

Large Pilocytic Astrocytoma May Be Aggressive

BY AMY ROTHMAN SCHONFELD
Contributing Writer

CHICAGO — Imaging characteristics can help physicians distinguish the more aggressive pilomyxoid astrocytoma from a pilocytic astrocytoma and thereby guide treatment decisions, according to Dr. Luke Linscott, who presented his findings at the annual meeting of the American Society of Neuroradiology.

“If you see a patient with a presumed pilocytic astrocytoma [PCA] who is either very young or an adult, with a large, bulky tumor in an atypical location for PCA and, especially if that tumor demonstrates hemorrhage, the most likely diagnosis is aggressive pilomyxoid astrocytoma [PMA],” said Dr. Linscott of the University of Utah, Salt Lake City.

In what is the largest case series to date on PMA, Dr. Linscott and colleagues reviewed the images, pathology reports, and clinical information of 21 patients with pathology-confirmed PMA. The average age was 5 years, with a range from 9 months to 46 years, and there was a slight predominance of males. Researchers contributed cases from the United States, Canada, Norway, and South Africa.

The tumor’s anatomic location is one diagnostic clue. Although PCAs are most commonly found in the posterior fossa and less commonly in the hypothalamus and optic chiasm, PMAs are more likely to

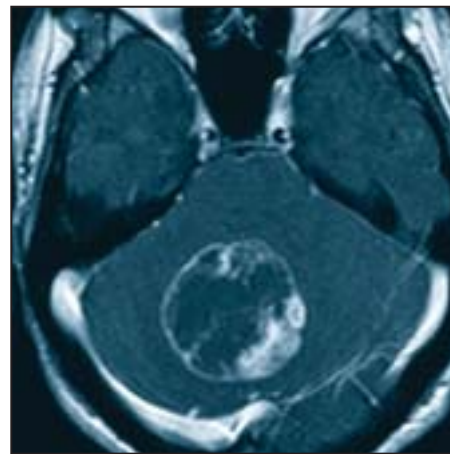
be located in the hypothalamic/optic chiasm region, according to Dr. Linscott. However, in this series, more than 40% of PMAs were found in atypical locations such as the cerebral cortex (4 of 21), cerebellum (2 of 21), basal ganglia (2 of 21), and area around the fourth ventricle (1 of 21). “These atypical locations are more common than previously reported and are more common in older patients,” said Dr. Linscott.

Intratumoral hemorrhage is another important distinguishing feature. Although evidence of hemorrhage was noted in 20% of PMAs, it is extremely rare in PCAs, according to Dr. Linscott.

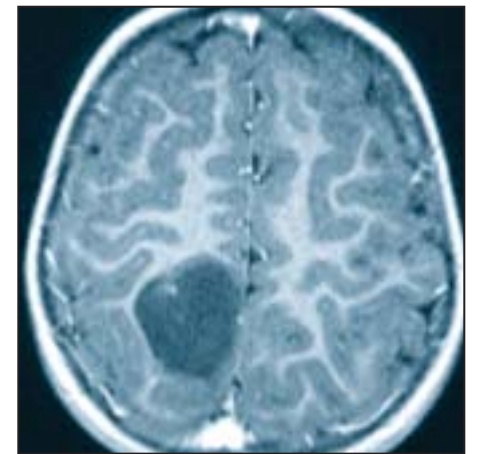
Rim enhancement on contrast-enhanced CT is also characteristic of PMA. In this series, 48% of cases showed heterogeneous rim enhancement, 43% showed uniform enhancement, and 9% showed no enhancement at all. Two cases showed cerebrospinal fluid dissemination.

Calcification is a characteristic finding of PCA. In this series, calcification was noted in only one case of PMA, making the diagnosis of PMA less likely, Dr. Linscott said.

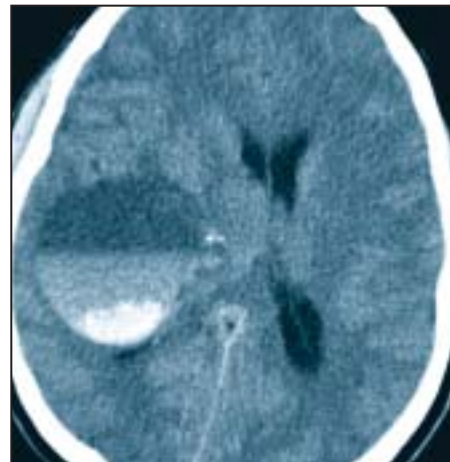
Identifying a PMA has important clinical consequences. Because PMA is a clinically more aggressive tumor than PCA, distinguishing between these two tumor types may change the surgical and medical management of the patient, including more aggressive adjuvant chemotherapy and radiotherapy. ■



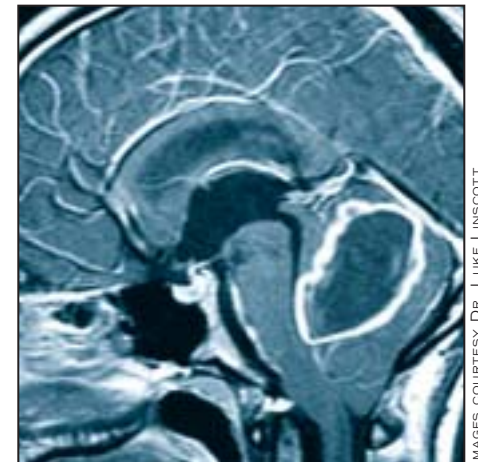
Cerebellar vermis tumor in 17-year-old boy on contrast-enhanced axial T1WI.



