

# Malignant glioma in laboratory workers

G N Rutty, M Honavar, B Doshi

## Abstract

**In 1989 an increased risk of cancer, with a higher than expected incidence of brain tumours, was reported in laboratory workers at the Pasteur Institute, Paris. Three cases of primary brain tumours occurring in three laboratory workers from one laboratory in a district general hospital also came to light. Although this may have been due to coincidence or geographic clustering, the need for stringent safety standards in all laboratories is reiterated, and it is proposed that a national register should be established to record the causes of death in laboratory workers.**

The reported incidence of intracranial malignant gliomas ranges from 3.8 per 100 000 to 16 per 100 000, but precise data are not easily available, in contrast to malignant tumours in general.<sup>1</sup>

The aetiology of brain tumours is also poorly understood. Experimental studies show that carcinogenic hydrocarbons and N-Nitroso compounds are absorbed from their site of application and have a role in cerebral tumours. Epidemiological evidence of an occupational risk of cerebral tumours has been reported in rubber workers, chemists, vinyl chloride and petrochemical workers.<sup>2</sup>

An increased risk of cancer among laboratory workers under the age of 50 involved in biomedical research, with a higher than expected incidence of brain tumours, has been reported at the Pasteur Institute, Paris.<sup>3,4</sup> We report the details of three technicians who worked in the same laboratory between 1979-1989 at a district general hospital in the South East of England and who died as a result of primary brain tumours.

## Case reports

### CASE 1

A 52 year old female laboratory technician had worked in biochemistry from 1982 to 1986. She presented in December 1986 with a short history of increasing confusion, dysphasia, worsening headaches and inability to cope. A computed tomography brain scan showed a hyperdense, enhancing, well defined tumour in the midline, extending to the medial side of the left frontal region, with pronounced oedema of the surrounding cortex.

Preoperative smears showed high grade malignant glioma, probably glioblastoma. This was confirmed on paraffin wax sections

which showed glioblastoma multiforme containing multinucleated giant cells, giant nuclei, perivascular pseudo-rosetting by tumour cells, areas of necrosis, endothelial proliferation and occasional mitoses. Immunohistochemical examination was performed using the avidin-biotin peroxidase complex (ABC) method, with rabbit anti-cow glial fibrillary acid protein (GFAP; Dakopatts). The cytoplasm of many of the tumour cells was strongly positive. The patient died within six months.

### CASE 2

A 22 year old female laboratory technician, who worked in haematology from 1983 to 1987, presented in February 1987 with a six month history of increasing headache, nausea and vomiting, diplopia and episodes of visual blurring. A computed tomogram showed a large mass of mixed density, enhancing with contrast, occupying almost all of the right frontal lobe and extending posteriorly.

A right frontal lobectomy was performed and histological examination showed an anaplastic astrocytoma (figure). The tumour cells showed nuclear pleomorphism and abundant mitoses. Mild endothelial cell proliferation was present, but there was no necrosis. The patient died shortly afterwards (the exact date is not known).

### CASE 3

A 43 year old male laboratory technician, who worked in haematology from 1979 to 1989, presented in November 1988 with a major seizure. An initial computed tomography brain scan was normal. He was readmitted in March 1989 following increasing right frontal headaches, impairment of memory and concentration, speech difficulties, confusion, increasing drowsiness and hiccups.

A repeat scan showed a very large, irregular, partly cystic mass in the right temporal-parietal region that was associated with severe oedema and shift of midline structures to the left.

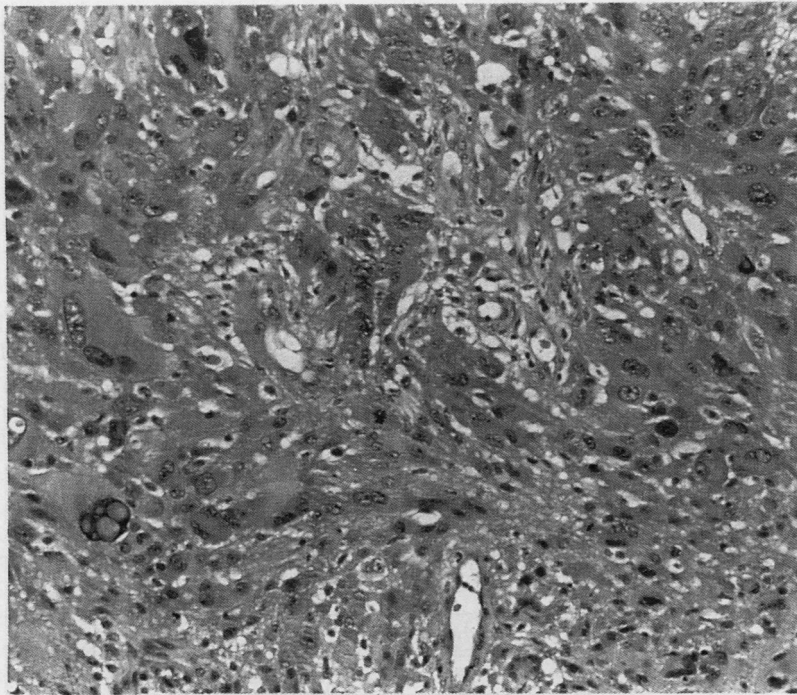
A craniotomy with debulking was performed and histological assessment of the tumour showed a moderately cellular, high grade malignant astrocytoma (grade III) containing many gemistocytic astrocytes, patchy endothelial proliferation, and small areas of necrosis. Nuclear pleomorphism was present but mitoses were scanty. The patient died in February 1990.

