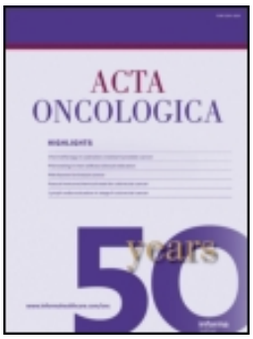

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LETTERS TO THE EDITOR

Papillary serous carcinomas of the uterine cervix and paraneoplastic cerebellar degeneration: A report of two cases

DEREK GERARD POWER[1], GERARD PAUL McVEY[2], DAVID WILLIAM DELANEY[3], DAVID REA[4], THOMAS D'ARCY[5], PETER AUGUSTINE DALY[1] & MICHAEL JOHN KENNEDY[1]

[1]*Academic Unit of Clinical and Molecular Oncology, St. James's Hospital, Dublin, Ireland,* [2]*Department of Radiation Oncology, St. James's Hospital, Dublin, Ireland,* [3]*Department of Pathology, St. James's Hospital, Dublin, Ireland,* [4]*Department of Radiology, St. James's Hospital, Dublin, Ireland,* [5]*Department of Gynaecology, St. James's Hospital, Dublin, Ireland*

To the Editor

Paraneoplastic cerebellar degeneration (PCD) is a debilitating neurodegenerative disease and is a rare complication of cancer. Its association with gynaecological malignancies is well described. Papillary serous carcinomas are aggressive neoplasms more commonly of ovarian and endometrial origin, but primary endocervical papillary serous carcinomas are recognised, and should be distinguished from metastases from common primary sites, though this is not always possible [1]. Endometrial serous carcinomas display a high incidence of abnormal p53 expression and a low incidence of PTEN mutations when compared to conventional endometrial carcinoma [2]. Similarly, many primary cervical papillary serous carcinomas exhibit abnormal p53 expression when compared to more conventional adenocarcinomas of cervical origin, which may account for the more aggressive nature of these tumours [1]. The two cases described here demonstrate the aggressive and unpredictable course of papillary serous carcinomas and a rare association with PCD.

A 59-year-old female presented with a two month history of post-menopausal bleeding and abdominal fullness, and was diagnosed with a bulky grade II papillary serous adenocarcinoma of the endometrial cervix (Figure 1A, B). Magnetic resonance imaging (MRI) showed parametrial extension, a left adnexal/ovarian mass and pelvic bone metastases (Figure 2A, B). The cancer antigen (CA) 12–5 level was 242 units (normal <34 units/ml). After six cycles of paclitaxel and carboplatin chemotherapy the CA 12–5 fell to 13 units/ml and radiology showed stable disease by response evaluation criteria in solid tumours (RECIST). A gynaecology opinion recommended an expectant approach. Progressive lower limb dysfunction developed leading to cerebellar ataxia and dysarthria six months from completion of chemotherapy and CA 12–5 rose to 141 units/ml. MRI brain showed marked cerebellar atrophy (Figure 3). Computed tomography (CT) scan showed enlargement of the adnexal mass and a reduction in the size of the cervical mass. Work up for this abnormal neurology included thyroid function tests, vitamin B12 levels, folate levels, serum protein electrophoresis, autoimmune screen and infectious screen, all of which were negative. The patient had never consumed alcohol and was a non-smoker. A lumbar puncture was attempted but was unsuccessful. Paraneoplastic anti-onconeruonal antibodies, including anti-Yo, anti-Ri, and anti-Hu were negative. Debulking surgery was performed and the histology confirmed our previous finding. Post-operative CA 12–5 fell to 36 units/ml, but rose to 132 units/ml within five months. Neurological symptoms worsened and radiology showed disease progression in bone. The patient died ten months after her initial uterine cervix carcinoma diagnosis.

