Study examines use of bevacizumab among patients with hereditary blood vessel disorder

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In a small study that included 25 patients with hereditary hemorrhagic telangiectasia (a genetic disorder that leads to abnormalities of blood vessels) and severe liver involvement with this disease, patients who received the drug bevacizumab had improved cardiac output and a reduction in the duration and number of episodes of nose bleeds, a potentially life-threatening complication for patients with this disorder, according to a study in the March 7 issue of *JAMA*.

Hereditary hemorrhagic telangiectasia (HHT) is a dominantly inherited genetic vascular disorder that may affect many organs, including the lungs, gastrointestinal tract, liver, and brain. Hepatic (liver) involvement is observed in up to 74 percent of patients, with liver vascular malformations resulting in several complications, including high output cardiac failure, according to background information in the article.

Sophie Dupuis-Girod, M.D., Ph.D., of Hopital Louis Pradel, Bron, France, and colleagues analyzed the efficacy of the drug bevacizumab in severe hepatic forms of HHT associated with high cardiac output. Bevacizumab is an anti-vascular endothelial growth factor treatment that is thought to be potentially effective for treatment for HHT. The single-center, phase 2 trial included 25 patients who had confirmed HHT, severe liver involvement, and a high cardiac index related to HHT. Participants received bevacizumab every 14 days for a total of 6 injections. The total duration of the treatment was 2.5 months; patients were followed up for 6 months after the beginning of the treatment. The primary outcome measure for the study was a decrease in cardiac output

at 3 months after the first injection, evaluated by echocardiography.

Of the 24 patients who had echocardiograms available for reread, there was a response in 20 of 24 patients with normalization of cardiac index (complete response) in 3 of 24, partial response in 17 of 24, and no response in 4 cases. The median (midpoint) cardiac index at the beginning of the treatment significantly decreased after 3 months. The median cardiac index at 6 months was significantly lower than before treatment. Average duration of epistaxis (bleeding from the nose), which was 221 minutes per month at inclusion, had significantly decreased at 3 months (134 minutes) and 6 months (43 minutes). Quality of life also significantly improved.

"In conclusion, this preliminary study suggests that bevacizumab may be a therapeutic option in the treatment of HHT. Our results demonstrated improved cardiac output and reduced epistaxis. Toxicity was moderate. We do not know if this treatment could be definitive or a bridging therapy while patients are waiting for a liver transplant. Longer follow-up studies are necessary to determine the duration of HHT efficacy and whether maintenance therapy is required," the authors write.

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