Case Report

Access this article online

Quick Response Code:

Website: www.ijhonline.org

DOI: 10.4103/ijh.ijh_20_22

Pernicious anemia with unusual associations

C. A. Mansoor

Abstract:

Pernicious anemia (PA) is an autoimmune disease due to vitamin B12 deficiency secondary to Intrinsic Factor deficiency. A 65-year-old man presented with left lower limb swelling and pain for one week. He had loss of appetite and fatigue for one month. Investigations showed lower limb deep vein thrombosis and bicytopenia. On further evaluation, he was found to have PA, duodenal carcinoids, and primary biliary cirrhosis. He was managed with heparin (followed by warfarin), parenteral Vitamin B12, and ursodeoxycholic acid. He was referred to the gastroenterology department for management of duodenal carcinoid. On follow-up his blood counts were normal. We present a patient with PA who had three unusual associations simultaneously at the time of presentation which was never reported in the literature previously, to the best of our knowledge.

Keywords:

Deep vein thrombosis, duodenal carcinoids, pernicious anemia

Introduction

Pernicious anemia (PA) is an autoimmune disease due to vitamin B12 deficiency secondary to Intrinsic Factor deficiency. Venous thromboembolism, hyperhomocysteinemia, gastric neuroendocrine cell disorders, and liver disorders (primary biliary cholangitis, autoimmune hepatitis, and Interferon-treated hepatitis C) are diseases that have an association with PA. We report a patient who had all these complications together at the time of presentation.

Case Report

A 65-year-old man presented with left lower limb swelling and pain for 1 week. He had loss of appetite and fatigue for 1 month. He had type 2 diabetes mellitus (on glimepiride and metformin) and hypertension (on cilnidipine) for 10 years. He was not a smoker and had no other addictions. On examination, he had pallor and left lower limb swelling. The rest of the examination was unremarkable.

Hemoglobin was 3.4 g/dl (macrocytic), total leukocyte count 4900/ml, platelet count 67,000/ml, and erythrocyte sedimentation rate 45 mm in1 h. Peripheral smear showed macrocytic red blood cells, leukopenia, hypersegmented neutrophils [Figure 1a], and thrombocytopenia but there were no immature or abnormal cells. Biochemical parameters were normal except for high alkaline phosphatase and hypoalbuminemia. The chest X-ray was normal. Ultrasonography of the abdomen showed chronic liver disease, splenomegaly, and mild bilateral pleural effusion. Lower limb venous Doppler revealed deep vein thrombosis. HIV, hepatitis B, and hepatitis C serology were negative. Antimitochondrial antibody was positive but other autoantibodies for autoimmune hepatitis were negative.

Bone marrow aspirate showed marked erythroid hyperplasia with megaloblastic maturation [Figure 1b]. Bone marrow

Department of General Medicine, Nizar Hospital, Valanchery, Kerala, India

Address for correspondence:
Prof. C. A. Mansoor, Department of General Medicine, Nizar Hospital, Valanchery, Kerala, India.
E-mail: drcamans@gmail.com

Submission: 27-04-2022
Accepted: 30-05-2022
Published: 25-10-2022

How to cite this article: Mansoor CA. Pernicious anemia with unusual associations. Iraqi J Hematol 2022;11:189-91.

biopsy showed erythroid hyperplasia with megaloblastic maturation and reduced megakaryocytes [Figure 1c]. Upper gastrointestinal endoscopy showed antral gastritis, multiple large sessile nodular lesions of about 1 cm size in the duodenum, and hiatus hernia. There were no esophageal varices. The plasma level of cobalamin was low (125 pg/ml. normal range 211–911), folate was normal and homocysteine level was high 46.78 μmol/L (normal range 5.46–16.20). Anti-intrinsic factor and parietal cell antibodies were positive. Endoscopic biopsy showed a well-differentiated neuroendocrine tumor (enterochromaffin-like cell hyperplasia strongly positive for synaptophysin) with no evidence of invasion of the muscularis layer [Figure 1d]. His blood coagulation profile was normal. There was a heterozygous mutation in the methylenetetrahydrofolate reductase (MTHFR 677) gene. The immunoglobulin G (IgG) and IgM anti-cardiolipin antibodies, IgG and IgM beta2 glycoprotein, and lupus anticoagulant tests were negative. Factor V Leiden and prothrombin G20210A were not detected. His serum levels of protein C and protein S were normal.

The patient was diagnosed to have pernicious anemia (PA) (megaloblastic anemia and positive anti-intrinsic factor and parietal cell antibodies) with deep vein thrombosis, primary biliary cirrhosis (chronic liver disease, high alkaline phosphatase, and positive antimitochondrial antibody), and nonfunctioning duodenal carcinoids (histopathology). He was managed with heparin (followed by warfarin), parenteral Vitamin B12, and ursodeoxycholic acid. He was referred to the gastroenterology department for management of duodenal carcinoid. On follow-up, his blood counts were normal.

