Cerebellar haemangioblastoma and genitourinary tumours

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SYNOPSIS In a series of 24 patients with cerebellar haemangioblastoma two subsequently developed renal carcinoma and one was found to have an epididymal tumour. The association between renal carcinoma and cerebellar haemangioblastoma is discussed. Repeated investigation of the genitourinary tract is advised in all cases of cerebellar haemangioblastoma to detect renal carcinoma before metastases have developed.

Lindau (1926) described an association between cerebellar haemangioblastoma and 'benign' tumours in several organs; retinal angiomas, adenomatous cysts of the pancreas, kidney, adrenal gland, and epididymis, and 'benign' renal hypernephroma. Since then, metastasizing renal carcinoma has been reported in cases of cerebellar haemangioblastoma with a positive family history of similar disorder (Olivecrona, 1952; Tønning *et al.*, 1952) but seldom in non-familial cases. Although Lindau (1926) referred to a single patient with an epididymal tumour, only three further cases appear to have been described (Melmon and Rosen, 1964).

Since 1965, 24 cases of cerebellar haemangioblastoma have been investigated in this Centre. Of these, one patient, with no family history of similar disorder, had three craniotomies for recurrent cerebellar haemangioblastoma and later developed renal carcinoma with pulmonary metastases. A second patient, with a positive family history of Lindau's syndrome, had a craniotomy for excision of a cerebellar haemangioblastoma and 20 years later developed a renal carcinoma which metastasized to the cerebellum, and a third patient, who had undergone excision of recurrent cerebellar haemangioblastoma, later developed an epididymal tumour.

CASE 1

D.B., a 47 year old man, presented to the Wessex Neurological Centre, Southampton, with a history of

headache, unsteadiness, and discomfort in the neck for three weeks. On examination, tenderness was detected in the right hypochondrium and renal angle, but no mass was palpated. Bilateral lateral gaze nystagmus and intention tremor were present and the gait was broad based with a tendency to fall to both sides. Postoperatively, an ophthalmologist demonstrated a small peripheral retinal angioma which was photocoagulated.

Seventeen years previously the patient had been admitted to the National Hospital for Nervous Diseases, Queen Square, London, complaining of headache and unsteadiness. Cerebellar signs were present on examination and ventriculography demonstrated a space-occupying lesion in the left cerebellar hemisphere. Posterior fossa craniotomy was performed and a cystic tumour was excised, which proved microscopically to be a typical haemangioblastoma.

For seven years he remained well but was readmitted to the National Hospital complaining of recurrent headache and unsteadiness. Cerebellar signs were detected and vertebral angiography revealed appearances indicating a second haemangioblastoma in the contralateral cerebellar hemisphere. An intravenous pyelogram was normal. A second tumour was removed from the right cerebellar hemisphere which again showed the histological structure of a haemangioblastoma. Postoperative progress was uneventful and he had remained asymptomatic for nine years until admission to the Wessex Neurological Centre.

Routine urinalysis and peripheral blood picture were normal and chest radiography showed normal lung fields. Vertebral angiography revealed four areas of pathological 'tumour staining' in the

FIG. 1. *Case 1. Cerebellar haemangioblastoma. Note resemblance to clear cell carcinoma of kidney but more prominent vascular component.*

FIG. 2. *Case 1. Typical clear cell renal carcinoma with acinar structure.*

posterior cranial fossa. At craniotomy six weeks later three separate cerebellar tumours were removed, two solid and one cystic, which were confirmed histologically to be typical haemangioblastomata (Fig. 1).

Five days postoperatively the patient developed pyrexia and a mass was palpated in the right hypochondrium. A chest radiograph, taken two months after the preoperative radiograph, demonstrated multiple nodules throughout both lung fields suggesting metastatic tumour deposits. Intravenous

pyelography and renal angiography demonstrated a mass in the right kidney. At right radical nephrectomy, through an abdominal incision, a tumour 7 × 6 cm was found in the centre of the kidney invading and extending along the right renal vein into the inferior vena cava. The pancreas appeared normal. Histological examination of the renal tumour and its extension into the vena cava showed the structure of a typical clear cell renal carcinoma (Fig. 2).