Axial T1WI shows nonenhancing posterior parietal tumor in a 2-year-old boy.



CT shows fluid-fluid levels in an acute intratumoral hemorrhage of a PMA.



T1 image with contrast shows teen's rim-enhancing lesion of the posterior fossa.

IMAGES COURTESY DR. LUKE LINSOTT

Early Results of Aricept Study Hint at Autism Improvement

BY BETSY BATES
Los Angeles Bureau

STANFORD, CALIF. — Preliminary analysis of a randomized, double-blind, placebo-controlled study of donepezil suggests the Alzheimer’s drug may slightly improve neuropsychologic function in children with autism, Dr. Antonio Hardan said at a pediatric update.

At the halfway point in a 20-week trial, improvements were seen in scores on some, but not all, neurocognitive tests among 10 autistic children aged 7-17 years receiving the drug, compared with 10 receiving placebo.

Specifically, children somewhat improved their performance on tests aimed at measuring spatial executive functioning (the Design Fluency Test), selective atten-

tion (the Color-Word Interference Test) and the California Verbal Learning Test.

“We didn’t see magic improvement or large improvements,” emphasized Dr. Hardan, director of the Autism and Developmental Disabilities Clinic at Lucile Packard Children’s Hospital of Stanford (Calif.) University. No improvement was seen on the Expressive One-Word Vocabulary Test, which measures language skills.

At the pediatric update, sponsored by Stanford University, Dr. Hardan emphasized that the trial is small and incomplete, and the results should be interpreted with caution. “But what is nice about this is it opens up a whole group of medications to study,” he said.

The use of donepezil (Aricept) in autism was first studied by Dr. Hardan at the University of Pittsburgh in an open-label study of eight children, half of whom demonstrated improvement on the Aberrant Behavior Checklist and Clinical Global Impression Scale. Improvements were suggested in irritability and hyperactivity, but not in inappropriate speech, lethargy, or stereotypies, he reported (*J. Child Adolesc. Psychopharmacol.*2002;12:237-41).

Another novel study is ongoing at Indiana University, Indianapolis, where a broad-spectrum antibiotic once used to treat tuberculosis led to improvement in social withdrawal in a pilot study. A randomized, double-blind study pitting d-cycloserine, a partial agonist of the N-methyl-D-Aspartate (NMDA) glutamate receptor subtype, against placebo is underway.

Although these are small studies, it is encouraging to see research into existing drugs to determine whether they might be effective in treating children with autism spectrum disorders, he said.

It took 15 years for risperidone (Risperdal) to be approved for autism-related irritability, noted Dr. Hardan.

Parents who must wait so long for drug approval feel they are “losing a lot of time,” he said. “That’s why they jump at any opportunity [to use a treatment, even one] that could be potentially hazardous for their child.”

Dr. Hardan stressed that research must be driven by theories that make scientific sense, followed by proof-of-concept studies to see whether evidence exists that an agent may be helpful.

He pointed to “the [high] price of shortcuts,” such as secretin, hailed as a possible treatment based on one uncontrolled observational study that hinted it may have improved behavior in three children undergoing gastrointestinal procedures. No verification was made to determine whether the children actually met diagnostic criteria for autism, he noted. “Based on this, secretin was unfortunately the most studied medication in autism.”

Fifteen randomized, double-blind studies eventually produced uniformly negative results.

The scientific community must “get realistic and not waste our resources,” when it comes to allotting funding for potentially beneficial treatments, he urged. ■

Is Autism Prevalence Truly on the Rise?

An apparent increase in the prevalence of autism and autistic spectrum disorders may be explained by differences in diagnosis, said Dr. Hardan.

Much of the increase in prevalence is among children with mild symptoms: children with high-functioning autism, Asperger’s syndrome, and pervasive developmental disorder, not otherwise specified.

“Fifteen or 20 years ago when somebody was verbal, it was very unlikely people were going to consider this an autism spectrum disorder,” he said. On the other hand, children with moderate to severe mental retardation were given that diagnosis in the past. Today many receive an autism diagnosis instead.

Traditionally, autism spectrum disorders were exclusively made in school-age children. “Now people in their 20s

and 30s who are struggling in daily living activities come to us and ask: ‘Do I have an autism spectrum disorder?’ Sometimes, some people do,” said Dr. Hardan. An adulthood diagnosis would have been unthinkable years ago.

Another contributor to the apparently increasing prevalence of autism is simple misdiagnosis, he said. Children with ADHD very often have social deficits, difficulties in developing peer relationships, and “poor coherence between visual and verbal behaviors.”

Children misdiagnosed as autistic include those with severe anxiety symptoms and early-onset personality disorders. Children with reactive attachment disorders, often adopted from overseas, have features that could mistakenly lead a clinician to diagnose autism, including severe social deficits and stereotypical behaviors, he said.