

Treatment Options for Paraneoplastic Neurological Disorders

By Carolyn Z. Lawrence

Paraneoplastic Neurological Disorders (PNDs) can be extremely complex and difficult to treat. The most important part of treatment is to get a proper and rapid diagnosis of both the underlying cancer and the type of Paraneoplastic disorder involved. This knowledge can help doctors provide more targeted and effective treatment that can ultimately improve both life expectancy and quality of life.

Diagnosis of Paraneoplastic Neurological Disorders

The diagnosis stage of treatment for PNDs involves two focuses:

- Identifying the type of underlying cancer
- Identifying the type of PND associated antibody

Often, doctors consider a range of other medical conditions with similar symptoms before testing for PNDs. For the most common forms of PND, a blood test can identify antibodies associated with different forms of PNDs. In more difficult cases, spinal taps can also be used to identify antibodies. MRIs, PET scans, and other imaging exams are also used to look for underlying cancers when PND is suspected.

In some patients, an underlying cancer can be difficult to find. This should not, however, automatically rule out the possibility of a PND. When a patient experiences the rapid onset of severe neurological symptoms, a Paraneoplastic Neurological Disorder should always be considered a possibility until further testing rules out the presence of common Paraneoplastic antibodies. In some cases, when a PND-associated antibody is found it may suggest the likelihood of a certain cancer type, and further cancer testing may be indicated.

Common Paraneoplastic-associated antibodies include:

- Anti-Yo - Most commonly found in women with gynecological and breast cancers, related to Cerebellar Paraneoplastic Degeneration
- Anti-Hu - Expressed by a number of cancers, including small cell lung cancers, neuroblastomas, and other forms of cancer.
- Anti-Ri - Most commonly associated with breast cancer, but can also be found in patients with lymphomas.

However, there are also a number of other antibodies associated with different forms of Paraneoplastic Neurological Disorders. Be sure to discuss the type of antibody found with your doctor, as it can affect the choice and success of any treatment.

Once a Paraneoplastic Neurological Disorder is confirmed, a patient's treatment plan will depend on:

- The type and stage of any underlying cancer
- The type of Paraneoplastic Neurological Disorder

Typically, PND patients will be treated by an oncologist (a doctor specializing in cancer) and a neurologist (a doctor specializing in neurological disorders). A neuro-oncologist (a doctor trained in treating the neurological effects of cancer) may also be involved. Physical therapists, speech therapists and occupational therapists should also be involved when a patient is diagnosed with a PND. Their assistance can greatly improve quality of life and help slow down neurological deterioration. Finally, because Paraneoplastic Neurological Disorders are rare, PND patients should, whenever possible, seek treatment at major cancer treatment centers where there is a greater likelihood of finding medical specialists with the greatest experience in treating PND patients with the most current treatments.

Questions to Ask Your Doctor

When consulting with a doctor about PND treatment, patients and caregivers should ask their doctors the following questions:

- What type of Paraneoplastic Neurological Disorder do I have? Which antibodies and cancers are associated with this type of Paraneoplastic Neurological Disorder?
- Do you have recent experience treating patients with my type of Paraneoplastic Neurological Disorder? If so, how many patients have you treated, which treatments were used, and what was the outcome of treatment?
- Are you willing to consult with or make referrals to Paraneoplastic specialists and researchers? If so, which specialists and researchers do you recommend?
- What treatment options do you recommend for my specific case? What are the expected outcomes for these treatments? What are the potential side effects of these treatments?
- Will your primary focus be on treating the underlying cancer, or will you also recommend treatment to address my neurological symptoms?
- What is your overall treatment philosophy for Paraneoplastic patients? How aggressive are you when it comes to treating Paraneoplastic patients and trying different treatment options?

Treating the Underlying Cancer

Paraneoplastic disorders are most common in patients with lung, breast, ovarian, and lymphatic cancers, but many other types of cancers can also be involved.

Because there have been some reported cases where the symptoms of PND have been abated after the cancer has been controlled, doctors usually suggest standard cancer treatments such as chemotherapy, tumor incision, and radiation as a first step in treating PND patients. Some PND patients may undergo many rounds, or even years, of cancer treatment.

Important Note: Some chemotherapy treatments can have neurological side effects. It is very important, therefore, that PND patients and caregivers always ask about the potential neurological side effects of any recommended cancer treatments. Whenever possible, avoid any risk of additional neurological problems.

