Rare disease

The role of breast MRI in the investigation of anti-Yo positive paraneoplastic cerebellar degeneration

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Summary

Paraneoplastic neurological syndromes are a group of rare and heterogeneous disorders complicating cancer through immune-mediated mechanisms. They typically arise before the diagnosis of malignancy, thus constituting its first clinical manifestation. A thorough search for the underlying tumour is necessary, as adequate tumour management is essential for both neurological prognosis and overall survival. The authors present the case of a 43 year-old woman who presented with a subacute cerebellar syndrome associated with the paraneoplastic anti-Yo antibody. Although paraneoplastic aetiology was immediately suspected, the diagnosis of the underlying tumour was not straightforward, as is often the case. This case report highlights the importance of directing tumour search for the most probable anatomic locations, according to patient demographics and risk factors as well as the type of onconeural antibodies present, and also the need to use the most sensitive diagnostic modalities appropriate for each target organ.

BACKGROUND

Paraneoplastic neurological syndromes (PNS) are a group of rare and heterogeneous disorders complicating cancer through immune-mediated mechanisms.¹ They typically arise before the diagnosis of malignancy, thus constituting its first clinical manifestation. The diagnosis of a PNS should therefore prompt a search for the underlying tumour, as adequate tumour management is essential for both neurological prognosis and overall survival. The diagnosis of the underlying tumour in patients with PNS is often a challenge, even though some clinical clues assist in directing the search for specific anatomic locations, namely the type of onconeural antibodies present.

CASE PRESENTATION

A 43 year-old woman, with no significant medical background except for a previous history of light smoking and a family history of breast cancer in a first degree relative, developed an altered sensation over the right side of the face. Approximately 3 months later the patient developed loss of balance, which evolved in the following months to a severe ataxic disorder with loss of ambulation. On admission to the Department of Neurology, the patient presented with severe dysarthria, horizontal gaze evoked multi-directional nystagmus, severe dysmetria in all four limbs and truncal ataxia; hyperactive deep tendon reflexes and extensor plantar responses were also present. The rest of the physical examination was unremarkable.

INVESTIGATIONS

The initial diagnostic investigation revealed a positive anti-Yo antibody. Antithyroid antibodies were mildly elevated, but thyroid function tests and ultrasound were normal. An elevated carbohydrate antigen 19.9 was also present (202 U/ml; normal <37). The cerebrospinal fluid (CSF) analysis

revealed a normal cell count (2 white cells/ μ l) and an elevated protein concentration (1.24 g/l; normal <0.45). A positive pattern of CSF oligoclonal bands was present, indicating intrathecal antibody production. A brain MRI revealed no significant abnormalities. A chest x-ray, a mammogram and breast and pelvic ultrasounds were performed, with no significant abnormalities. The pap smear was negative for intraepithelial lesions and malignancy. The thoracic, abdominal and pelvic CT scan and finally the whole-body fludeoxyglucose positron emission tomography (FDG-PET)/CT scan also failed to detect the underlying tumour, although cerebellar hypometabolism was evident on PET. Approximately 1 month after discharge, the patient had a contrast-enhanced breast MRI, which revealed an oval shaped mass-like lesion with irregular margin, measuring approximately 10 mm in maximum diameter, and two adjacent areas of non-mass-like enhancement (figure 1). The mass-like lesion was subjected to ultrasound-guided core needle biopsy, which revealed the presence of a high grade ductal carcinoma insitu (DCIS).

DIFFERENTIAL DIAGNOSIS

This patient fulfilled criteria for definite paraneoplastic cerebellar degeneration (PCD).²

TREATMENT

A course of high dose intravenous methylprednisolone (1 g/day for 5 days) followed by oral prednisolone (1 mg/kg) and a pulse of intravenous immunoglobulins (20 g/day for 5 days) were initially attempted, with no significant benefit.

After the detection of high grade DCIS on the right breast, the patient was further subjected to a unilateral mastectomy with sentinel lymph node excision. Additionally, treatment with intravenous cyclophosphamide (600 mg/

Figure 1 Breast contrast-enhanced MRI depicting images suggestive of malignancy, later confirmed to be ductal carcinoma insitu on histology. (A) Dynamic study subtraction image (axial): *oval shaped mass-like lesion with irregular margin in the right breast, measuring ~ 10 mm in maximum diameter; **area of non-mass-like clumped linear enhancement in the inferolateral periareolar region of the right breast, extending posteriorly. (B) Contrast-enhanced T1-weighted image (sagittal): area of non-mass-like segmental enhancement in the posterior inferolateral region of the right breast, extending to the middle depth of the breast (arrow).

m² every 3 weeks for 6 months) was initiated, as well as physical and speech therapy.

