A population-based study of the incidence and survival rates in patients with pilocytic astrocytoma

CHRISTOPH BURKHARD, M.D., PIER-LUIGI DI PATRE, M.D., DANIELLE SCHÜLER, GEORGES SCHÜLER, M.D., M. GAZI YAŞARGİL, M.D., YASUHIRO YONEKAWA, M.D., URS M. LÜTOLF, M.D., PAUL KLEHIUES, M.D., AND HIROKO OHGAKI, PH.D.

International Agency for Research on Cancer, Lyon, France; Department of Pathology, University Hospital, Geneva; Cancer Registry, Canton of Zürich; Departments of Neurosurgery and Radiology, University Hospital Zürich, Switzerland; and Department of Neurosurgery, College of Medicine, Little Rock, Arkansas

Object. The incidence of pilocytic astrocytomas and the rate of patient survival were analyzed in a population-based study in the canton of Zürich, Switzerland.

Methods. Between 1980 and 1994, 987 astrocytic and oligodendroglial tumors were diagnosed, of which 55 (5.5%) were pilocytic astrocytomas. The incidence rate, adjusted to the World Standard Population, was 4.8 per 1 million per year. The mean age at clinical diagnosis was 19.6 ± 12.7 years, and the male/female ratio was 1.12. The most frequent tumor sites were the cerebellum (40%), followed by supratentorial locations (35%), the optic pathway and hypothalamus (11%), and the brainstem (9%). The mean follow-up period was 12 years. Observed survival rates were 100% at 5 years and 95.8% at 10 years after diagnosis (relative survival rate at 10 years: 96.8%). Seven patients (13%) received postoperative radiotherapy, but this did not significantly affect survival. In all patients the tumors were histologically classified as WHO Grade I, except in two patients who had anaplastic pilocytic astrocytoma (Grade III), one of whom died after 7 years, whereas the other was still alive after 10 years.

Conclusions. This population-based study shows that, because of the benign biological behavior of pilocytic astrocytomas and advances in microneurosurgery, the survival rates for patients with these tumors are excellent, regardless of postoperative radiotherapy.

KEY WORDS • pilocytic astrocytoma • survival • tumor incidence • population-based study

Pilocytic astrocytoma is a circumscribed, benign, slow-growing lesion, and it is the most common glioma in children. Current knowledge of the incidence of pilocytic astrocytomas and patient survival is available in hospital-based studies, which may be subject to selection bias. We performed a population-based study of astrocytic and oligodendroglial brain tumors that had been diagnosed in inhabitants of the canton of Zürich (population ~ 1.16 million) between 1980 and 1994, regardless of patient age and tumor site. Patients were followed up until the end of 1999. In this report we present, on a population-based level, the incidence of pilocytic astrocytoma, patients’ survival rates, sex and age distribution, and the location of the tumors.

Clinical Material and Methods

Patient Population

The Cantonal Cancer Registry of Zürich actively collects information on cancer occurrence by using clinical and histopathological data and death certificates. We collected and evaluated data obtained in inhabitants who received diagnoses of astrocytic and oligodendroglial tumors between 1980 and 1994. The patients’ preoperative history was estimated on the basis of hospital records. The dates of clinical diagnosis were based on the dates of computerized tomography scanning or magnetic resonance imaging. The dates of the first operation and histological diagnosis were also noted for each patient. We were able to follow up on patients with pilocytic astrocytoma until the end of 1999 or until they died. Only two patients who emigrated from Switzerland were lost to follow up, one at 1.8 and one at 16.3 years after diagnosis. The original histological specimens were reevaluated according to the new WHO classification of tumors of the nervous system by two neuropathologists (P-L.D.P. and P.K.) who had access to patients’ clinical data.

All patients underwent microneurosurgery (performed by M.G.Y. and Y.Y.), usually at the Neurosurgery Department of the University Hospital of Zürich, which aimed at maximum tumor removal.

Statistical Methods

The canton of Zürich had a registered population of ap-
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approximately 1.12 million in 1980, 1.16 million in 1990, and 1.18 million in 1996. The 1990 population was selected as representative for the whole study period because its size and age distribution did not change significantly between 1980 and 1990. The mean annual incidence rate per 1 million population was age-adjusted to the World Standard Population, and was calculated using 5-year age groupings. The starting point for the survival analysis was the date of the histological tumor diagnosis, and the outcome of interest was death. Annual follow-up intervals were used. The estimation of expected survival rates (survival in population) was based on official life tables for Switzerland for the calendar periods of 1978 to 1983 and 1988 to 1993. Relative survival rates were calculated using the SURV2 program of the Finnish Cancer Registry (http://www.cancerregistry.fi/surv2/).