Department of  
Neuropathology,  
Brook General  
Hospital,  
London SE18 4LW  
G N Rutty  
B Doshi

Department of  
Neuropathology and  
Institute of  
Psychiatry, London  
M Honavar

Correspondence to:  
Dr G N Rutty, Department  
of Histopathology,  
Mount Vernon Hospital,  
Northwood, Middlesex  
HA6 2RN

Accepted for publication  
7 March 1991



*Glioblastoma multiforme showing highly pleomorphic cell nuclei, multinucleated tumour giant cells, endothelial proliferation with a fibrillary stroma (haematoxylin and eosin).*

### Discussion

Epidemiological data on primary brain tumours are scanty. In one such study Baker, using population adjusted figures, showed an excess of cases of grade 1–2 astrocytoma, but did not relate these to any specific occupation.<sup>5</sup> In the Public Health report of 1987 for our district, which has a total population of 219 000, the cause of death was recorded as stroke in 9.8% and cancer in 22.7%.<sup>6</sup> Primary brain tumour as a cause of death was not recorded.

It is essential to carry out well controlled epidemiological studies before associating brain tumours with a particular occupational group. Harrington *et al*, in a review of the cause of death in pathologists and laboratory scientists, found no excess mortality due to cerebral tumours in either occupational group.<sup>7</sup> This is in contrast to their subsequent paper, which documented a higher incidence of cerebral tumours in British pathologists.<sup>8</sup> Stroupe *et al*

also reported a higher incidence of brain tumours in American anatomists.<sup>9</sup> The cases documented in the Royal College of Pathologists register were histologically confirmed.<sup>7</sup> All our cases were also confirmed as high grade astrocytomas, both by histology and immunohistochemistry.

Carcinogenic and mutagenic properties of formaldehyde have been reported in animals, leading to speculation of their possible role in human carcinogenesis.<sup>10</sup> None of our patients worked in histopathology for any length of time and exposure to formaldehyde is not a prominent factor in their occupation. They would have been exposed, however, to blood, blood products, pathogens and various volatile substances.

Our observation may reflect genetic susceptibility, mere coincidence, or possible geographic clustering. As all three patients had worked in the same laboratory, we would like to emphasise that stringent safety standards must be maintained in all laboratories and that a national register to record cause of death in laboratory workers should be established.

We acknowledge with gratitude the help given to us by technical staff in Neuropathology, Brook General Hospital, and the Greenwich District Medical Photographic Department.

- 1 Russell DS, Rubinstein LJ. Incidence, pathogenesis and other general aspects. In: *Pathology of tumours of the nervous system*. Fifth Ed. London: Edward Arnold, 1989: 2.
- 2 Moss AR. Occupational exposure and brain tumours. *J Toxicol Environ Health* 1985;16:703–11.
- 3 Anonymous. Concern over deaths of Cancer Research Workers. [Editorial]. *Med Lab World* 1989;1.
- 4 Cordier S. Risk of cancer among laboratory workers. *Lancet* 1990;335:1097.
- 5 Barker DJ, Weller RO, Garfield JS. Epidemiology of primary tumours of the brain and spinal cord: A regional survey in southern England. *J Neurol Neurosurg Psychiatry* 1976;39:290–6.
- 6 Annual Report of the Director of Public Health. Dartford and Gravesham Health Authority, 1989.
- 7 Harrington JM, Shannon HS. Mortality study of pathologists and medical laboratory technicians. *Br Med J* 1975;i:329–32.
- 8 Harrington JM, Oakes D. Mortality study of British pathologists 1974–1980. *Br J Ind Med* 1984;41:188–91.
- 9 Stroupe EN, Blair A, Erikson GE. Brain cancer and other causes of death in anatomists. *JNCI* 1986;77:1217–23.
- 10 Soffritti M, Maltoni C, Maffei F, Biagi R. Formaldehyde: An experimental multipotential carcinogen. *Toxicol Ind Health* 1989;5:699–729.