associated predominantly with hemangioblastomas of the central nervous system (HbI), angiomatosis retinæ (AR), renal cysts, renal cancer, pancreatic cysts, pheochromocytoma and epididymal cystadenoma. Since paraneoplastic production of erythropoietin (EPO) or of erythropoiesis stimulating factors has been described in cerebellar HbI, renal cancer, renal cysts, and pheochromocytoma, we investigated whether the serum EPO concentration is an indicator of HLS, which might facilitate an early diagnosis of affected individuals.

Our study included 44 patients (23 females, 21 males) with positive gene carrier status of HLS. Their mean age was 38.7 (16–79) years. Five of the patients had HbI, 25 had AR, two had renal cancer, three had renal cysts, seven had phaeochromocytomas; four had a history of surgical treatment for HbI, and 11 for pheochromocytoma. Fifteen subjects presented with multiple lesions. Three asymptomatic individuals were identified as gene carriers by pedigree analysis.

Serum for EPO radioimmunoassay was prepared from venous blood sampled without anticoagulant. The assay was carried out in duplicate using human urinary EPO standard, 125I-labelled recombinant human EPO (specific activity 11–33 TBq/mmol; Amer sham Buchler, Braunschweig, Germany) and antiserum (1:5000) from a rabbit immunised with human urinary EPO. The antibody-bound 125I-EPO was precipitated with polyethylene glycol 6000 (160 g/l). The mean within and between assay coefficients of variation were 7% and 19% in the EPO range 40–50 mU/ml. The detection limit was 5 mU/ml. Comparative measurements of immunoreactive EPO were performed on serum samples from 14 normal subjects (five females, nine males; age 20–38 years). Their EPO values were essentially normally distributed with a mean (1 SD) of 18.1 (7.5) mU/ml. Thus with the assay described, 95.5% of all normal values are in the range 3.1–33.1 mU/ml, mean (2 SD).

Serum EPO was elevated (>3.1 mU/ml) in two of five (40%) patients with HbI, in two of 25 (8%) with AR, in one of seven (14%) with pheochromocytoma, but in none of the patients with renal and pancreatic lesions. No significant correlation was found between elevated EPO values and serum haemoglobin concentrations. One patient with AR and one patient with a history of pheochromocytoma surgery presented with erythrocytosis (haemoglobin >180 g/l), but serum EPO was normal in both cases.

We conclude that EPO is not a suitable marker for identifying patients affected with HLS, either in asymptomatic or in symptomatic individuals, and subsequently does not support our recently published clinical screening programme.

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Application of gadolinium-DTPA magnetic resonance imaging for detection of a filum terminale myxopapillary ependymoma allowing successful surgical resection

Myxopapillary ependymomas of the spinal cord are histologically distinct low-grade gliomas which arise almost exclusively in the regions of the conus medullaris and filum terminale. Radiographic confirmation of these tumours has traditionally relied upon myelography and, more recently MRI. We report a further case that demonstrates the diagnostic value of Gadolinium-DTPA enhanced MRI.

A 41 year old male teacher of gymnastics presented with a one and a half year history of low back pain which radiated intermittently and alternatingly to the right and left buttocks and thighs, and was exacerbated by valsalva manoeuvres. He did not complain of focal motor weakness, sensory or sphincteric disturbances.

Physical examination of the patient’s lumbosacral region as well as his neurological examination were unremarkable. He had normal strength, sensation and rectal tone, as well as active and equal deep tendon reflexes throughout, with downgoing plantar reflexes and a normal gait. Leseuge’s test was negative bilaterally.

Plain radiographs and unenhanced CT scans of the entire lumbosacral spine were repeated at our institution and were unremarkable. Intravenous enhanced lumbosacral (L1–S1) CT also failed to show any intraspinal enhancing mass. Spin-echo

Figure (a) Spin echo pulse sequence, T1 (TR/TE = 600/20) and (b) T2 (TR/TE = 2500/80) weighted sagittal MRIs of the lumbar spine: the tumour was not apparent on T1, however, on T2 weighted image an intradural tumour extending from approximately mid L2 to the superior border of L3 could be seen. Note the signal intensity of the CSF below the mass which was brighter than the CSF above the tumour. (c) Post Gd-DTPA injection T1-weighted sagittal MRI of the lumbar spine: the location, margin and extent of the intradural tumour was readily identifiable due to the striking enhancement of the tumour. (d) Light microscopy of the tumour revealing papillary low columnar cells surrounding a central core of hyaline containing small vessels (Haematoxylin and Eosin ×40).

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sequence T1-weighted sagittal and axial MRIs (TR = 600 ms; TE = 20 ms, matrix size 256 × 256, scan thickness 5 mm) obtained from a GE 1.5 Tesla super conductive (Sigma) were non-specific and the tumour was not visualised, as the signal intensity of the mass was nearly isointense with the surrounding CSF (fig a).

The T2s (TR = 2500 ms; TE = 80 ms), however, revealed an intraspinral lesion which was outlined by the different signal intensities of the CSF above and below the tumour (fig b). The CSF was dominant intraspinally brighter with the CSF superior to the tumour. There were no discernible signal differences between tumour and CSF, cephalad to the tumour. Thus the entire margin of the tumour was not well delineated (fig b). Following the injection of IV Gd-DTPA, at the dose of 0.2 ml/kg (0-1 mmol/kg) the T1-weighted MRI showed marked enhancement of the tumour with its margins well delineated from the surrounding CSF (fig c). The tumour extended from the middle of L2 caudal to the upper border of L3 and measured 14 mm in the AP dimension of which 32 mm in height. It was an intradural extramedullary lesion. Ependymoma and neurofibroma were the major differential diagnoses.