Results

Histological Review

In the period between 1980 and 1994, 987 cases of astrocytic and oligodendroglial tumors were detected in the canton of Zürich. Of these, 791 cases (80%) were diagnosed histopathologically, whereas 196 (20%) were only clinically diagnosed on magnetic resonance images or computerized tomography scans. Fifty-five tumors were diagnosed as pilocytic astrocytomas; 53 (96%) were classified as WHO Grade I and two (4%) as anaplastic pilocytic astrocytoma (WHO Grade III).

In 41 cases (75%), the original diagnosis of pilocytic astrocytoma was confirmed on histological review. Of the other 14 cases (25%), six were originally diagnosed as astrocytoma (fibrillary or not otherwise specified); four as anaplastic astrocytoma, two as oligoastrocytoma; and one each as subependymal giant-cell astrocytoma, or malignant juvenile small-cell glioma.

Incidence Rate

For the calendar period of 1980 to 1994, the incidence rate of pilocytic astrocytomas, age-adjusted to the World Standard Population, was 4.8 per 1 million per year (3.8 if adjusted to the European Standard Population). The incidence of pilocytic astrocytomas in children (< 15 years old) for the whole calendar period of 1980 to 1994, when age-adjusted to both the World and European Standard Population, was 8.3 per 1 million per year.

Pilocytic astrocytomas accounted for 5.5% of all oligodendroglial and astrocytic tumors including glioblastomas, and represented 6.6% of all astrocytomas. Overall, pilocytic astrocytomas represented 20 (2.8%) of 722 cerebral and 23 (92%) of 25 cerebellar astrocytomas. Pilocytic astrocytomas in children accounted for 21 (62%) of 34 astrocytomas in this age group.

Three patients with pilocytic astrocytoma (5.5%) suffered from neurofibromatosis Type 1, and one case (1.8%) occurred in the setting of tuberculous sclerosis; in the other patients there was no evidence of an inherited tumor syndrome.

Sex and Age Distribution

Male and female patients were similarly affected (29 males compared with 26 females), with a male/female ratio of 1.12. The patients’ age at diagnosis ranged from 2 to 49 years. The mean age at histological diagnosis of pilocytic astrocytoma was 19.6 ± 12.7 years (mean ± standard deviation). The age distribution was similar for both sexes: 21 patients (38%) were children (< 15 years old), 12 (22%) were adolescents (15–19 years old), and 22 (40%) were adults (≥ 20 years old).

Localization of Tumors

Pilocytic astrocytomas developed most frequently in the cerebellum (23 tumors, 42%) and supratentorial structures (20 tumors, 36%). Other, less frequent localizations were the brainstem (five cases, 9%), the optic pathway and hypothalamus (five cases, 9%), and the spinal cord (one case, 2%). In one tumor the location was unknown.

Correlation Between Patient Age and Tumor Localization

The cerebellum was the most frequent tumor site in children (14 [67%] of 21 cases); only two lesions developed in supratentorial structures (two [9.5%] of 21 cases; p = 0.0003). In patients older than 35 years of age, there was no significant difference between cerebellar and supratentorial location (55 compared with 33%, p = 0.6372). In no patient younger than 12 years of age did a pilocytic astrocytoma develop supratentorially (Fig. 1).

Preoperative History

The preoperative history was assessed in all but one case. In more than 70% of patients, the time from clinical to histological diagnosis was less than 1 month. In 50% of patients the preoperative history was less than 4.9 months (range 0.4–125 months), and was significantly longer in patients with supratentorial pilocytic astrocytomas (median 1171
Patients with pilocytic astrocytoma died within 10 years of diagnosis. Only two patients with pilocytic astrocytoma compared with low-grade astrocytoma and glioblastoma from the same population-based study. The mean follow-up period for patients with pilocytic astrocytoma does not generally include adjuvant radio- or chemotherapy. Of the 55 patients in this study, seven (13%) underwent postoperative radiotherapy. The total applied dose (2 Gy/fraction, five fractions/week) was 20 Gy (one case) or 60 Gy (six cases). In these patients, the initial diagnoses were malignant juvenile small-cell glioma (one case), anaplastic astrocytoma (one case), and anaplastic (pilocytic) astrocytoma (two cases). In the other three patients pilocytic astrocytomas were diagnosed. One of these was located in the pineal region, and was tentatively diagnosed as a germinoma and preoperatively irradiated; the second case occurred in a patient with neurofibromatosis Type I. In the third case, the reason for adjuvant radiotherapy remained unclear.

