

Oligodendrogliomas A report of 35 cases

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Abstract

Introduction: Oligodendrogliomas are not common intracranial neoplasms. We retrospectively reviewed all of the gliomas operated in Ghaem Hospital between the years 1981 and 2000 and found only 35 cases of oligodendrogliomas (7.6% of total gliomas). survival analyses were performed on possible prognostic factors including: patient age and sex, presence of seizure, site, size, side, and treatment(extent of surgical resection , radiation dose, chemotherapy).

Materials and Methods: Thirty-five patients with supratentorial oligodendrogliomas consisting of 27 males (77.1%) and 8 femals (22.9%) ranging in age from 4 to 68 years (mean age 36.9 years). Seizures were present in 20 patients (57%), headache in 20 patients (57%),vomiting and papilledema in 15 patients (43%), hemiparesis in 12 patients (34.3%).The surgical treatment of the 35 patients included gross total removal in ten patients (28.8%)and subtotal removal (including one patient who had only a biopsy) in 25 patients (71.2%). All patients had subtotal resection received postoperative radiation(median5000 rad), in patients whose tumors were progressed (ten patients) received further surgery and chemotherapy treatment were necessary.

Result:Thirty-five patients with supratentorial oligodendrogliomas underwent surgery plus postoperative radiation and chemotherapy between the years 1981-2000. The median survival time and the 5-10 and 15 year survival rates for these 35 patients were 5.6years,54%, 34%, and 24% .

Conclusion: Patients with pure oligodendrogliomas had better median survival time, approximately 5.6 years, respectively , compared with 3.2 years for those anaplastic oligodendrogliomas. The ten patients who underwent gross total resection of their tumors had a better median survival time compared with the 25 patients who had subtotal resection. Patients with partially resected lesions appeared to benefit from postoperative radiotherapy. The median survival period after subtotal tumor resection was better than patients without radiotherapy.

Keywords: Oligodendrogliomas, Glial tumors, Combined, Treatment Modality.

Introduction

The first description of an oligodendrogliomas was published in an historic classification of the glioma group by Bailey and Cushing in 1926 (1,2,3).

Pure oligodendrogliomas are uncommon gliomas and considered to be intermediate in grade between low-grade gliomas and

anaplastic astrocytomas (2).

They represent approximately 4-7% of all primary intracranial gliomas (Rubinstein 1972, Mork et al 1985) (4, 5).

Typically, they occur in middleaged adults who present with a severalyear history ofseizures,and are shomn by computerized tomography(CT) scan or magnetic resonance

image (MRI) to be supratentorial, frequently calcified mass lesions (6).

The following analysis is a retrospective review of our patients having pure oligodendrogliomas, seizures, and are shown by computerized mixed oligodendrogliomas and anaplastic oligodendrogliomas who received either surgery alone or surgery with postoperative radiation, and adjuvant chemotherapy between the years 1981 and 2000 in Ghaem Medical Center.

Material and Methods

All patients with supratentorial oligodendrogliomas, mixed oligodendrogliomas and anaplastic oligodendrogliomas operated on during a 20-years period (1981 through 2000) were identified from the files of the Ghaem Medical Center.

Patient population

Characteristics of patients were obtained from their charts. The 35 oligodendroglioma patients consisted of 27 males (77.1%) and 8 females (22.9%) (table 1) ranging in age from 4 to 68 years (median 36.9 years).

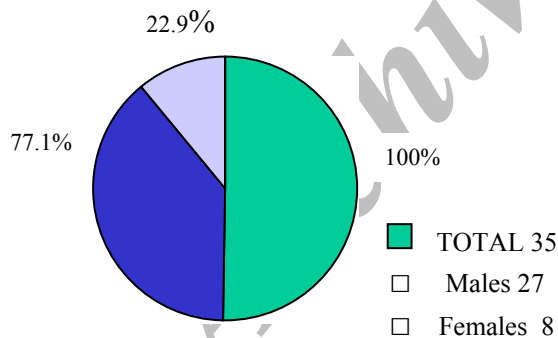


Chart 1: Patients with supratentorial oligodendrogliomas.