OUTCOME AND FOLLOW-UP

No invasive carcinoma could be detected on histology. After 2 years of follow-up, there was no evidence of residual tumour on contrast-enhanced breast MRI and no clinical evidence of metastatic disease. The anti-Yo antibodies are currently undetectable. The patient is neurologically stable, but no significant improvement was achieved, with the patient currently remaining wheelchair-bound and dependent in activities of daily living.

DISCUSSION

Paraneoplastic cerebellar degeneration consists of a pancerebellar disorder of subacute onset that is often severely disabling.³⁻⁵ Although there have been reports describing improvement after immunotherapy,⁶⁻¹³ the neurological outcome is generally poor regardless of immunomodulatory or effective tumour treatment, with most patients remaining severely disabled. In contrast, improved survival was found in patients receiving efficacious tumour treatment,⁵ which reinforces the need for an accurate diagnosis of the underlying tumour. Paraneoplastic cerebellar degeneration associated with the onconeural anti-Yo antibody is most frequently associated with ovarian cancer, breast cancer and other gynaecological malignancies.³⁻⁵ Consequently, previous European guidelines on the management of PNS recommended a mammography and a pelvic CT scan, followed by FDG-PET scan if the initial evaluation was negative.¹⁴ Several authors have also suggested that surgical exploration and removal of the pelvic organs may be warranted when initial investigation fails to reveal a malignancy in these patients.^{3 10 14} However, this is an invasive procedure that should be avoided if no gynaecological malignancy can be clearly demonstrated, as the tumour could also be located elsewhere.

Taking our patient's onconeural antibody profile and family history into account, we considered the possibility of an occult breast carcinoma. Although PET and PET/CT scans with FDG have shown to improve tumour detection in patients with PNS,¹⁵⁻¹⁷ in relation to breast cancer several studies have demonstrated a variable sensitivity that

is influenced by tumour size and histology. In particular, false negative results can occur with small breast lesions and in situ carcinoma.¹⁸ In contrast, dynamic MRI of the breast has proven a highly sensitive technique in disclosing malignant tumours, including lesions <10 mm.^{19 20} In a recent study, breast MRI has furthermore demonstrated a sensitivity of 98% in the detection of high-grade DCIS, thus substantiating its role in the diagnosis of primary malignant breast lesions.²¹ In accordance to its higher sensitivity in the detection of breast cancer, breast MRI allowed the detection of DCIS in our patient, thus avoiding an invasive exploratory surgical procedure of the pelvis. The superiority of breast MRI in detecting breast malignancy has been recently recognised by a European Federation of Neurological Societies Task Force.²²

In conclusion, this case report demonstrates the advantage of including breast MRI in the routine investigation of female patients with PCD associated with anti-Yo antibodies. Such a targeted diagnostic approach may ultimately allow a more rapid detection of the underlying tumour, with obvious implications for prognosis.

Learning points

- ▶ PNS are rare immune-mediated complications of cancer that most commonly manifest before the detection of the underlying malignancy, thus constituting its first manifestation.
- ▶ The detection of the underlying tumour is crucial for prognosis, but this is often a challenging task.
- ▶ The type of onconeural antibodies is the most important factor in directing the investigation to specific organs.
- ▶ Paraneoplastic cerebellar degeneration should always be suspected in a female patient with subacute pancerebellar dysfunction.
- ▶ The most frequent underlying tumours in anti-Yo positive PCD are ovarian and breast cancer; in this context, breast MRI must always be considered first line investigation, along with transvaginal ultrasound and/or pelvic CT.

Competing interests None.

Patient consent Obtained.

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Please cite this article as follows (you will need to access the article online to obtain the date of publication).

Real R, Oliveira A, Nadais G, Loureiro J, Garrett MC. The role of breast MRI in the investigation of anti-Yo positive paraneoplastic cerebellar degeneration.

BMJ Case Reports 2012;10:1136/bcr.11.2011.5225, Published XXX

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