CASE REPORT

Paraneoplastic cerebellar degeneration as a marker of endometrial cancer recurrence

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SUMMARY

An 84-year-old woman developed a cerebellar syndrome having undergone a total abdominal hysterectomy and bilateral salpingo-oophorectomy for endometrial cancer 1 year previously. She was found to be anti-Yo antibody positive and was diagnosed with paraneoplastic cerebellar degeneration (PCD). A subsequent positron emission tomography scan and lymph node biopsy identified recurrence of her endometrial cancer. This case illustrates how PCD can be an indicator of cancer recurrence, underlines the significance of PCD as a prompt to search for underlying malignancy, and highlights the difficulties PCD poses to the clinician in terms of diagnosis and management.

BACKGROUND

Paraneoplastic syndromes represent a diverse group of disorders characterised by non-metastatic systemic effects caused by underlying malignant disease. Paraneoplastic cerebellar degeneration (PCD) is a rare condition which leads to global cerebellar dysfunction[1] and has a preponderance to affect females over males.[2] Three main autoantibodies related to PCD have been identified: anti-Hu, anti-Yo and anti-Tr, which may be present in patient serum or cerebral spinal fluid, and each autoantibody is strongly associated with a different primary site of malignancy.[3] The most common autoantibody seen in PCD is anti-Yo. It is frequently implicated in gynaecological cancers, but can rarely be seen in other cancers also.[4] Interestingly, PCD can precede the presentation of cancer by months to years,[5] or as in the case we describe, PCD can also be a marker of cancer recurrence.

CASE PRESENTATION

An 84-year-old Caucasian woman was referred to geriatric outpatients with a 6-month history of recurrent falls. She described a loss of balance and bilateral weakness initially limited to her legs which progressed to involve both arms. On examination, she had slurring of speech, upper limb proximal muscle weakness, lower limb distal muscle weakness, and normal tone and reflexes.

Thirteen months prior, she had been diagnosed with a high-grade serous endometrial carcinoma (T1b) and had undergone a total abdominal hysterectomy and bilateral salpingo-oophorectomy, along with postoperative radiotherapy. A whole body CT scan carried out 8 months after surgery demonstrated no residual disease.

INVESTIGATIONS

Thyroid function tests, inflammatory markers and drug history did not yield diagnostic clues. MRIs of the brain and spine were unremarkable and electromyography was normal. Her serum, however, was positive for anti-Yo antibody.

Before her follow-up appointment for the results of her investigations, she was admitted to hospital with worsening falls and an inability to cope at home. In the 2 months following her initial clinic appointment, she had become a wheelchair user and on examination, she now exhibited pronounced dysarthria with an unsafe swallow, bilateral dysdiadochokinesis, bilateral intention tremor, horizontal nystagmus and marked ataxic gait.

A repeat CT scan of the abdomen and pelvis did not identify a recurrence of malignancy. Therefore, a whole body positron emission tomography (PET) scan was organised, which revealed increased uptake in the left anterior cervical lymph nodes. A biopsy was arranged which confirmed metastatic endometrial nodal deposits, with identical histology to that seen following her hysterectomy.

TREATMENT AND OUTCOME

A trial course of high-dose steroids was initiated, but unfortunately the patient did not receive any clinical benefit. On discussion with the patient, it was decided that no further therapies were to be attempted. A year earlier, she had been mobilising independently with no carers; however, her disability was now such that she required nursing home support on discharge.

DISCUSSION

Neurological paraneoplastic syndromes are uncommon, affecting 1–3% of patients with cancer. Of these, 25% are related to PCD, making it the most common paraneoplastic syndrome affecting the brain.[4] When considering PCD as a diagnosis, other more common conditions should first be excluded. Nevertheless, for patients with no risk factors for cerebellar disease, the possibility of PCD should be investigated.[5] In fact, it has been identified that in female patients aged over 50 presenting with a cerebellar syndrome, approximately two-thirds of cases are due to PCD.[6]

It should be noted that dedicated cerebellar imaging has limited value in the diagnosis of PCD. Though an MRI of the brain is helpful in excluding other pathologies, in PCD it is often normal.[7] For established disease, diffuse cerebellar atrophy may be seen, which correlates with the

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neuropathological hallmark in PCD of Purkinje cell destruction.[7]

Diagnosis of PCD should initiate a thorough search for underlying malignancy. Although the presence of PCD leads to a diagnosis of cancer in 63% of cases, the search can be challenging.[6] Associations between autoantibodies and specific cancer types can guide further investigation. The presence of anti-Yo antibodies in this case, for example, corresponds with the patient's history of endometrial malignancy.[3]

For patients in whom initial screening shows no evidence of malignancy, further investigation with a PET scan is recommended.[8] While CT scan and MRI may miss small lesions, a PET scan can detect lesions over 1 cm[5] and has been shown to have a sensitivity of >83% for detecting malignancy in patients with PCD.[8]

If, after an extensive search, no malignancy is detected, patients should be closely followed up with repeat interval imaging.[7] It has also been suggested that in these cases without a proven cancer, diagnostic laparoscopy and removal of the pelvic organs may be indicated.[2] However, cases such as those presented by Scheid *et al*,[7] in which a woman with PCD, who was eventually diagnosed with invasive ductal carcinoma of the breast, was inappropriately offered an ovariectomy because her initial whole body PET showed no evidence of malignancy, raise significant doubts about such an approach.

In most cases, the outcome in patients with PCD is not favourable, with 75–80% of patients eventually becoming unable to walk without assistance.[1] Treatment of the cancer does not lead to an improvement in neurological symptoms, although it has been shown to arrest further deterioration. Interestingly, it has been demonstrated that autoantibodies persist indefinitely, even after the precipitating cancer has been successfully treated.[2]

There are no agreed protocols for the treatment of PCD. Options available include plasma exchange, intravenous immunoglobulin and immunosuppression. However, little evidence exists to support their use.[5] Swift initiation of treatment has been shown to be beneficial, with patients treated within 1 month of becoming symptomatic having the best outcomes, and patients treated after 3 months of developing symptoms having a generally worse prognosis.[9]

Learning points

- Paraneoplastic cerebellar degeneration is a rare phenomenon, but must be considered in elderly patients presenting with a subacute or acute cerebellar syndrome.
- Diagnosis of paraneoplastic cerebellar degeneration should prompt a comprehensive search for underlying malignancy or recurrence of malignancy.
- Prognosis is generally poor; however, early diagnosis and prompt treatment can improve outcomes.

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