Seizures were present in 20 patients (57%), headache in 20 patients (57%), vomiting and papilledema in 15 patients (43%), hemiparesis in 12 patients (34.3%) (Chart 2).

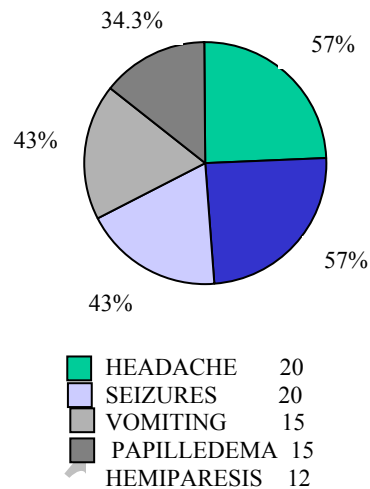


Chart 2: Symptoms and signs

Tumor characteristics including site, side, and size were identified from operative reports, and imaging data included plain skull x-ray films, CT scan and MRI.

The presence or absence of calcification was variably assessed on plain skull X-ray films, CT scans or histological sections.

The distribution of sites involved was as follows: Frontal lobe, 20 patients (57.12%); Temporal lobe, 8 patients (22.88%); Parietal lobe, 5 patients (14.3%); and multiple lobe, 2 patients (5.7%) (Chart 3).

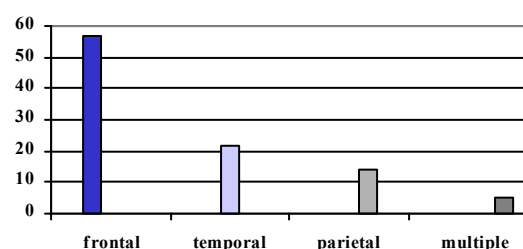


Table 3: Distribution of lobes involved

The right side left side in 19 patients (54.2%) (Chart 4).

Calcifications were present in 25 tumors (71.4%).

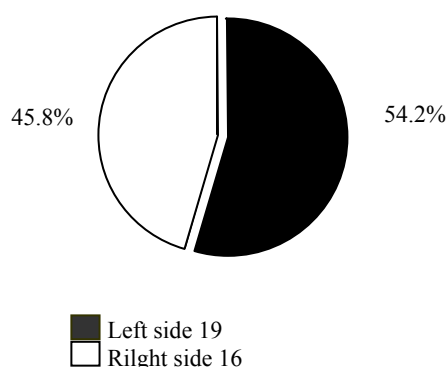


Table 4: Distribution of involved sides

Treatment

The extent of surgical resection was determined solely from information in the operative report. No consideration was given to postoperative imaging studies. The surgical treatment of the 35 patients included gross total removal in ten patients (28.8%) ; and subtotal removal (including one patient who had only a biopsy) in 25 patients (71.2%) All patients had subtotal resection , received postoperative radiation therapy (median 5000Rad). The median number of treatment, dose per fraction and treatment days were 25 treatments, and 200 Rad and 25 days, respectively. ten patients whose tumors were progressed received further surgery and chemotherapy treatment .

Result

At the time of the analysis 26 patients (74%) died. The median follow-up time for the nine patients who remained alive was seven years (range six months to twenty years).

The median survival time and the 5-10 and 15 year survival rates for these 35 patients were 5.6 years, 54%, 34% and 24%.Tumor progression was documented clinically, radiographically (by CT or MRI).

The median time to tumor progression was five years.The tumor recurred intracranially in fifteen patients whose disease progressed. Ten of the fifteen patients who had tumor

progression received further treatment (treated with surgery and chemotherapy).

Three of these patients died of further progression six months, nine months and two years later.

