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장기간 Sunitinib 복용 후 발생한 만성 혈전미세혈관병증

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Histologically Documented Chronic Thrombotic Microangiopathy Secondary to Sunitinib

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Inhibition of vascular endothelial growth factor (VEGF) signaling has become an innovative therapy in solid cancer. However, the VEGF antagonists can induce renal side effects because VEGF pathway expressed in the kidney is also blocked. Bevacizumab, recombinant humanized monoclonal antibody that target soluble VEGF, is well known to induce proteinuria, hypertension as well as thrombotic microangiopathy. Sunitinib can interrupt several tyrosine kinase receptors, including VEGF receptors. We report a case of histologically documented thrombotic microangiopathy (TMA) after treatment with sunitinib.

A 75 years old man with progressive azotemia was referred to nephrologist. The patient had a medical history of hypertension. 4 years earlier, he had undergone small bowel resection for bowel perforation by gastrointestinal stromal turmor (GIST). And he received imatinib therpay for liver metastasis. When imatinib therapy was initiated, there were mild azotemia (glomerular filatration rate 53.9 mL/min/1.73m^2) on blood tests and trace proteinuria on dipstick urine analysis (specific gravity 1.014). 2 years earlier, the treatment was changed to sunitinib due to resistance for and skin toxicity by imatinib. Sunitinib was given daily 50mg on a 4-week-on and 2-week-off schedule. His blood pressure and renal function were stable. However, because of hand-foot syndrome, dose of sunitinib tapered slowly and was changed to daily 25mg on a 2-week-on and 1-week-off schedule 19 weeks after treatment with sunitinib. His blood pressure began to rise. 7 months later, dipstick urine analysis showed proteinuria 3+. 22 months after initiation of sunitinib, glomerular filatration rate deteriorated to 31.8 mL/min/1.73m^2 and the protein/creatinine ratio in a random urine was 3.42 mg/mg. A renal biopsy was performed to evaluate the cause of aggravation of proteinuria and renal impairment. Light microscopy study showed capillary loops thickened with subendothelial widening and double contour, mesangiolysis, mild tubular atrophy with interstitial fibrosis. Immunofluorescence study revealed IgG, IgM, C1 and C4 depostis. Electronic microscopy demonstrated subendothelial widening associated with electron dense deposits. Diffuse effacement of epithelial foot process was also seen. Signs of hemolysis and thrombocytopenia were not detected on blood tests. The diagnosis of TMA was confirmed histologically, and sunitinib was discontinued.

Key Words : Sunitinib, 혈전미세혈관병증
Sunitnib, Thrombotic microangiopathy