Resistant Lymphatic Disease Responds to Novel Drug Treatment

Clinical History and Presentation

Born with diffuse soft tissue microcystic lymphatic malformations, a young boy was experiencing swelling and chronic pain in his right upper chest and truncal area. A biopsy performed by a dermatologist in his hometown revealed that the cutaneous malformation on his chest was a microcystic lymphatic malformation. He was then referred to the Hemangioma and Vascular Malformation Center at Cincinnati Children’s Hospital Medical Center for further evaluation and treatment.

Our Approach

The child was placed under the care of Denise Adams, MD, medical director of the center, who led a team of specialists in surgery, otolaryngology, dermatology, radiology and pain management in plotting a course for treatment. Since the boy was asymptomatic upon his initial evaluation, the decision was made to not actively treat him but to closely watch for changes in his condition. In a follow-up appointment several months later, an MRI exam was ordered after it was noted he had new discoloration on the front and back of the lesion. The MRI revealed a thickening of the boy’s chest wall and mediastinal adenopathy, which was determined to be lymphatic disease. Although still asymptomatic and experiencing no discomfort, this change in his condition led Dr. Adams to prescribe interferon and Celebrex® (for its matrix metalloproteinases-inhibitive properties). The patient continued this therapy for the next 10 months.

During his 10 months on interferon and Celebrex®, the boy was admitted to Cincinnati Children's numerous times for recurring streptococcal infections. Each recurrent infection and insertion of chest tubes caused the development of pleural effusions secondarily. During these stays, he also underwent several rounds of sclerotherapy with doxycycline to reduce the proliferation of the malformations as well as several thoracentesis procedures to remove pulmonary scarring. With each of these hospitalizations, when his fluids had decreased to an acceptable level, his chest tube was removed prior to discharge; however, he continued to contract infections, resulting in weight loss and failure to thrive.

At this point, it was apparent that neither the interferon nor the Celebrex® was providing relief for his lymphatic disease, so Dr. Adams made the decision to put him on an off-label treatment plan of rapamycin. Her team had achieved remarkable results with off-label use of rapamycin for a previous patient suffering from kaposiform hemangioendothelioma. A few days after beginning treatment with rapamycin, the boy was sent home with his chest tube.

This complex case illustrates the need for innovative thinking when all other treatment options have been exhausted.
Results and Follow Up

Almost immediately upon beginning rapamycin, the child’s pain diminished. Within two weeks, his chest tube was removed and no infection was found. Within one month his pleural fluid had decreased, while his activity level and weight had increased. At two months, an X-ray revealed his right pleural effusion had decreased by approximately 50 percent and the lower right lobe atelectasis had cleared in the interim. At three months, his right pleural effusion was minimal.

His condition has continued to improve over the two years he has been on rapamycin. Beginning in spring 2010, he was weaned from the drug.

Discussion and Lessons Learned

This complex case illustrates the need for innovative thinking when all other treatment options have been exhausted. It also emphasizes the need for additional studies to find effective treatments for these conditions. The fact that there are no widely accepted protocols or FDA-approved drugs for the treatment of vascular malformations has made it difficult for physicians to find answers that will help children with these conditions. Basic scientists and clinical investigators need to collaborate to identify pathways to better treat these lesions that can cause significant morbidity and mortality.

Phase II Study for Safety and Efficacy of Rapamycin

With the scarcity of studies in this area, due to the lack of patient volume and funding, physicians have had to gauge the effectiveness of a drug or therapy by looking at images of a treated child after the fact. Recently, Dr. Adams was awarded a four-year grant from the FDA to conduct a Phase II study to assess the efficacy and safety, as well as the biological markers, of rapamycin in the treatment of complicated vascular anomalies. For more information about the study, visit www.clinicaltrials.gov.

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