Discussion

The first description of an oligodendrogliomas was published in an historic classification of the glioma group by Bailey and Cushing in 1926 (1), and a later more complete description by Bailey and Bucy in 1929 (2,3).

Oligodendrogliomas (WHO grade 11) is a well-defferentiated diffusely infiltrating tumor composed of cells resembling normal oligodendroglial (7). Anaplastic (WHO grade 111malignant) or polymorph- ous Oligodendrogliomas extremely resemble glioblastomas(7,8) loss of heterozygosity of chromosome 1q,19q' and only rarely of 17p,characterize the molecular genetic of oligodendroglial tumors (7,9).

Oligodendrogliomas represent approximately 4-7% of all primary intracranial gliomas (Rubinstein 1972, Mork et al 1985), with occasional series reporting a higher incidence (10-15% Burger et al 1991; 18.8% Zulch 1986)(10).

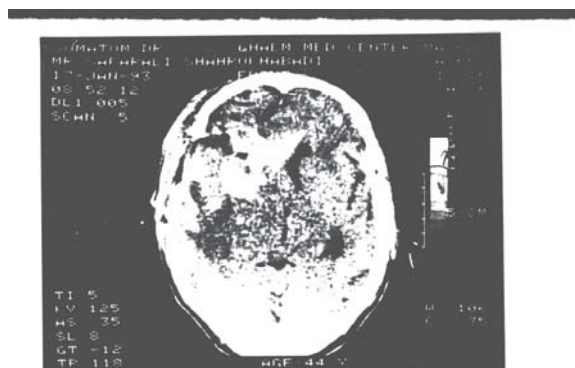
They represent the third most common gliomas following glioblastoma and astrocytoma (4). oligodendrogliomas are slow-growing tumors, current immunocytochemical (ICC) techniques have demonstrated that many tumors with the histologic appearance of astrocytoma will partially or completely lack staining for GFAP, and thus are now diagnosed as mixed oligoastrocytomas or oligodendrogliomas respectively. Thus, using these newer criteria the incidence of oligodendrogliomas has increased (6,8).

In our series oligodendrogliomas account for about 7.6 percent of intracranial gliomas. Rubinstein (1972) reported them to be equally distributed between the sexes although others reported a higher incidence in males (male: females 3:2,2:1) (5,8).

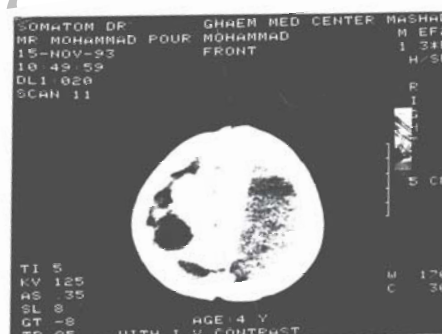
In our series there were 27 males and 8 females. They most frequently occurred in the third, fourth and fifth decades. There is a biphasic age distribution to the tumors, with two peak incidences at 6-12 years old and 26-46 years old (4). Oligodendrogliomas arise predominately in the white matter of cerebral hemispheres from which tumor cells usually extend into the overlying cortex (10). The adjacent leptomeninges may also be infiltrated, and have a slight predilection for the frontal lobes. Posterior fossa involvement is unusual, and spinal cord involvement is rare. Macroscopically and on neuroimaging oligodendrogliomas tend to appear circumscribed (7).

Patients with oligodendrogliomas have a long interval between the appearance of symptoms and diagnosis. The mean interval is about four years, and the range of means from various series is 28 to 70 months, in our series was 35-55 months. Seizure is the initial symptom in 50 percent of patients with oligodendrogliomas and about 10 percent of the tumors that cause seizures are oligodendrogliomas (11-14), in our series 20 patients (57%) had seizures. Elevations of intracranial pressure and focal neurological deficits are usually present by the time of diagnosis. In a combined series of over 600 patients, headache (80%), mental change (50%) and extreme weakness (45%) were the most commonly observed symptoms at presentation. Hemiparesis (50%), mental change (50%) and papilledema (50%) were the most commonly noted signs (15). In our series headache (57%), papilledema (43%) and hemiparesis were 34.3%.