Discussion

PA is autoimmune gastritis due to the destruction of gastric parietal cells by intrinsic factor and parietal cell antibodies resulting in intrinsic factor deficiency. The prevalence of PA is 0.1% in the general population, which can be up to 1.9% in the elderly population.[1]

Venous thrombosis (deep vein thrombosis and pulmonary embolism) was reported in association with PA previously.[2] B12 deficiency has prothrombotic potential which is secondary to increased plasma levels of homocysteine. Several cases of PA presenting as venous thrombosis was reported previously.[3] Homocysteine causes decreased binding of antithrombin III to endothelial heparan sulfate, an increased affinity between lipoprotein (a) and fibrin, induction of tissue factor activity in endothelial cells, and inhibition of inactivation of factor V by activated protein C.

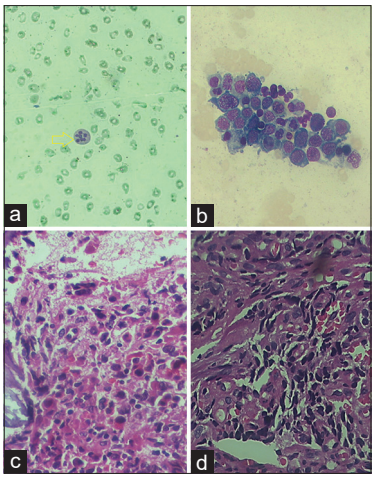

Figure 1: Peripheral smear showing macrocytic red blood cells and hypersegmented neutrophils (a). Bone marrow aspirate showing marked erythroid hyperplasia with megaloblastic maturation (b). Bone marrow biopsy showed erythroid hyperplasia with megaloblastic maturation (c). Endoscopic biopsy showing neuroendocrine tumor (d)

The association between PA and various liver diseases has been rarely reported. Primary biliary cholangitis (PBC), autoimmune hepatitis, interferon-treated hepatitis C, and cryptogenic cirrhosis were previously reported in association with PA.[4] PBC is a chronic immune-mediated disease that can coexist with other extrahepatic autoimmune manifestations. Cases reporting co-existence between PA and PBC are extremely rare in the literature.[5]

Patients diagnosed with PA have an increased risk of developing gastrointestinal malignancies such as gastric adenocarcinoma, carcinoid tumors, or esophageal squamous cell carcinoma.[6] PA associated with gastric carcinoids was reported previously several times. Duodenal carcinoids account for less than 2% of all gastrointestinal carcinoids.[7] The association of duodenal carcinoid with PA was not reported previously.[8]

Conclusion

Our patient presented with lower limb deep vein thrombosis and bicytopenia. On further evaluation, he was found to have PA, duodenal carcinoids, and primary biliary cirrhosis. This case reminds the readers of the unusual associations of PA. We present a patient with PA who had three unusual associations simultaneously during the presentation. To the best of our knowledge, this was never reported in the literature previously.

Compliance with ethical standards

All procedures performed in studies involving human participants were by the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards.

Informed consent

Informed signed written consent was taken from the patient involved.

Acknowledgment

I would like to thank Dr. Asik siddik of pathology whose comments and suggestions were immensely valuable for improving this case report.

Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent forms. In the form, the patient has given his consent for his images and other clinical information to be reported in the journal. The patient understand that name and initials will not be published and due efforts will be made to conceal identity, but anonymity cannot be guaranteed.

Financial support and sponsorship

Nil.

Conflicts of interest

There are no conflicts of interest.

References

1. Yousaf F, Spinowitz B, Charytan C, Galler M. Pernicious anemia associated cobalamin deficiency and thrombotic microangiopathy: Case report and review of the literature. Case Rep Med 2017;2017:9410727.
2. Ammouri W, Tazi ZM, Harmouche H, Maamar M, Adnaoui M. Venous thromboembolism and hyperhomocysteinemia as first manifestation of pernicious anemia: A case series. J Med Case Rep 2017;11:250.
3. Melhem A, Desai A, Hofmann MA. Acute myocardial infarction and pulmonary embolism in a young man with pernicious anemia-induced severe hyperhomocysteinemia. Thromb J 2009;7:5.
4. Yan X, Gao R, Hu Y, Jin J. Pernicious anemia associated with cryptogenic cirrhosis: Two case reports and a literature review. Medicine (Baltimore) 2018;97:e12547.
5. Shizuma T. Pernicious anemia in patients with primary biliary cirrhosis, autoimmune hepatitis, and chronic viral hepatitis. J Liver 2015;4:2167-0889.
6. Toh BH, Chan J, Kyaw T, Alderuccio F. Cutting edge issues in autoimmune gastritis. Clin Rev Allergy Immunol 2012;42:269-78.
7. Spoelstra-de Man AM, Wagenaar SS, van der Sluys Veer A, Brouwer CB. Relationship between pernicious anaemia and gastric neuroendocrine cell disorders. Neth J Med 2000;56:56-62.
8. Abraham A, Singh J, Siddiqui G, Prasad A, Rashid S, Vardaros M, ***et al.*** Endoscopic management of a primary duodenal carcinoid tumor. Case Rep Gastroenterol 2012;6:135-42.