Five patients (9%) underwent a second operation because of tumor recurrences 1 to 12 years after the first intervention. In all cases, the diagnosis was again that of a pilocytic astrocytoma. In no patient did the lesion progress from pilocytic astrocytoma (WHO Grade I) to anaplastic pilocytic astrocytoma (WHO Grade III).

Survival of Patients With Pilocytic Astrocytoma

The mean follow-up period for patients with pilocytic astrocytoma was 12 years (range 1.8–20.5 years). Only two patients died before the end of 1999, 6 and 7 years after their diagnosis. For both of these, the cause of death is not known; one tumor was diagnosed as anaplastic pilocytic astrocytoma and was treated with radiotherapy after the first biopsy, and the other was a pilocytic astrocytoma (Grade I) with no record of radiation treatment. The cumulative observed survival rate was 100% at 5 years and 95.8% at 10 years (relative survival at 10 years: 96.8%). The Kaplan–Meier plot (Fig. 2) compares the survival rate in patients with these tumors with those for low-grade astrocytomas (WHO Grade II) and Grade IV glioblastomas diagnosed in the canton of Zürich during the same period, 1980 to 1994 (unpublished results).

Discussion

In this study, we determined the incidence rate of pilocytic astrocytomas as 4.8 per 1 million per year (age-adjusted to the World Standard Population) in the canton of Zürich, Switzerland. This rate is higher than the value of 2.9 recorded in the CBTRUS for the period 1992 to 1997, adjusted to the World Standard Population (2.3 if adjusted to the 2000 US standard population). Whether this reflects a significant difference in incidence between the US and Switzerland/Europe remains to be seen. To some extent, the histological review of more than 80% of gliomas registered in the canton of Zürich during the period from 1980 to 1994 may be responsible, because approximately 20% of cases were added after histological review.

The fraction of brain tumors diagnosed as pilocytic astrocytomas varies considerably, possibly because of a selection bias and the application of different clinical and histopathological criteria. In the present study, pilocytic astrocytomas represent 6.6% of all astrocytomas (3% of cerebral and 92% of cerebellar astrocytomas) in all age groups, and 62% of all astrocytomas in children.

According to data from the CBTRUS, pilocytic astrocytomas amounted to 1.9% of all CNS tumors in all age groups in the US between 1970 and 2000. Similar data were shown based on 3221 CNS tumors from the files of 13 pathology institutes in Korea between 1997 and 1998 by Suh, et al.,26 who reported that pilocytic astrocytomas amounted to 2.1% of all CNS tumors in all age groups. In the study by Suh, et al., pilocytic astrocytomas comprised 6.5% of all CNS tumors in children and 11.4% of astrocytic brain tumors in all age groups. Of 3268 brain tumors registered in the German Childhood Cancer Registry, pilocytic astrocytomas amounted to approximately 15% of all CNS tumors and 38% of all astrocytic brain tumors in children.15 Rickert and Paulus23 surveyed brain tumors in children diagnosed at the Institute of Neuropathology in Münster, Germany, between 1984 and 2000 and performed a metaanalysis of 15 additional international investigations in patients 15 to younger than 20 years of age. Astrocytomas were the most common entity throughout childhood and adolescence (47% of all lesions), with pilocytic astrocytomas accounting for 24% of all pediatric CNS tumors. Of 1014 glioma cases entered in the Tohoku Brain Tumor Registry in Japan between 1979 and 1990, 41 (4%) were pilocytic astrocytomas.16

Hospital-based studies may be biased toward more easily surgically accessible tumor sites. In this population-based study we show that in all age groups combined, the cerebellum (43%) and supratentorial structures (37%) excluding the optic pathway and hypothalamus were affected at a similar frequency. There appears to be a significant age factor, however. Our study shows that the majority of pilocytic astrocytomas in children were located in the cerebellum (67%), whereas those in adults most frequently involved supratentorial structures (55%). In two hospital-based studies derived from the Mayo Clinic Tissue Registry in Rochester, Minnesota, during the period between 1960 and 1984,13,14 the majority of pilocytic astrocytomas (105 cases,
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67%) were located in the cerebellum, and only 51 cases (33%) were observed in supratentorial locations.