On medroxyprogesterone therapy the patient feels improved, has gained weight, and a follow-up

FIG. 3. Case 2. Family tree.

FIG. 4. Case 3. Papillary cystadenoma of the epididymis.

radiograph shows regression of the pulmonary metastases.

CASE 2

W.B., at the age of 27 years, had been admitted to the United Birmingham Hospitals for excision of a left-sided cerebellar haemangioblastoma. Eighteen years later he developed haematuria, and at Poole General Hospital a clear cell renal carcinoma was removed at left nephrectomy.

At the age of 47 years he was admitted to the Wessex Neurological Centre complaining of difficulty with speech and unsteadiness. He was dys-

arthric with lateral gaze nystagmus and ataxia. Vertebral angiography suggested a left cerebellar space occupying lesion. At craniotomy a tumour, with microscopical appearances of renal carcinoma, was removed from the left cerebellar hemisphere. He died one month postoperatively and no postmortem examination was performed.

The patient's father, three brothers, a sister, and a niece have all undergone excision of cerebellar haemangioblastomata (Fig. 3).

CASE 3

N.A., at the age of 17 years, had been admitted to

Atkinson Morley's Hospital, Wimbledon, where at craniotomy a left cerebellar haemangioblastoma was excised.

When aged 26 years he was admitted to Poole General Hospital complaining of testicular pain. On examination the left testis and epididymis were enlarged and tender. At operation to exclude torsion of the testis two cystic nodules were found in the head of the epididymis which microscopy showed to be papillary cystadenomata of the epididymis (Fig. 4). An intravenous pyelogram was normal.

Four years later he was admitted to the Wessex Neurological Centre complaining of headache and unsteadiness. On examination nystagmus, ataxia, and incoordination of the left arm were detected. Vertebral angiography suggested a left cerebellar space occupying lesion and a tumour was excised at craniotomy which had the microscopical appearances of a haemangioblastoma. The patient has since remained asymptomatic, and there has been no family history of similar disorder.

DISCUSSION

In 1926 Lindau reported six patients with cerebellar haemangioblastoma and hypernephroma which he stated caused no symptoms in life being 'of a benign hypernephroid type' (Lindau, 1931). Metastasizing renal carcinoma in these patients was reported by Kernohan *et al.* in 1931, and there have been further reports, particularly in familial cases. Tonning *et al.* (1952) described a 35 year old woman with cerebellar haemangioblastoma who, at necropsy, was found to have renal carcinoma with pulmonary metastases. Her brother and sister had both developed cerebellar haemangioblastoma and her mother had died of an unverified brain tumour. A similar familial case was described by Olivecrona (1952) and further family studies (Melmon and Rosen, 1964; Christoferson *et al.*, 1961) have reported renal carcinoma in their kindred. Renal carcinomata in two women with Lindau's syndrome were described by Greene and Rosenthal (1951) and Kaplan *et al.* (1961) but no mention was made of the family histories, as in a possible further case reported by Stein *et al.* (1960). Lindau (1931) estimated a family history to be present in 20% of cases, and the literature suggests a higher incidence of renal carcinoma in patients with a family history of similar disorder. Case 1 appears to represent a nonfamilial form of Lindau's syndrome in

association with a renal carcinoma. A retinal angioma was detected and haemangioblastomata were excised from different parts of the cerebellum; this recurrent tendency is characteristic (Olivecrona, 1952). Case 2 was familial and developed a renal carcinoma, and case 3, though nonfamilial, is at risk, and also illustrates the little recognized occurrence of adenoma of the epididymis in these patients (Lindau, 1926; Melmon and Rosen, 1964).

These cases support the recommendation for renal angiography in Lindau's syndrome (Melmon and Rosen, 1964) and repeated intravenous pyelography (Isaac *et al.*, 1956) in patients with cerebellar haemangioblastoma to detect renal carcinoma before metastases have developed. The cerebellar lesion is histologically benign and potentially resectable, but the renal lesion may be malignant and presents an additional threat to the lives of these patients.

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