Neurologic complications of systemic cancer

**Overview**

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In a previous edition of *Cancer Forum* (1998 Jul;22(2)) we discussed the management of primary tumours of the central nervous system (CNS). A more common scenario for the oncologist is the patient with cancer who develops neurologic complications. The difficulty is to determine as quickly as possible the anatomical site (“where is it?”), which often helps to answer the second question of “what is it?”. Associations of certain tumours with particular complications can be helpful. For example, adenocarcinomas and melanoma are more common causes of leptomeningeal metastases, while small cell lung carcinoma (SCLC) is the tumour most likely to be associated with paraneoplastic neurologic phenomena.

Management of cerebral metastases

In this forum, Ryan has expertly summarised the issues regarding the management of this common complication. From a neurologic perspective, radiation encephalopathy is a real phenomenon and occurs more commonly in elderly patients. I have seen patients whose neurologic deterioration was rapid and progressive within weeks of radiation. Underlying vascular disease or diabetes may be additional risk factors. However, it is also true that progressive disease has an equally devastating effect on neurologic function. This debate has been seen in primary CNS lymphoma, in which longer survival with chemotherapy increases the risk of whole brain radiotherapy. Patients over the age of 60 are at particular risk. This certainly should inform the decision-making in prophylactic cranial irradiation of SCLC.

Another issue relates to what are appropriate endpoints in trials of brain metastasis therapy. In one pilot study of chemotherapy, patients came off study with progression without reaching the study’s endpoints. In the study of Motexafin Gadolinium that is currently being run in a number of sites in Australia, targeting patients with cerebral metastases associated with non small cell lung carcinoma (NSCLC), neuropsychologic assessments are included. In addition, a blinded panel of neurologists is being used to define patient progression. Imaging is not a criterion and not required! The US Food & Drug Administration has made it clear in these studies that radiologic response criteria are not rigourous or representative enough to ensure registration. In therapies that are not likely to improve the survival of one group, quality of life and neurologic function are appropriate and meaningful endpoints, but the assessment tools need to be improved.

Leptomeningeal metastasis

The data on management of this complication are limited to small and often retrospective data. Early diagnosis can be important as most fixed deficits are not reversible with therapy, except in patients with lymphoma. It is important to think of this condition to make the diagnosis.

Other potential approaches include a fortnightly intrathecal injection of slow-release Cytarabine that is associated with fewer injections. Others have used high dose Methotrexate to bypass problems with CSF flow obstruction. Siegal has discussed the importance of systemic therapy, and argued that this is as active as intrathecal therapies.

Neurosurgery and malignancy

Metastatic spinal cord compression is a true medical emergency and, as Rogers discusses, delayed diagnosis is associated with significant neurologic deficits due to paraplegia or quadriplegia. There is no simple formula for identifying which patients are suitable for surgery, but the Regine study certainly should encourage surgical consideration early.

The clinical warning signs include persistent back pain, with circumferential radicular referred pain and associated with contralateral sensory loss to pain and temperature. Pyramidal weakness of the limbs may follow.

The range of new neurosurgical approaches above that of laminectomy make the procedure applicable to more patients, with the potential to improve quality of life. It still remains difficult to lay out clear guidelines to decide who should, and should not, be operated.

Similarly, the ability to deal with painful brachial plexopathies surgically can make a difference to pain management. A multidisciplinary approach allows for improved management of these complex problems.

Neurologic complications of chemotherapy

As outlined in my paper, it is usually possible to identify specific syndromes associated with certain drugs. Less common reactions need to be considered, and as new drugs, including biological therapies, become available, we may discover new syndromes.

Paraneoplastic neurologic syndromes

While uncommon, these conditions can be devastating for the patient, and are a fascinating window into the interaction between cancer, the immune system and the brain. These syndromes can occur unrelated to malignancy, particularly
Lambert Eaton myaesthenic syndrome. Other examples are the cerebellar syndrome and opsoclonus-myoclonus.

As mentioned by Sutton, antineuronal antibodies may not be present and novel antineuronal antibodies can be found in individual patients whose significance is not clear. The most common antibodies (Hu, Ri, Yo) are available in Australia, but the more recently defined ones are not. It is possible to send specimens to one of the US labs such as that of Dr Josep Dalmau (jdalmau@aol.com).

It appears that the antibodies are not likely to be pathogenic, and recent evidence has focused on the role of killer T cells. One model suggests that apoptotic tumour cells are presented to dendritic cells, producing antigen-specific T cells.5

Hopefully, as our understanding improves therapies will also. We hope you find these papers a useful update of the diverse intersection between oncology and neurology.

**References**


