

Moving Research *into Treatment*

OLIGODENDROGLIOMA AND OLIGOASTROCYTOMA

“Glioma” is the name of a group of tumors that arise from the supporting cells in the brain, the ones that help “glue” the brain tissue together. Oligodendroglioma and astrocytoma are two specific types of gliomas. Each is named after the normal cell it most closely resembles.

Oligodendroglioma cells look like oligodendrocytes under the microscope—small round cells that have a “fried-egg” appearance. Astrocytomas are thought to arise from astrocytes, a star-shaped brain cell. Researchers believe that oligodendrocytes and astrocytes originate from the same parent cell, meaning that the tumors that arise from these cells are likely related biologically. Indeed, some gliomas contain a “mixture” of oligodendroglioma and astrocytoma cells. If an oligodendroglioma contains many astrocytoma-looking cells, the tumor is called an oligoastrocytoma.

Up to 25% of gliomas and nearly 4% of all brain tumors are oligodendrogliomas. Mixed gliomas, primarily oligoastrocytomas, account for 5% to 10% of gliomas and 1% of all brain tumors. Oligodendrogliomas and oligoastrocytomas develop in young and middle-aged adults (ages 30 to 50). Very few children are diagnosed with oligodendrogliomas or oligoastrocytomas.

A tumor’s most aggressive cell type usually determines its potential for growth. In oligoastrocytomas, it is the astrocytoma element that usually grows more quickly. Also, oligodendrogliomas and some oligoastrocytomas that contain anaplastic (malignant) cells will tend to multiply more rapidly than the low

grade versions of these tumors, which may take years to grow.

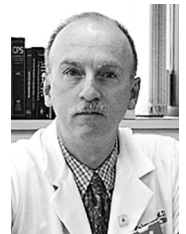
While the exact cause of these and other brain tumors is unknown, oligodendrogliomas and oligoastrocytomas begin to grow when a normal brain cell becomes abnormal, and that abnormal cell continues to reproduce itself. Researchers are studying the roles of abnormally functioning stem cells, proteins, enzymes or missing genetic material as possible causes for these tumors. Scientists now know that the absence of chromosomes 1p and/or 19q is a common characteristic of both oligodendrogliomas and oligoastrocytomas. In addition, more aggressive oligodendrogliomas appear to have abnormalities on chromosomes 7, 9, or 10, along with an unusual amount of growth factors and gene proteins believed to promote blood vessel growth around the tumor.

For low-grade, accessible oligodendrogliomas, surgery is the first line of treatment. Anaplastic oligodendrogliomas and oligoastrocytomas are best treated with surgery followed by radiation and chemotherapy. Under careful study is the treatment of tumors with deleted chromosomes 1p and 19q which often grow slowly despite anaplastic features. Temozolomide (Temodar), the drug combination called PCV (procarbazine, CCNU, and vincristine), or biodegradable polymer wafers soaked in the drug carmustine (Gliadel) are common chemotherapy options. (Note that the wafers are placed into the tumor cavity during surgery to remove the brain tumor, whereas the Temodar and PCV are given during or after radiation.) In clinical trials, some

patients with anaplastic oligodendrogliomas or oligoastrocytomas have been receiving intensive chemotherapy along with peripheral stem cell support (to replace blood cells lost during treatment).

Researchers continue to explore new drugs, drug combinations, and the role of MGMT (O6-Methylguanine-DNA Methyltransferase), in mediating resistance to chemotherapy in oligodendroglioma and oligodendrocytes. Ongoing studies are testing a drug called O6benzylguanine (O6BG), which when given prior to or with chemotherapy, may purposefully lower MGMT expression to make the chemotherapy more effective. Interestingly, MGMT is often silenced in those oligodendrogliomas that have lost chromosomes 1p and 19q, which may help explain their unusual chemosensitivity.

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