The most characteristic findings on plain x-ray films and CT scans were the frequent occurrence of prominent, irregular clumps of calcification within the tumor mass in approximately 40 to 60 percent of patients oligodendrogliomas have a higher rate of calcification than classic astrocytoma (fig 1,2).



Non-Contrast Enhanced C.T Reveals a Densey Calcified Oligodendroglioma in L. F Lobe.



Contrast enhanced C.T reveals a densey Calcified oligodendrogliomas in L.P lobe

On computed tomography scan part of an oligodendrogliomas is usually isodense or hypodense.

This region may or may not enhance after contrast medium administration. Magnetic resonance imaging (MRI) demonstrates a tumor that is hypointense on T1-weighted images and hyperintense on T2-weighted images. Except for regions of signal void that correspond to fragments of calcium (9).

oligodendrogliomas may also have cystic and hemorrhagic areas, their density and signal-intensity characteristics may be heterogeneous. The proton spectroscopic maps of oligodendrogliomas show depressed NAA values. Lactate is usually absent (7). Craniotomy for attempted gross total resection is the preferred initial therapy (16,17).

The mortality rate associated with operative treatment has been less than 3 percent, and the morbidity rate less than 5 percent (2,16,18). In our series two patients (5.1%) died two months after operation. When oligodendrogliomas have anaplastic features or recur aggressively after initial resection, radiation therapy is indicated (18-21).

For pure anaplastic oligodendroglioma or mixed anaplastic oligostocytoma combined treatment (surgery, postoperative radiation therapy and adjuvant chemotherapy) was effective with acceptable toxicity (22,23). Both extensive resection and radiation therapy increase duration of survival. Gross total resection results in longer survival than does subtotal removal (5,14,24). Use of postoperative radiation therapy increased the 5 year survival rate from 31 percent to 85 percent, the 10 years survival rate from 25 percent to 55 percent, and the median duration of survival from 2.8 years to 8 years (25,26).

Prognostic factors in oligodendrogliomas are: age at surgery, extent of surgical resection, year of surgery, postoperative karnofsky score and MIB-1LI (Immunohistochemical parameters), MIB and PCNA labeling indexes [LIS] were associated with survival in both unit and multivariate analysis, so some clinical and therapeutic factors together with MIB-1 LI play a prognostic role (26). The number of cell in the deoxyribonucleic acid synthesis phase of the cell cycle is also predictive of outcome (27), fifty to seventy five percent of oligodendrogliomas are found to be more anaplastic at reoperation. About 15 percent of recurrent tumors are of the glioblastoma multiform type. The period of remission after treatment of recurrent tumor is often brief (9).

Conclusion

Oligodendrogliomas are not common intracranial neoplasms. The survival periods of patients like those with other infiltrative

gliomas are significantly shorter than expected, and are associated primarily with tumor grade. Selected patients who undergo gross total resection, particularly younger patients with low-grade tumors, may not require postoperative radiation therapy. All other patients appear to benefit from postoperative radiation therapy which significantly prolongs the median survival time but does not influence the cure rate in oligodendrogliomas patients with subtotal surgery.

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References

- 1- Bailey P, Cushing H. Classification of tumors of the glioma group on a histogenetic basis with a corresponding study of prognosis. Philadelphia: JB Lippincott; 1926.
- 2- Bailey P, Bucy PC. Oligodendrogliomas of the brain. J pathol-bacteriol 1929;32:735-751.
- 3- Balko MG, Blisad KS, Samaha FJ. Oligodendrogliomas gliomatosis cerebri. J Hum pathol 1992;23:706-709.
- 4- Kaye Andrew H, Laws Edward R. Brain tumors. London: Churchill Livingstone; 1997. p. 479-490.
- 5- Mork SJ, Lindegaard KF, Halvorsen TB et al. Oligodendrogliomas: Incidence and biological behavior in a defined population. J of Neurosurg 1985;63:881-889.
- 6- Ludwig CL, Smith MT, Godfrey AD et al. A clinicopathological study of 325 patient with oligodendrogliomas. Ann Neurol 1986;19:15-17.
- 7- Yumans H, Winn R. Neurological Surgery. Philadelphia: W.B. Saunders company; 2003. p. 453, 664, 698, 847, 952.
- 8- Schiffer D, Dutto A, Cavalla P, Bosone I, Chi OA, Villani R, Bellotti C. Prognostic factors in oligodendroglioma. J Neurol Sci Nov 1997; 24(4):313-319.

- 9- Youmans H, Julian R. Neurological Surgery. Philadelphia: W.B. Saunders Company; 1996. p. 2659-2663.
- 10- Tindall GT, Cooper PR, Barrow DL. The practice of Neurosurgery, Williams and Wilkins; 1996. p. 612-621.
- 11- Chin how, Hazel JJ, Kim TH et al. Oligodendrogliomas: A clinical study of cerebral oligodendrogliomas. Cancer 1980; 45:1458-1466.
- 12- Stenhou D. Plain radiography of the skull in the diagnosis of intracranial tumors. Br J Radiol 1948; 21:287-300.
- 13- Weir B, Elvidge AR. Oligodendrogliomas: An analysis of 63 cases. J Neurosurgery 1968; 22:500-505.
- 14- Rengachary W. Neurosurgery. 2nd ed. New York: McGraw-Hill; 1996. p. 763-768.
- 15- McKernan RO, Thomas DGT. The clinical study of gliomas. Brain tumors: Scientific basis, clinical investigation and current therapy. Boston: Butterworth; 1980. p. 194-230.
- 16- Cairncross J, Perrier NJ. Low-grade glioma. To treat or not to treat. Arch Neurology 1990; 46:1238-1239.
- 17- Kyritsis AP, Yung WK, Burner J, Gleason MJ, Levin M. The treatment of anaplastic Oligodendrogliomas and mixed gliomas. J of Neurosurgery 1993; 32:365-371.
- 18- Lindegaard KF, Mork SJ, Elde GE et al. Statistical analysis of clinicopathological features radiotherapy and survival in 170 cases of oligodendroglioma. J of Neurosurgery 1987; 61: 224-230.
- 19- Bullard DE, Rawlings CE, Philips B et al. Oligodendrogliomas: An analysis of the value of radiation therapy. Cancer 1987; 60: 2179-88.
- 20- Sheline GE, Boldrey E, Karlsberg et al. Therapeutic considerations in tumors affecting the central nervous system. Oligodendrogliomas Radiology 1964; 82: 84-89.
- 21- Wallner KE, Gonzales M, Sheline GE. The treatment of Oligodendrogliomas with or without postoperative irradiation. J of Neurosurgery 1988; 68:684-688.
- 22- Glass JG, Hocheberg FH, Gruber ML, Louis DN, Smith D, Rattner. The treatment of oligodendrogliomas and mixed oligodendrogliomas-astrocytomas with PCV chemotherapy. J of Neurosurgery 1992; 76: 741-745.
- 23- Jeremic B, Shibamoto Y, Grujicic D, Milicic B, Stojanovic M, Nikolic N, Dagovic A, Aleksandrovic J. Combined treatment modality for anaplastic oligodendrogliomas. A phase II study. Neuro Oncol 1999; 43(2):179-185.
- 24- Russel DS, Rubinstein LJ. Pathology of the tumors of the central nervous system, 5th ed. Baltimore: Williams and Wilkins; 1989. p. 1012.
- 25- Sheline GE. Radiation therapy of brain tumors. Cancer 1977; 39:873-881.
- 26- Sunzmn Gnkas, Shitarn N, Akanuma A, Takakura K. Factors possibly influencing the prognosis of Oligodendroglioma. Neurosurgery 1988; 22:886-891.
- 27- Coons SW, Johnson PC, Pearl DK et al. Prognostic significance of flow cytometry deoxyribonucleic acid analysis of human oligodendrogliomas. Neurosurgery 1994; 34: 680-687.

