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Case Report

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Gastric Antral Vascular Ectasia as a Rare Complication of Nintedanib in Fibrotic Lung Disease: A Case Report

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Key words:
Gastric antral vascular ectasia GAVE; Upper gastrointestinal bleeding; Anemia; Fibrosing interstitial lung disease (ILD); Anti-fibrotic therapy; Tyrosine kinase inhibitor; Argon plasma coagulation (APC).

Abstract:

Nintedanib is an oral tyrosine kinase inhibitor targeting VEGF, PDGF, and FGF receptors and is approved for idiopathic pulmonary fibrosis and other fibrosing interstitial lung diseases. Gastrointestinal adverse events are common, but severe upper gastrointestinal bleeding and gastric antral vascular ectasia (GAVE) are rarely described. A 76 year old woman with fibrosing interstitial lung disease, treated with nintedanib 150 mg twice daily for over two years, presented with melena, dyspnea, edema, and profound anemia (hemoglobin 4.0 g/dL). Endoscopy revealed classic GAVE, successfully treated with argon plasma coagulation. Extensive evaluation excluded cirrhosis, systemic sclerosis, malignancy, peptic ulcer disease, and other secondary causes of GAVE. Nintedanib was discontinued, after which melena resolved and hemoglobin stabilized without recurrence of bleeding. Given nintedanib's anti VEGF and anti PDGF effects and prior case reports of GAVE under nintedanib and other TKIs, a probable causal association was considered. This case highlights GAVE as a rare but potentially life threatening and under recognized complication of long term nintedanib therapy and underscores the need for vigilance and early endoscopic evaluation in antifibrotic treated patients presenting with unexplained anemia or upper GI bleeding.

Introduction

Nintedanib is an orally administered tyrosine kinase inhibitor (TKI) targeting multiple pathways including vascular endothelial growth factor (VEGF), platelet-derived growth factor (PDGF), and fibroblast growth factor (FGF). It is one of the two FDA approved medications available for idiopathic pulmonary fibrosis (IPF) till now[1]. The most frequently reported adverse effects are gastrointestinal, including diarrhea, nausea, elevated liver enzymes, and weight loss[2,3]. However, gastrointestinal bleeding, particularly due to gastric antral vascular ectasia (GAVE), is extremely rare.

GAVE is an uncommon cause of upper gastrointestinal (GI) bleeding, characterized endoscopically by red, dilated blood vessels in the

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gastric antrum arranged in a striped pattern (often said "watermelon stomach"). Its pathogenesis remains unclear but is thought to involve mucosal ischemia and increased mucosal VEGF expression. While GAVE has been associated with systemic sclerosis, cirrhosis, and chronic renal failure[4], its occurrence in patients on antifibrotic therapy such as nintedanib is rarely documented in literature.

Here, we report a case of life-threatening anemia due to GAVE in an elderly female with diffuse parenchymal lung disease (DPLD) who had been receiving nintedanib. We review the proposed mechanisms and prior reports, emphasizing the need for vigilance in antifibrotic-treated patients.

Case Report

A 76-year-old female with a diagnosis of DPLD (radiologically and clinically consistent with fibrosing ILD) since 2022 had been on nintedanib 150 mg twice daily for over two years. She had mild baseline symptoms including intermittent dry cough and exertional dyspnoea, and she had tolerated the medication well without dose modification.

She presented to the Respiratory Medicine Department of Bangladesh Specialized Hospital with complaints of progressively worsening shortness of breath over one week, multiple episodes of melena, and bilateral lower limb swelling. Her oxygen saturation was 87% on room air. She was pale, tachypneic, and had bilateral pedal edema, respiratory examinations revealed bilateral basal crackles.

Initial investigations showed: Hemoglobin: 4.0 g/dL, Mean Corpuscular Volume (MCV): 87, Platelets: Normal, Reticulocyte count: Elevated (suggestive of ongoing blood loss), Liver and renal function: Normal, NT-proBNP: 9500 pg/mL, Chest X-ray: Bilateral pleural effusions along with ground glass opacities, honeycombing, traction bronchiestesis. She was managed with oxygen, transfusion of packed red blood cells, and intravenous furosemide. Following hemodynamic stabilization, an upper GI endoscopy was performed, which revealed gastric antral vascular ectasia (GAVE) — multiple ectatic vessels in a linear pattern in the antrum. Argon plasma coagulation (APC) was done successfully.

Other potential causes of anemia, including gastrointestinal malignancy, peptic ulcer, chronic liver disease, megaloblastic anemia, varices, and parasitic infections, were excluded. Colonoscopy was normal. There was no history of NSAID or anticoagulant use. Autoimmune screen was negative, ruling out any connective tissue disease. Liver ultrasound was normal, and there was no evidence of bleeding disorder.

Given the absence of underlying connective tissue or hepatic disease, and the long-term use of nintedanib with known anti-VEGF activity, a causative link between nintedanib and GAVE was considered plausible. The medication was discontinued.

The patient's melena resolved, and she remained hemodynamically stable. At 2-month follow-up, she reported no recurrence of GI symptoms, had stable hemoglobin (~11.5 g/dL), and her respiratory symptoms remained unchanged.

