A randomized prospective controlled trial reported by Gerritsen et al. documents the efficacy of open carpal tunnel release for patients with carpal tunnel syndrome (CTS), and demonstrates that surgery is much more effective than splinting alone for long term relief of symptoms (JAMA 288:1245-1251, 2002). The study randomly assigned 176 people with CTS to treatment by either open surgery or wrist splinting at night, designed as an intention-to-treat analysis with primary outcome measures of patient-reported improvement in symptoms evaluated at 1, 3, 6, 12 and 18 months. Analysis for the two groups was first done on a strict intention-to-treat basis (i.e. if a patient randomized to splinting did poorly at 3 months, had surgery and did well at 18 months, the good outcome was attributed to the splinting group). Additional analyses were done to address this problem.

One month into the study, patients randomized to splinting had improved more. At 3, 6, 12 and 18 months, however, the surgical group had greater improvement. By 18 months treatment was successful in 90% of patients who had randomized to surgery and 75% of those who had randomized to splinting. If the patients in the splinted group who subsequently crossed over to surgery were counted as “no improvement with splinting,” the success rate from splinting at 18 months dropped from 75% to 37%. Thirty-two of the 89 patients who initially randomized to splinting crossed over to surgery and 30 of these patients (94%) had a successful outcome at 18 months. Adverse effects were common, but mild, in both groups. One surgical patient developed reflex sympathetic dystrophy.

It should be noted that the option of initial treatment with splinting followed by surgery in those who fail conservative treatment resulted in a 94% long term successful outcome. This is not significantly different from those patients who immediately went to surgery. Blinding was not possible, introducing potential biases, especially in patient-reported outcomes or their elucidation by therapists. Another instructive feature of this study is that a strict decision-to-treatment analysis, naively interpreted, would have grossly overestimated the benefit of splinting.

Robert E. Harbaugh, M.D.
OUTCOMES & POPULATION SCIENCE

Splinting vs Surgery in Carpal Tunnel Syndrome

T he inactivation of oncogenes has become a recent target strategy in the treatment of cancer. In a recent report (Science 297: 102-104, 2002) Jain et al. describe a fascinating project in which they pharmacologically inactivated the MYC oncogene in transgenic mice that are prone to the development of osteogenic sarcomas. These tumors are similar to human osteogenic sarcomas and are known to overexpress the MYC oncogene. In both in vitro and in vivo models, the authors used doxycycline (dox) to pharmacologically inactivate MYC. Upon withdrawal of the dox, contrary to the original hypothesis that the discontinuation of the inactivating agent would cause the tumor cells to revert to their proliferative and tumorigenic state, 95% of the tumor cells instead underwent apoptosis. The remaining 5% of cells retained a morphology and phenotype consistent with that of mature osteoblasts, suggesting the differentiation of osteogenic tumor cells into mature bone. Less than 1% of the tumor cells regained tumor-like properties.

The results demonstrate a promising role for oncogene inactivation in the treatment of cancer. In addition, the findings disprove the notion that cessation of pharmacologic inactivation of an oncogene results in tumor regrowth, which has previously been a major challenge to the proposed utility of oncogene inactivation in the treatment of certain tumors. The findings may potentially be very useful in managing tumors of the central nervous system (CNS). Not only has the deregulation of various oncogenes been shown to play a role in CNS tumorigenesis, but also aberrations in MYC have specifically been implicated in the development of astrocytomas, oligodendrogliomas (1), medulloblastomas (2-4), glioblastomas (5), pituitary adenomas (6), neuroblastomas (7), CNS lymphomas (8); and primitive neuroectodermal tumors (PNETs) (9).

In recent years, cancer therapies involving anti-angiogenesis or alterations in the local tumor environment have shown promise, but these strategies target the tumor environment rather than the tumorigenic cell. A therapy such as the one presented here, which actually specifically targets and selectively induces apoptosis in tumor cells, is highly desirable, potentially very safe, and may have a significant application in the treatment of CNS tumors.

Deepa Soni, M.D. and Robert M. Friedlander, M.D.
BASIC SCIENCES RESEARCH

References: