Offering Hope to Patients with ALS

Relaying news of a diagnosis of ALS. Allaying fears. Providing multi-disciplinary care and support for patients and their families. These are everyday undertakings of neurologists, nurses, and other health professionals – including those at the Kesslenich Family MDA ALS Center at the University of Miami Miller School of Medicine – who look after ALS patients. Offering patients a future without ALS, is an essential element to providing comprehensive care.

Michael Benatar, MD, PhD, associate professor of neurology, chief of the Neuromuscular Division, and the Walter Bradley Chair in ALS Research at the Miller School believes that, in the absence of effective treatments for patients with ALS, the opportunity for research participation offers the best hope for patients and their families.

Benatar, who leads an active program of research at the University of Miami, studies patients with sporadic ALS as well as more than 400 families across the U.S. with the familial form of this disease (www.als-research.org). In an effort to identify the genetic cause of ALS in these families, a key step towards development of therapeutic and even preventive strategies, Benatar and his team joined forces with an international consortium led by Bryan Traynor, MD, of the NIH. The collaboration led to the important discovery last year that mutations in the VCP gene, although uncommon in patients with familial ALS, were a shared cause of ALS, FTD, and IBMPFD (Inclusion Body Myopathy, Paget disease, and Frontotemporal Dementia) (Neuron, December 9, 2010). More recently, the international consortium made the landmark discovery that mutations in the C9ORF72 gene on chromosome 9 are the most common cause identified to date of not only familial ALS, but also a significant minority of patients who appear to have the sporadic form of the disease. The pathogenic mutation is a hexanucleotide repeat expansion believed to exert its effect by interfering with RNA processing, a mechanism increasingly recognized to be central to the pathophysiology of ALS. The C9ORF72 discovery was reported in the September 22, 2011 issue of the journal Neuron, with Benatar and colleague Joanne Wu, ScM, as the Miller School co-authors on this publication. A team from Mayo Clinic Jacksonville has also independently identified the same repeat expansion as a genetic cause of FTD/ALS; their study is reported in the same issue of Neuron.

In addition to these groundbreaking genetic discoveries, Benatar and his team are at the forefront of many other research efforts, including pioneering the first-ever clinical trial (of a drug called arimoclomol) in patients with familial ALS due to mutations in SOD1, which until recently were the most common known cause of ALS. Benatar also leads the Pre-fALS study, a prospective observational study of unaffected family members of patients with familial ALS; these pre-symptomatic individuals are at risk for developing ALS because they carry mutations in genes known to cause ALS (SOD1, C9ORF72, TARDBP, VCP etc.). Participants in Pre-fALS and the arimoclomol trial are also systematically evaluated using novel imaging and electrophysiological biomarker techniques. Most recently, Benatar has launched a new study to further elucidate the relationship between ALS and IBMFFPD. All three studies are actively recruiting participants (see contact information below) from across the U.S., with the costs of genetic testing and travel to the University of Miami covered by the research program.

These are indeed exciting times in the field of ALS research. New genetic discoveries in the last five years have shed light on new links between familial and sporadic ALS, unmasked important connections between ALS and other degenerative disorders, uncovered important disease mechanisms that had previously been overlooked, and paved the way for new therapeutic development targeting these newly discovered pathogenic pathways.

Through their participation in research, an often fulfilling and self-empowering experience, ALS patients and their families hold the key to scientific advancement. This-together with the recognition that palpable progress in ALS research is being made, even if the translation into effective therapy is an arduous process—is cause for optimism and hope.