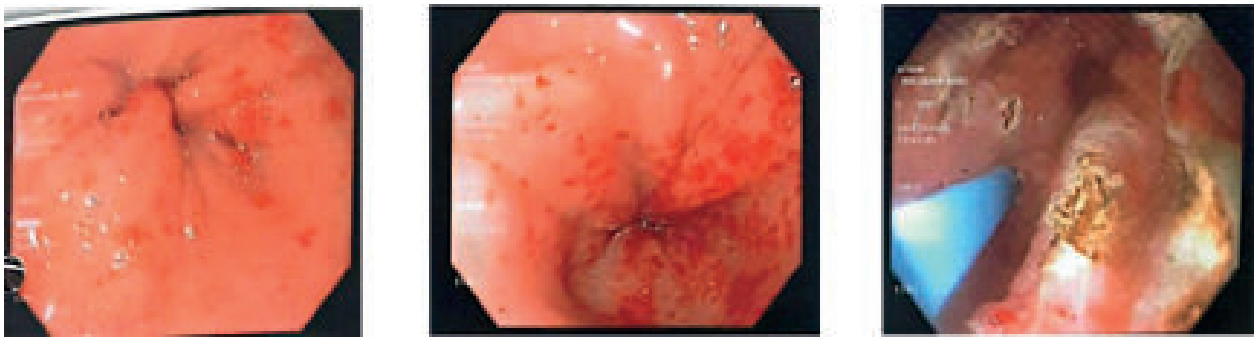

Fig.: *Upper gastrointestinal endoscopy demonstrating numerous vascular ectatic lesions localized to the gastric antrum, consistent with GAVE, last one showing argon plasma coagulation (APC) of the lesions.*

Discussion

The pathogenesis of GAVE involves mucosal vascular ectasia, which may arise due to impaired gastric mucosal perfusion, mechanical stress, or elevated local VEGF levels[4,5]. Nintedanib's inhibition of VEGFR could theoretically lead to microvascular injury or aberrant mucosal angiogenesis contributing to GAVE. Additionally, PDGF inhibition may impair mucosal repair, exacerbating vascular injury. Ogawa et al. (2021) reported a patient with idiopathic pulmonary fibrosis (IPF) who developed recurrent GAVE after starting nintedanib, with bleeding resolving after drug discontinuation[6]. Kuwano et al. (ERS 2019) presented a case series of suspected nintedanib-related gastric bleeding, one of which was confirmed as GAVE endoscopically[7]. Another Japanese retrospective study noted rare but serious GI bleeding events in IPF patients on nintedanib but lacked histologic confirmation of GAVE[8].

These findings suggest GAVE is an exceedingly rare but potentially under-recognized complication of antifibrotic therapy.

Common causes of upper GI bleeding were ruled out in our patient. There was also no exposure to medications known to cause GAVE (e.g., chemotherapeutics, immunosuppressants). Thus, the temporal relationship with long-term nintedanib, the known anti-angiogenic mechanism, and the resolution upon withdrawal support a probable causal association.

Conclusion:

Nintedanib has a well established gastrointestinal toxicity profile dominated by diarrhea and mild bleeding, while serious upper GI bleeding is uncommon. This case adds to emerging evidence that GAVE can occur in association with long term nintedanib exposure and, similar to other TKIs, may resolve after drug withdrawal. Clinicians should consider GAVE in nintedanib treated patients with iron deficiency anemia or melena, promptly arrange endoscopy, and weigh drug discontinuation or modification if GAVE is confirmed. Early recognition may prevent life threatening hemorrhage while allowing individualized decisions about ongoing antifibrotic therapy.

Conflict of Interest:

The authors stated that there was no conflict of interest in this study

Funding:

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Consent:

For the purpose of publishing this case report and any related photos, the parents were written informed consent was acquired.

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References:

1. Richeldi L, du Bois RM, Raghu G, et al. Efficacy and Safety of Nintedanib in Idiopathic Pulmonary Fibrosis. *N Engl J Med*. 2014;370(22):2071–2082.
2. Corte TJ, Bonella F, Crestani B, et al. Safety of nintedanib in patients with progressive fibrosing interstitial lung diseases: data from the INBUILD trial. *Respir Res*. 2020;21(1):147.
3. Maher TM, Corte TJ, Fischer A, et al. Pirfenidone in patients with unclassifiable progressive fibrosing interstitial lung disease: a double-blind, randomized, placebo-controlled, phase 2 trial. *Lancet Respir Med*. 2020;8(2):147–157.
4. Sebastian S, O'Morain CA, Buckley M. Review article: current therapeutic options for gastric antral vascular ectasia. *Aliment Pharmacol Ther*. 2003;18(2):157–165.
5. Junquera F, Saperas E, De Torres I, et al. Increased expression of vascular endothelial growth factor in gastric antral vascular ectasia (watermelon stomach). *Endoscopy*. 2003;35(5):391–395.
6. Ogawa K, Miyake Y, Takeda K, et al. A case of gastric antral vascular ectasia induced by nintedanib in a patient with idiopathic pulmonary fibrosis. *Respirol Case Rep*. 2021;9(9):e00829.
7. Kuwano K, et al. Gastric antral vascular ectasia in nintedanib-treated patients with IPF. *Eur Respir J*. 2019;54(Suppl 63):PA4207.
8. Mouri K, Saito Y, Suzuki S, et al. Gastrointestinal bleeding in patients receiving nintedanib for idiopathic pulmonary fibrosis. *Respir Investig*. 2017;55(3):229–232.