Short report

Concordant cerebral oligodendroglioma in identical twins

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SUMMARY A case of concordant oligodendroglioma in monozygotic twins is reported. The twins were also concordant for uterine leiomyoma and one twin partner had fibroadenoma and lipoma of the breast and myelofibrosis. As very few cases of concordant glioma in monozygotic twins have been published and no such cases in dizygotic twins, a genetic influence in the aetiology of glioma can only be suggested.

Four histologically proven cases of concordant glioma in monozygotic twins have been published so far, amongst which there was no case of oligodendroglioma.¹⁻⁴ Study of concordant and discordant brain tumours may shed light on the contribution of genetic and non-genetic factors to the pathogenesis of these tumours. Therefore, we report on a twin pair concordant for oligodendroglioma and uterine leiomyoma.

Case histories

The female twins were born in 1928. The parents were healthy and non-consanguineous. At time of delivery paternal age was 36 years and maternal age 38 years. Data about placenta(s) and the composition of fetal membranes were not available. The twins were of identical resemblance from their early childhood till in their fifties. Both had blood-group A Rhesus factor positive and they were right handed. They were reared and lived together till 1952. The younger sister is hypermetropic and has concomitant convergent squint of the left eye. The family history was negative for hereditary diseases.

Twin A

This twin has had hypermetropia, convergent squint and amblyopia of the left eye from early childhood. She acquired pulmonary tuberculosis during the second world war, com-

plicated by abdominal tuberculosis at the age of 26. She remained without offspring. At the age of 38 a uterine leiomyoma was removed. The first symptoms suggesting brain pathology consisted of paresthesiae in the right arm and leg at the age of 56 years. No other neurological abnormalities were evident. There were no signs of phacomatoses. Cytogenetic analysis of peripheral lymphocytes showed a normal karyogram (46, XX). On computed tomography of the brain an irregular hypodense area was seen in the left parietal lobe. At craniotomy a slight bulging of the left parietal bone was apparent. Only partial removal of the tumour was possible. Histological examination showed it to be an oligodendroglioma, grade B² (figs a). Radiotherapy was given with a megavolt apparatus at a dose of 6120 cGy in 34 sessions in 49 days. Twelve months after surgery there are still no clinical or CT scan signs of tumour recurrence.

Twin B

She had had hypermetropia, convergent squint and amblyopia of the right eye from early childhood. She had 4 children one of whom had an ovarian cyst. At the age of 30 and 47 years she suffered from psychiatric disturbances which were explained by environmental circumstances. At the age of 38 a uterine leiomyoma was removed. The first unequivocal symptom pointing to brain pathology was an attack of vertigo after a sudden head movement at the age of 56 years. No neurological abnormalities or signs of phacomatoses were found. Computed tomography of the brain showed a hypodense mass with hyperdense spots in the right frontal lobe. At craniotomy frontal lobectomy was carried out for radical removal of the tumour. Histological examination revealed an oligodendroglioma, grade D⁵ (fig. b). Radiotherapy was given with a telecobalt apparatus at a dose of 5000 cGy in 20 sessions in 21 days.

Six months after surgery severe anaemia was discovered.

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Fig (a) Oligodendroglioma grade B in twin A; (b) oligodendroglioma grade D in twin B, with increased cellularity, endothelial hyperplasia, pleomorphism and necrosis (not shown). (H & E, × 165.)

Bone marrow biopsy indicated myelofibrosis. Cytogenetic analysis of bone marrow cells showed polyploidy in 6 out of 10 metaphases. One and a half years after surgery a minimal left sided hemiparesis was detected. CT scan revealed hydrocephalus without signs of tumour recurrence. A Hakim CSF drainage system was inserted. Nevertheless, progressive deterioration followed. She died 22 months after craniotomy. At necropsy no residual tumour was found. The right hemisphere was softened. Microscopy revealed radionecrosis. The bone marrow was hypoplastic without features of a myeloproliferative disorder.