Contact:
General inquiry, Pre-fALS study, IBMFFPD-ALS study: fals@med.miami.edu, 1-888-413-9315
Arimoclomol trial: sod1@med.miami.edu

WHAT’S INSIDE

Pg. 2 - Mohamed Samy Elhamy, M.D.
  Jackson Memorial Neuro-ICU
  Clinical Trials
Pg. 3 - Unique Heat Shock Protein Vaccine (HSPPC-96)
Pg. 4 - In The News
  What’s Next
  Resident Spotlight -New Class Profile
Mohamed Samy Elhammady, M.D., now an instructor of clinical neurological surgery at the University of Miami Miller School of Medicine (UM), completed his residency, a neuroendovascular surgery fellowship and an open cerebrovascular and skull base surgery fellowship at UM/JMH. Dr. Elhammady earned his medical degree with highest honors from the University of Mansoura in Egypt. He began his neurosurgical training at the University of Mansoura before training in the U.S. at UM.

Dr. Elhammady specializes in the treatment of all aspects of cerebrovascular disease, including coiling and clipping of aneurysms, embolization and resection of arteriovenous malformations (AVMs), and stenting and endarterectomy for carotid stenosis. He is highly trained in brain and skull base tumors, including endovascular tumor embolization, minimally invasive endoscopic skull base approaches for pituitary tumors, resection of benign skull base tumors (such as meningiomas, schwannomas, acoustic neuromas and others) and malignant skull base tumors (such as carcinomas and others), as well as surgery for gliomas and brain metastases.

Dr. Elhammady runs an endovascular laboratory together with Ali Aziz-Sultan, M.D., where they are involved in researching novel methods for the treatment of aneurysms and AVMs, as well as the embolization and endovascular administration of chemotherapy for tumors. He is in the process of starting a microsurgical anatomical dissection and vascular laboratory for education, and a neurosurgeon at Jackson Memorial Hospital training, and research in anatomy of the brain, skull base approaches, and microvascular techniques.

For more information on Neurology clinical trials please call 1-877-977-7724.

Mohamed Samy Elhammady, M.D., joins the Department of Neurological Surgery as an instructor of clinical neurological surgery.
More than 17,000 new cases of central nervous system cancer are diagnosed annually in the United States, accounting for more than 13,000 deaths each year. Primary malignant brain tumors are nearly uniformly fatal, and the five-year survival rate for the highest grade of malignant glioblastoma, glioblastoma multiforme (GBM) remains poor. Improvements in conventional treatment modalities have provided only moderate extension of survival for patients harboring malignant gliomas, at times with undesirable side effects. As a result, experimental techniques such as immunotherapy are being applied to malignant glioma patients with increasing frequency.

To this end, the University of Miami joins a multicenter group to complete phase II of a clinical trial using heat shock protein vaccine (HSPPC-96) for patients with newly diagnosed glioblastoma multiforme (GBM). The trial, which is pioneered by the University of California San Francisco, revolves around cancer immunotherapy, an important new treatment modality, with HSPPC-96 being a novel approach to active specific immunotherapy. Immunotherapy is appealing because it offers the potential for specifically targeting tumor cells, without injury to normal neural and glial structures. The preliminary results using HSPPC-96 have been promising, thereby supporting the concept of active tumor and patient specific immunization with autologous tumor-derived heat-shock protein-peptide complex.

During surgery to remove suspected GBMs, University of Miami neurosurgeons will collect tumor tissue as part of their resection technique. The tissue sample will then be used to develop a vaccine specific to each patient’s tumor type through isolation and purification of the heat shock protein peptide complex. After pathologic confirmation of GBM, patients will receive standard of care radiotherapy and chemotherapy. The vaccine will be administered on a weekly basis along with maintenance temozolomide chemotherapy.

The heat shock protein vaccine has been refined over several years, being used in numerous animal models and clinical trials for the treatment of various systemic malignancies, such as renal cell carcinoma, pancreatic cancer, and lung cancer. Only recently, however, has this adjuvant therapy been employed in glioma patients. The preliminary results are encouraging, with earlier studies documenting increased overall survival and progression free survival in patients receiving the vaccine. Importantly, the vaccine has a favorable side effect profile, with no serious adverse events being reported to date. To be eligible, patients must be at least 18 years of age, functionally independent, and able to tolerate standard radiation and chemotherapy. They cannot carry the diagnosis of Human Immunodeficiency Virus, other concurrent malignancy, or systemic autoimmune disease and/or any history of immunodeficiency.

