Oligodendroglioma outcome

Among diffuse gliomas, oligodendrogliomas show relatively better prognosis, respond well to radiotherapy and chemotherapy, and seldom progress to very aggressive tumors. To elucidate the genetic and epigenetic background for such behavior and tumor evolution during tumor relapse, Aihara et al., comparatively analyzed 12 pairs of primary and recurrent oligodendrogliomas with 1p/19q-codeletion. Initial treatment for these patients was mostly chemotherapy alone. Temozolomide was used for 3, and procarbazine, nimustine and vincristine (PAV chemotherapy) were used for 7 patients. World Health Organization histological grade at recurrence was mostly stable; it was increased in 2, the same in 9, and decreased in 1 cases. Whole-exome sequencing demonstrated that the rate of shared mutation between the primary and recurrent tumors was relatively low, ranging from 3.2-57.9% (average, 33.3%), indicating a branched evolutionary pattern. The trunk alterations that existed throughout the course were restricted to IDH1 mutation, 1p/19q-codeletion, and TERT promoter mutation, and mutation of the known candidate tumor suppressor genes CIC and FUBP1 were not consistently observed between primary and recurrent tumors. Multiple sampling from different regions within a tumor showed marked intratumoral heterogeneity. Notably, in general, the number of mutations was not significantly different after recurrence, remaining under 100, and no hypermutator phenotype was observed. FUBP1 mutation, loss of chr. 9p21, and TCF12 mutation were among a few recurrent de novo alterations that were found at recurrence, indicating that these events were clonally selected at recurrence but were not enough to enhance malignancy. Genome-wide methylation status, measured by Illumina 450 K arrays, was stable between recurrence and the primary tumor. In summary, although oligodendroglioma displays marked mutational heterogeneity, histological malignant transformation accompanying events such as considerable increase in mutation number and epigenetic profile change were not observed at recurrence, indicating that noticeable temporal and spatial genetic heterogeneity in oligodendrogliomas does not result in rapid tumor progression [1)].

Oligodendrogliomas are generally felt to be incurable using current treatments. However compared to the more common astrocytomas, they are slowly growing with prolonged survival. In one series, median survival times for oligodendrogliomas were 11.6 years for grade II and 3.5 years for grade III.

However, such figures can be misleading since they do not factor in the types of treatment nor the genetic signature of the tumors. A recent study analyzed survival based on chromosomal deletions and the effects of radiation or chemotherapy as treatment, with the following results (both low-grade and anaplastic oligodendrogliomas): 1p/19q deletion with radiation = 121 months (mean), 1p/19q deletion with chemotherapy = over 160 months (mean not yet reached), no 1p/19q deletion with radiation = 58 months (mean), and no 1p/19q deletion with chemotherapy = 75 months (mean).

Another study divided anaplastic oligodendrogliomas into the following four clinically relevant groups of histology with the following results: combined 1p/19q loss = median survival was >123 months (not yet reached), 1p loss only = median survival was 71 months, 1p intact with TP53 mutation = median survival 71 months, and 1p intact with no TP53 mutation = median survival was 16 months.

Because of the indolent nature of these tumors and the potential morbidity associated with neurosurgery, chemotherapy and radiation therapy, most neurooncologists will initially pursue a course of watchful waiting and treat patients symptomatically. Symptomatic treatment often includes the use of anticonvulsants for seizures and steroids for brain swelling. PCV chemotherapy (Procarbazine, CCNU and Vincristine) has been shown to be effective and was the most commonly

used chemotherapy regimen used for treating anaplastic oligodendrogliomas, but is now being superseded by a newer drug: Temozolomide. Temozolomide is a common chemotherapeutic drug to which oligodendrogliomas appear to be quite sensitive. It is often used as a first line therapy, especially because of its relatively mild side effects when compared to other chemotherapeutic drugs.

Nevertheless, a retrospective study on 1054 patients with anaplastic oligodendroglioma, presented during the 2009 ASCO Annual Meeting, suggests that PCV therapy may be superior in efficacy to the newer temozolomide therapy. Median time to progression for patients with 1p19q co-deletion was longer following PCV alone (7.6 years) than with temozolomide alone (3.3 years); median overall survival was also longer with PCV treatment versus temozolomide treatment (not reached, vs. 7.1 years).

The standard dosing schedule of temozolomide is 5 consecutive days of daily dosing during 28 day cycles. However, different dosing schedules may produce better results, such as continuous daily dosing using lower amounts of drug (e.g. 21 day dosing during 28 day cycles). As an example of an altered dosing schedule, promising results have been shown using lower daily doses on each day for 7 weeks, followed by a 4 week off periods.

Regarding the duration of dosing, for oligodendrogliomas the duration prescribed by oncologists varies considerably and seems to range from 6 cycles to over 32 cycles (i.e. over 3 years). In one study, researchers compared patients who received temozolomide for at least 12 months on the 5/28 day cycle, dividing such patients into two groups: “short term” patients receiving temozolomide for 12-18 cycles and those “long term” patients receiving 19 or more cycles (range was 19 to 32 cycles). Researchers found that there was a statistically significant advantage for “long term” treatment (median progression free survival for “short term” patients was 95 weeks (follow up of 73 weeks), but for “long term” patients the median progression free survival was not yet reached (follow up of 134 weeks)).

Because of their diffusely infiltrating nature, oligodendrogliomas cannot be completely resected and are not curable by surgical excision. If the tumor mass compresses adjacent brain structures, a neurosurgeon will typically remove as much of the tumor as he or she can without damaging other critical, healthy brain structures. Surgery may be followed up by chemotherapy, radiation, or a mix of both, but recent studies suggest that radiation does not improve overall survival (even when age, clinical data, histological grading, and type of surgery are considered).

However, a recent long-term study does affirm that radiation combined with adjuvant chemotherapy is significantly more efficatious for anaplastic oligodendroglioma patients with 1p 19q co-deleted tumors and has become the new standard of care.

However, it is possible that radiotherapy may prolong the overall time to progression for non-deleted tumors.

Oligodendrogliomas, like all other infiltrating gliomas, have a very high (almost uniform) rate of recurrence and gradually increase in grade over time. Recurrent tumors are generally treated with more aggressive chemotherapy and radiation therapy. Recently, stereotactic surgery has proven successful in treating small tumors that have been diagnosed early.

Long-term survival is reported in a minority of patients.

With aggressive treatment and close monitoring, it is possible to outlive the typical life expectancies for both low grade and high grade oligodendrogliomas. Westergaard’s study (1997) showed that patients younger than 20 years had a median survival of 17.5 years.

Another study shows a 34% survival rate after 20 years. However, as discussed above, such figures can be misleading since they do not factor in the types of treatment nor the genetic signature of the tumors. As well, such historic data loses significance due to the relatively long survival of patients (compared to other types of brain tumors) and the introduction of newer treatment options over time.

http://en.wikipedia.org/wiki/Oligodendroglioma

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Aihara K, Mukasa A, Nagae G, Nomura M, Yamamoto S, Ueda H, Tatsuno K, Shibahara J, Takahashi M, Momose T, Tanaka S, Takayanagi S, Yanagisawa S, Nejo T, Takahashi S, Omata M, Otani R, Saito K, Narita Y, Nagane M, Nishikawa R, Ueki K, Aburatani H, Saito N. Genetic and epigenetic stability of oligodendrogliomas at recurrence. Acta Neuropathol Commun. 2017 Mar 7;5(1):18. doi: 10.1186/s40478-017-0422-z. PubMed PMID: 28270234; PubMed Central PMCID: PMC5339990.