Sometimes it can be very difficult to identify cancer in PND patients, even though Paraneoplastic antibodies are found. These patients are said to have "occult" or hidden cancers that are hard to detect even after many scans, blood tests and biopsies. Some doctors may still choose to use chemotherapy to treat suspected occult cancers when PND antibodies are present.

Treating the Paraneoplastic Neurological Disorder

Beyond treating any underlying cancer, doctors may also look for ways to slow or stop the auto-immune process associated with PNDs in order to improve the patient's neurological stability. It's important to understand that the success of these treatment options will vary depending on the type of PND and its associated antibodies.

There are three main treatments used to directly treat the neurological effects of Paraneoplastic disorders. The main goal of these treatments is to suppress the immune system. They are: Plasmapheresis, IvIg, and immunosuppressant medications. Sometimes a combination of treatments is used. None of these treatments are effective for all forms of PND.

Plasmapheresis

Plasmapheresis can be thought of as a "blood cleansing" process. During plasmapheresis blood is passed through a device called a separator, which removes Plasma, the part of the blood containing the PND antibodies. The rest of the blood is returned to the patient.

Plasmapheresis is generally not painful, although some patients may find the process uncomfortable. A small thin tube is placed in one large vein, usually in the arm, and another tube is placed in the opposite hand or foot. Blood is removed through one tube, goes through the separator, and is returned to the body in the other tube. Only a small amount of blood is outside of the body at any one time. The process takes several hours and can be done on an outpatient basis. Usually paraneoplastic patients undergoing plasmapheresis will receive several treatments spaced out over several weeks.

Risks associated with plasmapheresis include a drop in blood pressure, bleeding, and allergic reactions to the solutions used to replace the plasma. In some patients, excessive suppression of the immune system can temporarily occur.

Plasmapheresis has been shown to have mixed results in paraneoplastic disorders, usually resulting in only a temporary improvement unless the underlying cause of antibody production in the body (the cancer) has been found and alleviated.

Intravenous immunoglobulin (IVIG) therapy

IVIG therapy uses immunoglobulins, a type of protein that is found in human blood which helps to fight off harmful bacteria, viruses, and other germs. IVIG products are derived from the plasma of large numbers of individuals. All donors are tested for contagious diseases including HIV, and hepatitis.

During an IVIG treatment, the immunoglobulins are given intravenously. An IV catheter is placed into the patient's hand or lower arm and the IVIG solution is dripped into the vein. Side effects can include headache, flu-like fatigue, fever, chills and nausea.

Like plasmapheresis, results from IVIG can be mixed for paraneoplastic patients. Doctors usually advise patients that it can take several weeks to see results such as improvement in neurological function or the slowing of neurological deterioration. Many paraneoplastic patients will need follow up IVIG treatments.

Some research has suggested that IVIG may not be effective for some types of paraneoplastic disorders. Dr. Franz Blaes, a German researcher into paraneoplastic disorders, has noted, for instance, that anti-Hu antibody-associated syndromes are unlikely to respond to IVIG.

Immunosuppressant drugs

Many paraneoplastic specialists recommend a combination of immunosuppressant drugs. Immunosuppressant drugs are designed to suppress the body's production of the antibodies associated with paraneoplastic disorders.

Commonly used immunosuppressant drugs include cyclophosphamide, azathioprine, and rituxan. They are usually given orally.

Some specialists use these drugs in combination with plasmapheresis or IVIG. One study conducted by Dr. Steven Vernino at the Mayo Clinic found that out of 19 patients treated with a combination of oral cyclophosphamide and plasmapheresis, 53% experienced a positive response. Dr. Vernino noted that better outcome was achieved the earlier treatment began after diagnosis.

Other Medical Treatments Used to Help PND Patients

Paraneoplastic patients usually have a wide range of symptoms related to both the Paraneoplastic disease and their cancer. Doctors may prescribe a variety of drugs and therapies to address these issues. For example, if a patient has poor appetite, an appetite stimulant medication such as Megace can often improve appetite. Some doctors prescribe steroids like prednisone and anti-seizure medications such as Topamax to help with various symptoms. Anti-nausea medications may also be used to combat the side effects of chemotherapy and the effects of vertigo in PND patients.

Since depression is very common among PND patients, anti-depressant drugs may also be prescribed.