By targeting the immune system and activating a patient specific T-cell response, the vaccine offers a new avenue for glioma therapy. At the University of Miami, implementation of this vaccine is facilitated by multidisciplinary care and coordination between neurosurgeons, neurologists, and radiation oncologists. Our team is excited to be one of only 10 medical centers in the country, and the only one in Florida, to offer this treatment.

Jackson Memorial Hospital (JMH) is home to one of the largest Neuroscience Intensive Care Units (NSICU) in North America. The NSICU has 24 beds equipped with cutting edge neuromonoring equipment, including continuous video EEG for constant monitoring of cerebral electrical activity. Staffed by three full time neurointensivists, the unit provides state-of-the-art neurocritical care for patients with acute neurologic and neurosurgical disorders from across the United States and Caribbean Basin.

One such patient, Jerry Halabi, was transferred by air ambulance from his native island of Curacao to the NSICU for treatment in the fall of 2010. Mr. Halabi, a 32-year-old, presented with new seizures from epilepsy which could not be brought under control at the local hospital in Curacao. His family then decided to seek out the expertise of the JMH/UM specialists for a comprehensive evaluation of his condition and other possible treatment options. Upon arrival, he was placed on continuous video EEG monitoring and received escalating therapies with multiple anticonvulsants, sedatives and pentobarbital to control his seizures. Diagnostic testing, including MRI, was suggestive of encephalitis. Labs were drawn to test for viral encephalitis and serology was strongly positive for IgG for St. Louis encephalitis.

Several attempts to taper off the pentobarbital failed. His medical course was complicated by pneumonia and prolonged mechanical ventilation requiring a tracheostomy tube placement. Finally, after six weeks the barbiturate coma was successfully lifted and Mr. Halabi was able to wake up without continuous seizures. He began to follow commands although he remained extremely weak in his limbs due to a severe peripheral neuropathy.

Ten weeks after his admission to the intensive care unit, he was transferred to Kendall Rehabilitation Center for intensive physical therapy before returning to his home in Curacao. Mr. Halabi is now able to work again full time and can walk independently with only a slight limp due to hip pain. He is still being treated with two anticonvulsants to control his epilepsy, but at a significant lower dosage. Mr. Halabi has made a remarkable recovery in a short period of time. He has been able to return to his previous life, and spend time with his family and friends.

“He has made a fantastic recovery from refractory status epilepticus caused by a rare viral encephalitis. Seeing him do so well after such a difficult illness makes what we do in the Neuro-ICU incredibly rewarding,” said Kristine O’Phelan, M.D., director of neurocritical care and one of the primary specialists who treated Mr. Halabi.

Like many international patients, Mr. Halabi’s successful recovery was due to the treatment provided by a comprehensive team of specialists including neurologists, neuro-critical care nurses and clinical pharmacists—a highly-trained team that cannot be replicated in their home countries.

Want more? Check out these stories online and discover more about the University of Miami Miller School of Medicine and Jackson Memorial Hospital.
The Departments of Neurology and Neurological Surgery welcomed a new class of residents in July with an incredible array of backgrounds and experiences. Many new class members are graduates of top 50 medical schools and members of Alpha Omega Alpha Honor Medical Society. They come from a variety of international locations and from across the United States. Their experience and interests include research of hypothermia for traumatic brain injury (TBI), stroke and neuromuscular and movement disorders. The members of this year’s class are medical alumni of Tulane University School of Medicine, Washington University School of Medicine, University of Miami Miller School of Medicine, Albert Einstein College of Medicine, Medical College of Georgia School of Medicine, Indiana University School of Medicine, Howard University College of Medicine, The University of Texas Medical School at Houston and West Virginia University School of Medicine.

The Department of Neurology's residents are slated to graduate in June 2015 and the Department of Neurological Surgery's residents will graduate in June 2018.