Epidemiological data from the US for 1992 to 1997 show a mean age of 17 years at diagnosis in patients with pilocytic astrocytoma, a value somewhat lower than the mean age of 19.6 years observed in our study. Clark, et al. reported a mean age of 22 years at onset in 30 patients diagnosed between 1970 and 1980 at the Armed Forces Institute of Pathology in Washington, D.C.; this higher value is likely due to the fact that the study focused on pilocytic astrocytomas in the cerebral, that is, supratentorial location.

Pilocytic astrocytoma is histologically characterized by a biphasic tissue pattern with varying proportions of compact bipolar cells with Rosenthal fibers and loose-textured multipolar cells with microcysts and granular bodies. Although classified as WHO Grade I, pilocytic astrocytoma may occasionally show microvascular proliferation and even foci of necrosis that, in contrast to diffuse astrocytomas, are not signs of malignancy. We note that a significant fraction of pilocytic astrocytomas in our case collection, particularly those from the early 1980s, were initially misclassified, most frequently as low-grade astrocytoma or anaplastic astrocytoma, stressing the importance of accurate histological diagnosis to avoid overtreatment of this benign neoplasm. As shown in previous observations, there was no case in the present study that progressed from pilocytic astrocytoma (WHO Grade I) to anaplastic pilocytic astrocytoma (WHO Grade III), indicating that malignant progression is a very rare event.

Patients with pilocytic astrocytomas have an excellent overall survival rate. Hayostek, et al. analyzed 105 cerebellar pilocytic astrocytomas from the files of the Mayo Clinic Tissue Registry obtained between 1960 and 1984, and showed that survival rates for up to 5, 10, and 20 years were 85, 81, and 79%, respectively. Forsyth, et al. analyzed 51 supratentorial pilocytic astrocytomas diagnosed in the same calendar period and based on the same registry and found that survival rates for 10 and 20 years were 82%. Morreale, et al. reported on 54 cerebellar astrocytomas treated at the Mayo Clinic in Rochester, Minnesota, between 1978 and 1990. Of these, 39 (72%) were pilocytic astrocytomas. The survival rate of patients with pilocytic astrocytomas was 88% at 5 years and 50% at 10 years when residual tumor tissue was observed on postoperative imaging after the first operation. In contrast, a 100% 10-year survival rate was reported after resection without identifiable residual tumor tissue. Forty-one patients with pilocytic astrocytomas recorded in the Tohoku Brain Tumor Registry in Japan between 1979 and 1990 had survival rates of 98% at 2 years and 95% at 10 years. Pencalet, et al. conducted a retrospective review of 168 children who were surgically treated for cerebellar astrocytoma in the Hospital Necker-Enfants Malades in Paris between 1955 and 1995. Of these tumors, 93.5% were pilocytic astrocytomas. Based on a mean follow up of 7.7 years, the survival rate was 96%. Shaw, et al. analyzed a total of 196 low-grade gliomas and showed that 85% of patients with pilocytic astrocytoma survived for 5 years and 79% survived for 10 years.

One would expect population-based survival studies to show a somewhat less favorable prognosis than reports from specialized cancer centers. The CBTRUS data appear to confirm this, with relative survival rates for pilocytic astrocytomas of 91.4% at 2 years, 87.6% at 5 years, and 84.3% at 10 years. Our study shows the best survival rates reported to date, 100% at 5 years and 96.8% at 10 years after diagnosis. This favorable outcome may reflect the fact that in the canton of Zürich, virtually all patients were treated using microneurosurgery in a single, highly specialized University Medical Center.

Pilocytic astrocytomas are treated surgically, and gross-total resection carries the most favorable prognosis. If complete resection is not possible, adjuvant radiation therapy is applied in some centers. Because radiation may cause serious side effects, especially in the developing brain, its use is commonly restricted to treatment of optic, diencephalic, and brainstem lesions. Although some studies showed a beneficial effect of radiation in patients with pilocytic astrocytoma, others showed no effect on survival. Our study strongly supports the view that postsurgery adjuvant therapy is unnecessary, because in our study, in which there was a 100% 5-year survival rate, only seven (13%) of 55 patients received postoperative radiotherapy.

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Address reprint requests to: Hiroko Ohgaki, Ph.D., Unit of Molecular Pathology, International Agency for Research on Cancer, 150 cours Albert Thomas, 69372 Lyon Cedex 08, France. email:ohgaki @iarc.fr.