خلاصه

گزارش ۳۵ مورد اُلیگودندروگلیوما

دکتر علیرضا بیرجندی

مقدمه: اُلیگودندروگلیوما از تومورهای داخل جمجمه شایع نیستند. مطالعه گذشته نگر بر روی تمام گلیومهای مغزی عمل شده در بیمارستان قائم بین سال های (۲۰۰۰-۱۹۸۱، ۱۳۷۹-۱۳۶۰) انجام شده که ۳۵ مورد تومور اُلیگودندروگلیوما (۷/۶٪ تمام گلیومها) وجود داشته است. آنالیز بقاء روی فاکتورهای پیش آگهی احتمالی شامل سن بیمار، جنس، وجود تشنج، محل، اندازه و طرف ضایعه و درمان (میزان برداشت جراحی، دوز رادیوتراپی) انجام شده می باشد.

روش کار: ۳۵ بیمار با اُلیگودندروگلیوما بالای چادر مخچه تحت عمل جراحی، رادیوتراپی و کموتراپی بعد از عمل جراحی بین سال های ۱۹۸۱-۲۰۰۰ (۱۳۷۹-۱۳۶۰) قرار گرفته اند شامل ۲۷ مرد (۱/۷۷٪)، ۸ زن (۹/۲۲٪) و سن بیماران بین ۴ تا ۶۸ سال (میانگین سنی ۳۶/۹ سال) بودند. تشنج در ۲۰ بیمار (۵۷٪)، سردرد در ۲۰ بیمار (۵۷٪)، ادم پای در ۱۵ بیمار (۴۳٪) و ضعف نیمه بدن در ۱۲ بیمار (۳۴/۳) وجود داشته است. درمان جراحی در ۳۵ بیمار شامل برداشتن به ظاهر کامل تومور در ۱۰ بیمار (۲۸/۸٪) و به طور ناکامل (شامل یک بیمار که فقط بیوپسی شده) در ۲۵ بیمار (۷۱/۲٪) بوده است. تمام بیماران که به طور ناکامل تومور آن ها برداشته شده بعد از عمل جراحی رادیوتراپی (به طور متوسط ۵۰۰۰ راد) دریافت کرده اند در بیماران که تومور آن ها پیشرفت داشته (۱۰ بیمار) عمل جراحی مجدد و کموتراپی لازم داشته اند.

نتایج: ۳۵ بیمار با اُلیگودندروگلیوما بالای چادر مخچه تحت عمل جراحی همراه با رادیوتراپی و کموتراپی بین سال های ۱۹۸۱-۲۰۰۰ قرار گرفته اند متوسط زمان بقاء و میزان سال های بقاء ۱۵، ۱۰، ۵ سال برای ۳۵ بیمار ۵۴٪، ۳۴٪، ۲۴٪ برای ۵/۶ سال بوده است.

بحث و نتیجه گیری: بیماران با اُلیگودندروگلیوما خالص زمان بقاء متوسط در آن ها بهتر بوده تقریباً ۵/۶ سال در مقایسه با بیمارانی که اُلیگودندروگلیوما آناپلاستیک داشته اند ۳/۲ سال بوده است. بیمارانی که تحت عمل جراحی برداشتن به ظاهر کامل تومور قرار گرفته اند، در مقایسه با ۲۵ بیماری که برداشتن تومور آن ها به طور ناکامل بوده است، متوسط بقاء بهتری داشته اند. در بیمارانی که تومور آن ها به طور ناکامل برداشته شده به نظر می رسد رادیوتراپی بعد از عمل برای آن ها مفید می باشد.

واژه های کلیدی: اُلیگودندروگلیوما، تومورهای گلیال، چگونگی درمان های توم.