Hyperthyroidism in Kids Presents As Cardiac, Behavioral Symptoms

BY BETSY BATES

Cardiac symptoms in a child should raise a high index of suspicion of hyperthyroidism, based on the results of a single-center study that also found prominent behavioral and mood issues in many children with the diagnosis.

Hyperthyroidism was diagnosed in more than half the children referred for a work-up for cardiac symptoms, based on a retrospective chart study conducted at the University of California, Davis, by Dr. Lindsey Loomba-Albrecht, of the department of pediatric endocrinology, and her associates.

Further, cardiac symptoms—tachycardia/heart palpitations, shortness of breath on exertion, chest pain, and/or syncope—were present in nearly a quarter of 68 children diagnosed with hyperthyroidism over an 8-year period.

Goiter, weight loss, gastrointestinal and neurologic symptoms, and fever or heat intolerance were also represented as common presenting complaints among the diagnosed children, who ranged in age up to 18 years. A few were diagnosed as a result of screening laboratory tests or exophthalmos, Dr. Loomba-Albrecht reported at the Western regional meeting of the American Federation for Medical Research.

In pediatric textbooks, cardiac indications are listed as possible symptoms of hyperthyroidism but they appear far down on a list of symptoms that typically includes heat intolerance, emotional lability, short attention span, tremors, increased appetite, ophthalmologic symptoms, flushed skin, sweating, and muscle weakness.

"Delayed diagnosis occurred in many due to the time spent evaluating suspected cardiac disease," Dr. Loomba-Albrecht, said in an interview following the meeting.

Because of the high incidence of cardiac symptoms investigated in children with hyperthyroidism, Dr. Loomba-Albrecht and her associates are recommending that thyroid screening labs be considered in all children with cardiac symptoms.

Severe behavioral and mood symptoms were also strikingly common in the cohort, regardless of whether these symptoms brought the child to medical attention.

Mood and behavioral symptoms were the presenting concern in just 4 of 68 pediatric patients with hyperthyroidism, but 14 of the 68 (20.5%) had major psychological issues at the time of diagnosis, reported Dr. Loomba-Albrecht.

Four were in juvenile hall; seven had major depression, and three had demonstrated antisocial behavior (including one with concomitant severe anxiety).

The prevalence of mood and behavior disturbances in the children with hyperthyroidism was far greater than what was seen in gender-matched controls who were seen in the endocrinology clinic for pubertal or growth problems (20.5% vs. 1.5%), she noted.

"For comparison, 3% of children in the general population have a mood disorder and 1%-2% have generalized anxiety or panic disorder," she said.

Dr. Loomba-Albrecht highlighted the case of a 13-year-old boy brought into the emergency department with multiple injuries sustained while "car surfing," in which juveniles perform dangerous maneuvers while holding onto the outside of a vehicle.

During his stay in the emergency department, the teenager experienced sustained tachycardia "of unclear etiology." A CT scan of the neck revealed an enlarged thyroid gland, previously unnoticed because he had been placed in a protective cervical spine collar during transport.

Graves' disease was confirmed by a laboratory work-up.

Looking back, the boy's parents noted that his behavior had become quite erratic over the previous several months, resulting in plummeting school grades.

"The percent with behavioral problems prior to development of the hyperthyroidism is unknown, but the timing of symptoms suggests that the hyperthyroidism caused the behavior manifestations in most cases.

"Hyperthyroidism should thus be considered whenever a child is evaluated for behavior change," the team advised.

None of the researchers reported any conflicts of interest regarding the study. ■

Companies to Study Plavix's Inconsistency

BY ALICIA AULT

The Food and Drug Administration said that Sanofi-Aventis and Bristol-Myers Squibb Co. have agreed to conduct studies to better characterize the effectiveness of clopidogrel (Plavix) in patients with certain genetic factors. The two manufacturers also have said they will lead clinical trials to assess what effects other therapies, such as proton pump inhibitors, might have on clopidogrel's efficacy.

Several recent studies have raised doubts about the anticlotting agent's effectiveness in patients with certain genetic profiles. "The FDA is aware of published reports that clopidogrel is less effective in some patients than it is in others," said the agency.

