseminated squamous cell carcinoma. The clinical features of an acute ascending areflexic paralysis with sensory involvement and albuminocytogenic dissociation of CSF fill the Brighton Collaboration criteria for the diagnosis of GBS¹ and the presence of antiganglioside antibodies further strengthens the diagnosis and indicates an axonal subtype.² While it cannot be ruled out that the GBS was secondary to a preceding infective process, the absence of infective symptoms and negative antibodies to *C jejuni* and decreases the likelihood of this.

This lady was being treated palliatively for disseminated squamous cell carcinoma and so clearly had significant comorbidity. The ultimate cause of her death was a respiratory arrest, which we propose was owing to muscular weakness from GBS. This is supported by the pattern of ascending paraesthesia and weakness, together with the sequentially decreasing serial vital capacity measurements. However, it should be noted that respiratory arrest may have been owing to the underlying malignancy itself. Despite treatment with intravenous immunoglobulin, the patient still passed away. This case thus serves to highlight that GBS has potentially serious consequences with 20% of the affected patients suffering from permanent disability and with 5% mortality.³

There is still a controversy as to whether true paraneoplastic GBS exists. A single case-control study has demonstrated a positive association between GBS and cancer⁴ and several case reports describe GBS occurring alongside malignancy, including cancers of lung,⁵ bladder,⁷ blood,^{8–10} colon¹¹ and skin.¹² To our knowledge, we present the first case associated with squamous cell carcinoma. Furthermore, the authors have described cases of relapsing GBS which heralded the discovery of an underlying neoplasm which then improved following the resection of the tumour,⁷ suggesting a causal link between malignancy and neuropathy. However, while the onset of GBS and cancer may be simultaneous and even linked, there is an argument as to whether this fulfils the criteria for a true 'paraneoplastic' process, with no common identifiable marker between the reported cases and no apparent mechanism explaining how malignancy may cause pathology.¹³ With regard to our treatment for this patient, a recent Cochrane review shows moderate quality evidence that in severe disease, intravenous immunoglobulin started within 2 weeks of onset hastens recovery as much as plasma exchange, which is known to be more effective

Figure 3 Histology slide of left sacral alar. Immunolabelled with AE1/AE3 a cytokeratin marker.

than supportive care alone.¹⁴ However, we witness that the constant antigenic stimulation provided by the cancer in our patient was the reason that this was not effective, a feature absent in the resolving infections included in the Cochrane review.

We propose that the underlying malignancy should be considered in cases presenting with GBS especially when there is no apparent preceding infection, and conversely that GBS considered in any patient with cancer with neurological findings. Furthermore, we propose that further studies into this association may be of value in highlighting the link, and elucidating the pathophysiological mechanisms of this serious disease.

Learning points

- ▶ Guillain-Barre syndrome (GBS) can lead to significant morbidity and mortality, despite appropriate treatment with immunoglobulin.
- ▶ Neuropathy in patients with cancer should raise the suspicion of GBS.
- ▶ Antiganglioside antibodies and the presence of albuminocytogenic dissociation on lumbar puncture may prove important tests in confirming the diagnosis of paraneoplastic GBS, but it may not become positive until late in the disease process.

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