Pathology types of MS

Much of our knowledge about MS has come from the study of brain tissue from MS patients. This tissue comes from autopsies done on deceased patients or from brain biopsies. It is rare for patients to die from MS; rather, most MS patients die from diseases of aging. Thus, most autopsy specimens reflect disease that is often decades old and that does not represent the disease during an active phase. Most brain biopsies in MS patients are done because a brain tumor is suspected. Biopsy specimens usually demonstrate very active MS, though even this may be several days after the onset of the immune attack.

While these specimens have taught us much about the disease, the study of MS lesions during an active phase has been difficult. Recently, an effort was made to study autopsy and biopsy specimens that showed active lesions. These specimens were from both North America and Europe. These rare specimens have been crucial to furthering our understanding of the disease.

When these active lesions were studied they fell into four types. It should be emphasized that these types are based on the appearance of the disease under the microscope (pathology) which is different than the four types of MS based on the clinical course (See page on Subtypes of MS). Each patient had only one type of pathology on examination. There were very rare cases that had more than one biopsy, or a biopsy followed by an autopsy, and these patients had only one type of pathology over time.

Type I MS Lesion: this is the classic MS lesion with loss of myelin associated with the presence of lymphocytes (inflammatory cells) and macrophages (cleaning up the debris).

Type II MS Lesion: this type of lesion is similar to the classic type I lesion with myelin loss, lymphocytes and macrophages. In addition, there is deposition of immunoglobulins and complement. Immunoglobulin and complement indicate that not only are T cells from the immune system involved, but also B cells. B cells are the cells that make antibodies to fight infections.

Type III MS Lesion: this type of lesion has myelin loss, lymphocytes and macrophages like the first two types. However, the oligodendrocytes that make myelin appear to be dying from apoptosis. Apoptosis is a process by which cells self destruct. Apoptosis genes within the cell are turned on and produce enzymes that destroy the nucleus of the cell and eventually the cell contents. This is a mechanism that our bodies use to destroy cells that we don’t want during development, cancer cells or cells infected with viruses. Consistent with apoptosis, the myelin in type III lesions appears to be lost next to the axon first, and further out from the axon later (whereas an immune attack on myelin would first affect the exterior of the myelin). This type of lesion is consistent with an illness that affects the health of the oligodendrocyte that makes the myelin.
Type IV MS Lesion: this type of lesion has myelin loss, lymphocytes and macrophages similar to other types. It also resembles type III because oligodendrocytes are dying. However, they are dying through a process that does not involve apoptosis.

Currently, there is no way to determine what type of lesion a person with MS might have except through a brain biopsy, which would not be recommended. Clinical and MRI characteristics of patients are being studied to determine if any predict which pathology type a patient has, but to date none have proven adequate. The clinical course of MS (relapsing, secondary progressive, primary progressive and relapsing/progressive) does not predict which type of pathology a patient has.

The importance of these pathology types is that they give us clues to the causes of MS. Types III and IV suggest that factors other than an immune attack on the myelin may be important contributors to the disease. Viral, toxic or genetic factors may also contribute to the disease. Furthermore, this suggests that MS could even be more than one disease. Further understanding of these pathology types may one day lead to better treatment of the disease. For example, therapy could be directed against B cells in patients with type I pathology. The description of these pathology types has been a huge advance that will lead to much more research and eventually to better treatments for MS.