The second case is that of a 64-year-old female who presented in a similar manner with a CA 12–5 of 2,580 units/ml. Optimal surgical debulking revealed a stage IIIc grade II moderately differentiated papillary serous adenocarcinoma of the uterine cervix. Intermittent chemotherapy with carboplatin alone and in combination with paclitaxel, as well as hormonal therapy, over two years

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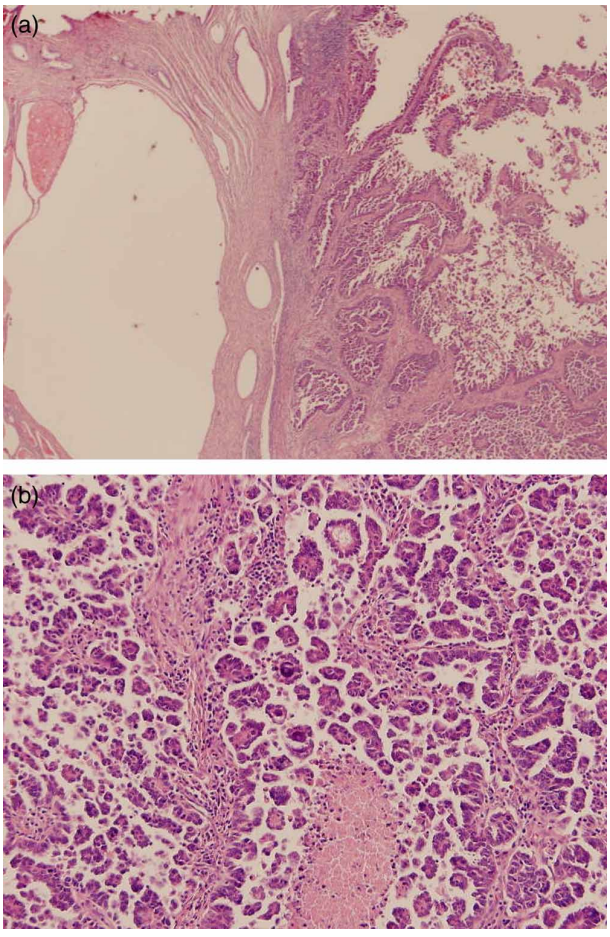

Figure 1. A – low power view of normal cervix on the left and endocervical adenocarcinoma on the right. B – papillary serous adenocarcinoma of uterine cervix with psamomma body formation.

ultimately resulted in a partial radiological response by RECIST and normalisation of CA 12–5. Four months later she presented with a two month history of slurred speech, ataxia, and inability to execute fine hand movements. On examination she had right gaze nystagmus, dysarthria, dysmetria, and hyporeflexia. Cognitive function, muscle tone and strength were well preserved. She had no clinical or radiological evidence of recurrence. MRI brain showed mild cerebellar atrophy. Work up was performed as in the first case, and was negative. Lumbar puncture showed a slightly raised protein level of 110 mg/dl (48–106 mg/dl), and a mild lymphocyte pleocytosis of 10×10^6 /ml ($6–23 \times 10^6$ /ml. Anti-onconeuronal antibodies were looked for in serum and cerebrospinal fluid but were not found. The patient underwent comprehensive rehabilitation, but six months later she deteriorated further and was referred to the palliative care services. She died three years following the diagnosis of PCD.

The majority of PCD cases associated with gynaecologic cancer cited in the literature have

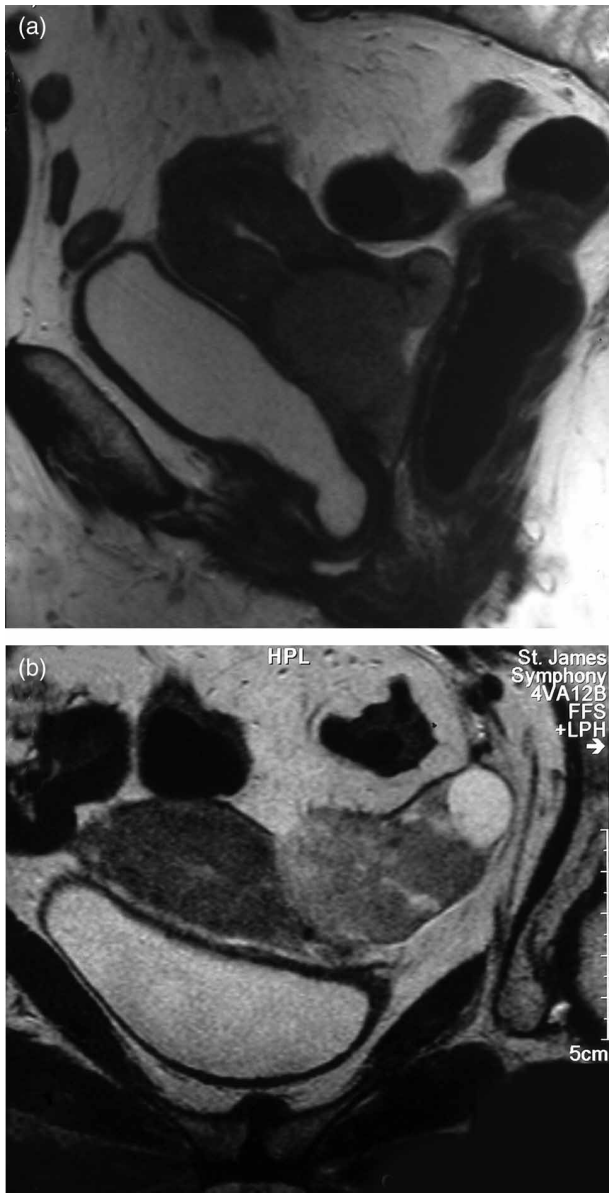

Figure 2. A – saggital T2-weighted pelvic MRI showing a mass in the lower third of the uterus relatively hyperintense to myometrium. B – saggital oblique T2-weighted sequence demonstrating a relatively hyperintense left adnexal mass medial to the left ovary.

ovarian adenocarcinoma with serous or endometrioid histology. We describe two cases of moderately differentiated papillary serous adenocarcinoma of the uterine cervix associated with antibody negative PCD diagnosed after an initial response to chemotherapy. PCD is a rare and unusual complication of cancer and accounts for about 10% of non-metastatic neurologic cancer-related complications [3]. Diagnosis can be difficult as presentation is varied and in over two-thirds of cases can precede the diagnosis of cancer [4]. PCD is a diagnosis of exclusion. Differential diagnoses include: leptomeningeal metastases, cerebrovascular disease, infec-

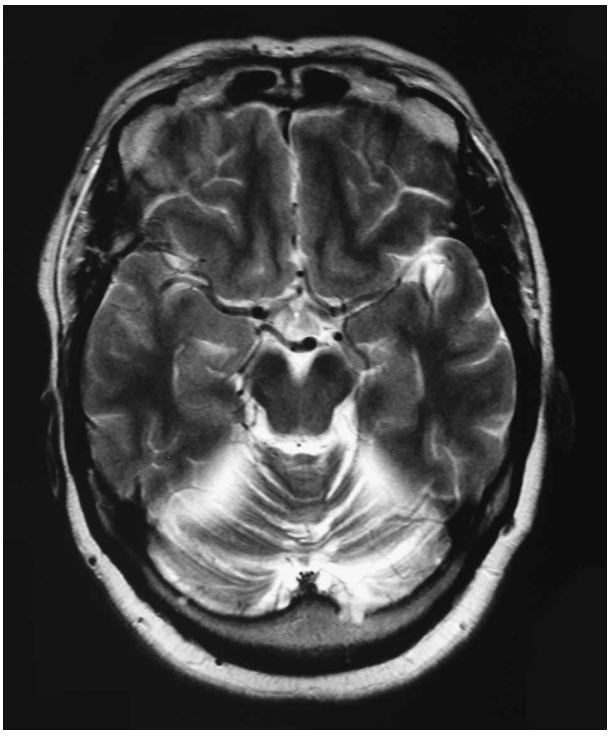

Figure 3. T2-weighted axial MRI-brain. CSF lies within the folia of the cerebellum secondary to parenchymal cerebellar loss.

tious causes, toxic causes (including alcohol and chemotherapeutic toxicity), demyelinating diseases, endocrine disorders or hereditary degeneration. Patients usually present in the sixth decade and there is a female preponderance [5].