Discussion

The identical resemblance of our twins and the mirror-imaging⁶ of tumour site and ophthalmological symptoms suggest monozygosity. Examination of their fetal membranes at birth had not been performed or remained unrecorded. Extensive comparison of bloodgroups and other marker genes was impossible because twin B had died in another hospital before onset of symptoms and admission of twin A. However, both twin partners had bloodgroup A, Rhesus factor positive, which is in accordance with presumed monozygosity.

The twins were concordant for oligodendroglioma and uterine leiomyoma, but discordant for fibroadenoma and lipoma of the breast and myelofibrosis. Concordance rate is defined as the percentage of twins of which both twin partners have the same disorder. Twin studies and in particular the comparison of concordance rates for certain diseases in monozygotic and dizygotic twins are usually considered as a powerful tool with which to assess the relative contribution of genetic and non-genetic factors.⁷ However, there are a number of theoretical objections against attaching too much value to twin studies and concordance rates.⁷⁻⁹ Concordance rates for gliomas in monozygotic or dizygotic twins are not available. There are only four published cases of concordant glioma in monozygotic twins (table). However, no such cases have been published in dizygotic twins. Because the numbers are small and based on uncontrolled case studies, these case reports only suggest a genetic influence. Evaluation of the literature concerning concordant cerebral tumours is difficult owing to the numerous and frequently changing classification systems. In this study we used the grading system of Smith *et al.*⁵ The report of Joughin⁴ (concordant glioma) lacks histological description. The case of Brady¹⁰ (concordant spongioblastoma) is not included in the table because of co-existing neurofibromatosis. Hereditary syndromes with tumour formation in the nervous system should be excluded in twin studies. To the best of our knowledge concordant oligodendroglioma of the brain in identical twins has not been reported before, but there are three reports of familial oligodendroglioma.¹¹⁻¹³ Although familial clustering of cases may suggest a genetic aetiological factor, the occurrence of a glioma in two or more members of one family may be coincidental depending on the frequency of the tumour in the population. In their extensive study of familial brain tumours Tijssen *et al*¹⁴ stated that up to now serial studies of twins did not support a genetic influence in the aetiology of gliomas. They concluded that many of these retrospective studies lack important data such as type of zygosity and proper

Table Proven cases of concordant gliomas in identical twins

Authors	Histological diagnosis	Age (yr)	Localisation
Joughin ⁴	Glioma	27	Left subcortical
	Glioma	32	Right temporal
Kjellin <i>et al</i> ²	Astrocytoma	33	Right temporal
	Astrocytoma	50	Right temporal
Fairburn and Ulrich ³	Mixed glioma	3	Brainstem, left cerebellar hemisphere
	Mixed glioma	7	Left frontoparietal
Clarenbach <i>et al</i> ¹	Subependymoma	22	4th ventricle
	Subependymoma	22	4th ventricle
Present case	Oligodendroglioma	56	Left parietal
	Oligodendroglioma	53	Right frontal

histological verification. In an earlier study¹⁵ an increased risk of developing a glioma in relatives of a glioma patient was indicated.

With respect to the associated disorders in our twins some facts are worth mentioning. Monozygotic female twins show a higher concordance rate for uterine leiomyomas.¹⁶ The twins and their sister had hypermetropia with squint and amblyopia. A higher concordance rate for squint in monozygotic twins,¹⁷ as well as familial clustering¹⁸ have been described. The discordance of our twins for tuberculosis is not in disagreement with their presumed monozygosity because the concordance rate for tuberculosis in monozygotic twins is estimated at 53%.⁷ The discordance for radionecrosis may be related to the different methods of radiotherapy applied in both cases and the short follow-up of twin A.

Our observation of concordant oligodendroglioma in a monozygotic twin pair suggests, as in other similar cases of concordant glioma, a genetic influence, although the number of reports is small. Accurate epidemiological studies may resolve the problem of nature and nurture.

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