According to the FDA's posting on its Web site, the two drug makers have agreed to complete the studies within a certain time frame. The agency did not elaborate but did say that, "it could take several months to complete the studies and analyze the results."

In the meantime, physicians should continue to prescribe clopidogrel, said the agency. Patients should not stop taking the drug but should talk with their physicians if they are currently taking a proton pump inhibitor or considering starting on one, including the over-the-counter omeprazole (Prilosec).

The agency cited six published reports looking at the effects of PPIs or certain polymorphisms on clopidogrel. Most were published in 2008. Missing from the FDA's reference list were three studies published at the end of December and in early January.

French researchers found that acute myocardial infarction patients with a CYP2C19 loss-of-function allele who took clopidogrel had a higher rate of cardiovascular events (N. Engl. J. Med. 2009;360:363-75). Another study found that patients with acute coronary syndromes who had the same polymorphism had lower levels of the active clopidogrel metabolite and thus a higher rate of cardiovascular events (N. Eng. J. Med. 2009;360:354-62).

A third study found that, in patients under age 45 years with the same polymorphism, clopidogrel also was less effective (Lancet 2009;373:309-17). ■

Aldosterone Blockers Viewed as Key Drugs in Obese Patients

BY MITCHEL L. ZOLER

NEW YORK — Two aldosterone receptor blocking drugs—spironolactone and eplerenone—have almost overnight become important, second-line antihypertensive drugs for obese patients.

"Aldosterone receptor blockers were never on the list [of major antihypertensive drug choices], and now [they're] listed as fourth line, but for me, in the subgroup of obese patients, [they're] second line," Dr. George L. Bakris said in an interview at a meeting sponsored by the American Diabetes Association.

"In obese patients I'll start them on a couple of drugs but [if they remain above their goal blood pressure], the second or certainly the third drug will be an aldosterone receptor blocker," said Dr. Bakris, professor of medicine and director of the hypertensive diseases unit at the University of Chicago.

His most common choice is spironolactone, given at the relatively low dosage of 25 mg b.i.d. At this low level gynecomastia, a common adverse effect of the drug, usually doesn't occur, he said. An alternative is to use eplerenone, which causes an even lower level of gynecomastia but also costs more than spironolactone, even though eplerenone is now available as a generic formulation.

If they remain above their goal blood pressure, the second or third drug should be an aldosterone receptor blocker.

DR. BAKRIS

With this treatment, Dr. Bakris said he has seen some obese patients respond with a systolic blood pressure reduction of more than 20 mm Hg. The treatment can also help resolve the mild hypokalemia that these patients may have because of an unusual form of a mild, secondary hyperaldosteronism that they develop because of their obesity. In fact, aldosterone receptor blockers were first used in patients of this sort in the early 2000s at the University of Alabama specifically to treat their hypokalemia. Dr. David A. Calhoun and his colleagues, who did this work, found that the treatment also led to huge blood pressure reductions, Dr. Bakris said (Am. J. Hypertens. 2003;16[pt.1]:925-30).

Subsequent basic sciences studies have determined what's going on. Subcutaneous adipocytes are not simply passive fat stores but function as a "miniendocrine organ," releasing a variety of enzymes called adipokines. A series of adipokine-triggered enzymes activate angiotensin II release and boost the sensitivity of adrenocortical cells, triggering aldosterone secretion and producing the mild hyperaldosteronism state, he explained (Int. J. Obesity 2007;31:1605-16).

This condition can occur in people with a body mass index of 30 kg/m^2 or higher, although it seems like the higher the body mass index, the more common the condition becomes. In these patients another frequent consequence of obesity is sleep apnea, which itself causes a dramatic increase in blood pressure that may be very responsive to treatment with continuous positive airway pressure.

A role for aldosterone receptor blockade in treating hypertension in obese patients began to appear recently in expert guidelines, such as a position paper on treating hypertension in patients with diabetes from the American Society of Hypertension that was published last September (J. Clin. Hypertens. 2008;10:707-13).

Dr. Bakris also said it is possible that adipocyte-triggered hyperaldosteronism and hypertension might even appear occasionally in leaner individuals. "I don't think it's necessarily the amount of fat, but the company it keeps—the metabolic milieu. How the patient got these cells is the key, and right now we don't know the details," he said. ■

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