PCD usually manifests as a rapid (hours to weeks) onset of pancerebellar dysfunction with associated truncal and appendicular ataxia, dysarthria, vertigo, nystagmus and diplopia. The syndrome can lead to profound disability, leaving many patients wheelchair bound and with unintelligible speech [6]. Pathological examination shows degeneration of Purkinje cells within the cerebellar cortex [7]. The CSF may be normal or have an elevated protein, a lymphocyte pleocytosis (usually T-cells), increased IgG, and oligoclonal banding. Specific anti-onconeuronal antibodies have been identified both in the CSF and in the sera of patients with PCD. A recent series shows that up to 77% of cases with paraneoplastic neurologic disease have positive anti-onconeuronal antibodies [5]. The anti-Yo auotoantibody can account for up to 50% of PCD patients and is associated almost exclusively (74%) with breast and pelvic cancers, i.e. ovarian and endometrial [6]. Anti-Yo is directed against cerebellar degeneration related (CDR) antigens expressed by Purkinje cells and cancer cells of patients with PCD. Such an immunological anti-tumour effect is said to explain the frequent finding of a low tumour burden in antibody positive PCD [7,8]. The frequency of anti-Yo in ovarian cancer patients is higher than the frequency of paraneoplastic syndromes, however it is not present in patients without cancer or with other forms of cerebellar disease and thus is a very specific marker for PCD [7,9]. Patients with PCD who do not have the anti-Yo antibody tend to have either lung cancer, breast cancer, or Hodgkin lymphoma, and tend to manifest neurological symptoms after the diagnosis of cancer. Lung cancer, usually small cell, is associated with the anti-Hu antibody. Breast cancer, and to a lesser extent small cell lung cancer is usually associated with the anti-Ri antibody, and Hodgkin lymphoma is associated with the anti-Tr antibody [6]. Thus, in a patient with neurological symptoms, detecting onconeuronal antibodies in serum or CSF can alert the physician to the possibility of an occult malignancy.

The treatment of PCD has been very disappointing. It has been estimated that up to 30% of PCD patients develop symptoms when the primary tumour is in remission. Thus treatment of cancer alone is not enough [10]. Only in small cell lung carcinomas has regression of cerebellar symptoms been reported after complete resection of tumour [11]. Immunologic therapy e.g. intravenous immunoglobulin, plasmapheresis, high dose steroids, and chemotherapies such as cyclophosphamide have all been tried, but with limited success [10,12]. Prompt recognition of neurological symptoms and institution of the above therapies seems to improve outcome in only a minority of cases. Recent reports using rituximab in antibody associated paraneoplastic neurological syndromes show some promise, but patient numbers are small and further studies are needed [13]. Proteasome antibodies and their association with anti-Yo antibodies is currently the focus of much research in PCD [14]. Reasons for such poor outcomes are unclear, however it does seem that there is a central production of autoantibodies that is unaffected by plasmapheresis, both cellular and humoral responses are involved, non-immune mechanisms play a role, and irreversible Purkinje cell death has occurred by the time neurological symptoms have developed [7]. Intense rehabilitation is vital to optimise the functional status of patients. Regular physiotherapy, speech therapy, and psychological support should be integral in the management of PCD [15].

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Clear cell sarcoma originating in a paraspinous tendon: Case report and literature review

RUSSELL GOLLARD[1], JERRY HUSSONG[2], JON BLEDSOE[3], LARRY ROSEN[4] & JOHN ANSON[5]

[1]*Cancer & Blood Specialists of Nevada, 58 N. Pecos Road, Henderson, Nevada, USA,* [2]*Laboratory Medicine Consultants, 3059 S. Maryland Pkwy., #100 Las Vegas, Nevada, USA,* [3]*Mayo Clinic-Department of Neurosurgery, 201 W. Center Street, Rochester, Minneapolis, USA,* [4]*Mike O'Callaghan Federal Hospital, 4700 Las Vegas Blvd. N., Nellis Air Force Base, Nevada, USA and* [5]*Western Regional Center for Brain & Spinal Surgery, 3061 S. Maryland Pkwy., Las Vegas, Nevada, USA*

To the Editor

Sarcomas are amongst the least common tumors clinical oncologists encounter; however even amongst soft tissue sarcomas, subsets requiring distinct treatment plans exist. Gastrointestinal stromal sarcomas (GIST) have undergone a revolutionary paradigm shift in treatment with the discovery of targeted kinase inhibitors; other less treatable soft tissue sarcomas also require distinct treatments, even as regimens continue to evolve [1]. Although clear cell sarcoma, being an uncommon entity, is not in the differential of common paraspinous tumors this rare presentation illustrates several important aspects of truncal sarcoma management for the practicing oncologist.

We report a rare paraspinous clear cell sarcoma. A 38-year-old African-American fireman was admitted to the hospital for severe pain beginning in the left subcostal region and radiating to the left upper quadrant. A magnetic resonance imaging (MRI) scan showed a paraspinous mass 2.0×5.0 cm in size (Figures 1 and 2)

Correspondence: Russell Gollard, Cancer & Blood Specialists of Nevada, 58 N. Pecos Road, Henderson, NV 89074, USA. Tel: +1 702 822 2000. E-mail: rgollard@hotmail.com

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