In addition to drugs and treatments, the PND patients who seem to do best, both in the short term and in the long term, are those that receive on-going physical therapy, occupational therapy, and speech therapy. Unfortunately, physical therapy may be stopped after a relatively short period of time because no apparent "improvement" has been seen. Doctors and physical therapists should understand that in PND patients stabilization, not improvement, may be the goal for physical therapy. Continuing PT on a regular basis can help patients maintain their balance and muscular control enough to make a large difference in their quality of life.

It is a good idea for all newly diagnosed patients to have at least a consultation with an occupational therapist and a speech therapist. The occupational therapist can help the patient and caregivers find ways to use adaptive techniques and technologies that keep the patient safer and more independent.

Since speech and swallowing can often be affected in some forms of PND, an initial consultation with a speech therapist soon after diagnosis can be useful for establishing a baseline for future speech difficulties. Speech therapists, Physical Therapists, and Occupational Therapists can help the patient minimize breathing, speech, and swallowing difficulties.

Homeopathic and Alternative Remedies

Many PND patients ask whether homeopathic or alternative treatments can help alleviate Paraneoplastic symptoms. **Homeopathic and alternative remedies should always be used with caution in PND patients, and only after consulting with a medical doctor familiar with the patient's PND and cancer.** Paraneoplastic patients already have a host of neurological and immunological issues, and there is always a danger that non-FDA approved preparations and remedies may exacerbate these issues.

PND patients and caregivers should also be cautious about information found on the Internet or in online discussion groups. The success of any treatment depends on the individual patient's overall health, and the type of PND and cancer involved. Claims made by non-medical professions regarding "cures" or "treatments" for PNDs or their symptoms should be viewed with skepticism, unless they are supported by medical research.

Paraneoplastic Neurological Disorders are extremely complex. The best source of medical information is always a medical professional who is familiar with the individual patient's cancer, PND, and medical symptoms.

PND Specialists and PND Clinical Trials

Because Paraneoplastic Neurological Disorders are rare, many doctors do not have extensive experience treating PND patients. Therefore, whenever possible, PND patients should consider consulting with specialists who do have experience with Paraneoplastic disorders. Many of these specialists understand that PND patients have difficulty travelling and are willing to consult with the patient's local doctors about treatment. **It never hurts to get a second opinion!**

There are also a number of medical researchers investigating the underlying causes of Paraneoplastic Neurological Disorders and conducting clinical trials of new treatment options.

Here is a list of some of the best known and most experienced PND specialists. This list, however, is by no means all-inclusive.

United States

Memorial Sloan Kettering Cancer Center, New York, New York (contact: Dr. Jerome Posner)

Rockefeller University, New York, New York – ongoing clinical research studies in Paraneoplastic Neurological Disorders (contact: Dr. Robert Darnell)

University of Texas Southwestern Medical Center, Texas (Contact: Dr. Steven Vernino, extremely willing to consult with local doctors)

Department of Neurology, Hospital of the University of Pennsylvania, Philadelphia, PA (Contact: Dr. Dalmau)

Mayo Clinic Neuro-Oncology Department, Rochester, Minnesota

Johns Hopkins Medical Center, Neurology Department, Baltimore, Maryland (Contact: Dr. Argye Beth Hillis)

Duke University Medical Center, Durham, North Carolina (Lambert Eaton Syndrome specialists available; also experience treating other forms of PND)

Cleveland Clinic Tausig Cancer Center, Cleveland, Ohio

Stanford School of Medicine, Neurology and Neurological Sciences, Palo Alto, California (contact: Dr. Kendra Peterson)

Division of Movement Disorders, Department of Neurology, University of Southern California, Los Angeles, California

Northwestern Medical Center/Northwestern University School of Medicine, Department of Neurology and Movement Science, Chicago, Illinois (Contact: Dr. Timothy Hain)

University of Wisconsin Medical Center, Madison, Wisconsin (Contact: Dr. Charles E. Kahn, specializes in Lambert Eaton Syndrome)

Canada

Princess Margaret Cancer Hospital, Toronto, Canada (Contact: Dr. Warren Mason, Pencer Brain Cancer Clinic)

Sunnybrook & Women's College Hospital, Toronto, Canada (Contact: Dr. James Perry)

University of Toronto, Toronto-Sunnybrook Regional Cancer Centre, Division of Medical Oncology (Contact: Dr. Ellen Warner)

Ottawa Regional Cancer Centre, Ottawa, Canada (Contact: Dr. Rakesh Goel)

Europe

For PND specialists and researchers in Europe, please visit the PNSeuronet website, which has an extensive list of Paraneoplastic doctors in Europe: <http://www.pnseuronet.org/>