An L1 through L4 lumbar laminectomy was performed exposing the dark-blush dura. The dura was opened and the encapsulated 5 × 1.5 cm bluish-brown tumour was easily identified. The CSF caudal to the tumour was xanthochromic and protein-aceous, and clear cephalad to the tumour. It arose from the filum terminale and invaded the conus medullaris. Sharp microscopic techniques were employed to resect the tumour completely. The filum terminale was amputated and a 1 mm ventrally located tumour feeding the artery was divided. The dura was closed in a watertight fashion. The patient made an uneventful recovery.

His neurological examination remained intact.

Light microscopic examination of the tumour using hematoxylin and eosin revealed papillary areas consisting of low columnar cells surrounding a central core of acellular hyaline and connective tissue containing small blood vessels (fig d). The architecture of the cells was orderly without mitoses and was consistent with the pathologic diagnosis of myxopapillary ependymoma. Gadolinium DTPA is a paramagnetic contrast material that decreases the relaxation time of T1 and T2 nuclei in tissues where it accumulates. T1 shortening increases the signal intensity of tissues, whereas T2 shortening decreases the signal. Fortunately, at lower concentrations, the T1 effect predominates. Like iodinated agents used for CT, Gd-DTPA serves as an indicator of blood-CSF barrier disruption for MRI. If this barrier is disrupted, the contrast molecules diffuse into the interstitial compartment producing T1 shortening and enhancement of T1-weighted images. Spin-echo pulse sequence T1-weighted images were not helpful in this case as the tumour and hypointense CSF had nearly similar signal intensities. Differences of signal intensity between the tumour and CSF on T2-weighted images allowed the visualisation of the CSF lesion. Brighter signals were observed from the CSF below the tumour secondary to its decreased flow, and increased protein content. Following Gd-DTPA injection, it was observed that the contrast agent entered the CSF and its margins were well delineated from the surrounding CSF and from the conus medullaris. Although its enhancing characteristic was not specific for either a neurofibroma or ependymoma, the true extent and location of the lesion was readily identifiable.

This case confirms a previous study documenting the superior imaging capacity of Gd-DTPA MRI compared with unenhanced T1 and T2 MRI in diagnosing spinal cord ependymomas\(^1\) and other hitherto radiologically elusive spinal cord lesions.\(^{2}\)

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Somatostatin receptors and the modulation of adenylyl cyclase activity in Alzheimer's disease

The most consistently reported neuropeptide dysfunction in Alzheimer's disease is that affecting somatostatin neurotransmission, as characterised by a loss of somatostatin-like immunoreactivity and decreased numbers of somatostatin receptor recognition sites.\(^3\) Such changes in the number of receptor recognition sites, however, give no information as to the functional integrity of the receptor in the disease state.\(^4\) A recent study on rat brain established that somatostatin modulation of neural function involves the inhibition of adenylyl cyclase activity by the occupation of receptor sites negatively coupled, via GTP-binding ("G")-proteins, to this enzyme.\(^5\) As a result, in our study, we have assessed the integrity of somatostatin receptor function in Alzheimer’s disease by assaying both the levels of receptor recognition sites and the ability of somatostatin to inhibit adenylyl cyclase activity.

Brains from a series of eight clinically diagnosed and histopathologically confirmed Alzheimer’s disease cases (mean SEM) age 81 (2) years, mean (SEM) post mortem delay 21 (8) hours and eight control subjects (mean age 75 (2) years, mean post mortem delay 23 (3) hours) were collected at necropsy. Tissue from the superior temporal cortex (Brodman area 22) was dissected, slowly frozen and stored at -70 °C. The procedure for the preparation of synaptic membranes. Adenylyl cyclase assays were performed on washed synaptic membrane fractions (10-15 μg protein) from each brain at 30 °C in assay buffer consisting of 80 mM Tris acetate (pH 7.4), 0.5 mM ATP, 10 μM GTP 1 mM theophylline, 0.3% BSA, 0.5 mM EGTA, 5 mM phosphatase, 30 unit units of phospholipase A2. The concentration of somato- statin-14 used (100 μM) was the same as that reported necessary to achieve inhibition of rat cortical membrane adenylyl cyclase.

Somatostatin receptors were determined using extensively washed and lysed membrane preparations (ca. 70 μg protein/assay) which were incubated for 60 minutes at 37 °C in 50 mM Tris HCl (pH 7.4) buffer containing 10 mM MgCl2, 1 mM BSA and 60 μg/ml bacitracin, with two different concentrations of [32P]-labeled somatostatin-14 (30 and 110 pM). Non-specific binding was defined using 1 μM unlabelled somatostatin-14. Incubations were terminated 10 minutes after trituration and tissue bound radioactivity determined following washing of the pellet.

In addition to these experiments, the effects of 10 μM neuropeptide Y-36 (NPY) on adenylyl cyclase activity were determined since this neuropeptide has also been shown to mediate inhibition of the enzyme.\(^6\) Such experiments were also considered important in view of the known co-localisation of somatostatin and NPY in some cortical neuronal sub-populations and the reported loss of NPY immunoreactive neurons in Alzheimer’s disease temporal cortex.

Basal adenylyl cyclase enzyme activities in the control and Alzheimer’s disease groups were not significantly different from each other (table). The large apparent difference (20%) between the control and Alzheimer’s disease group basal activities was due to a single control case showing high activity (138±2 pmol cAMP/min/mg protein).

<table>
<thead>
<tr>
<th>Table Somatostatin receptor function in Alzheimer’s disease</th>
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<tbody>
<tr>
<td><strong>Somatostatin binding</strong></td>
</tr>
<tr>
<td>[32P]-labeled somatostatin</td>
</tr>
<tr>
<td>30 pmol (100 pmol) somatostatin</td>
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<td>6 (2) (1)</td>
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**p < 0.05 compared to control.**

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