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Case Report

Localized gastric amyloidosis in a patient diagnosed with Hodgkin lymphoma- A case report and review of literature

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ABSTRACT

Gastrointestinal amyloidosis (GIA), a protein deposition disorder, has numerous etiologies and manifestations and poses a significant diagnostic and treatment challenge. GIA is either acquired or genetic, and it is most commonly caused by chronic inflammatory disorders (AA amyloidosis), hematologic malignancy (AL amyloidosis), and end-stage renal disease (Beta-2 amyloidosis). In AL amyloidosis, the amyloid forming protein is derived from the light chain component of a protein in the blood called monoclonal immunoglobulin. These light chains are produced by abnormal cells (known as plasma or B cells) found in the bone marrow. AL amyloidosis can be caused by abnormal light chains produced by lymphomas or chronic lymphocytic leukaemia(CLL) in rare cases. Hodgkin lymphoma has been found to be associated with systemic amyloidosis and particularly with renal amyloidosis with an incidence of less than 1%.

Here we report a rare case of a 61-year old female patient who was previously diagnosed with Hodgkin lymphoma and underwent chemotherapy, now presented with anemia, dypnoea and was found to have a non healing ulcer in the body of the stomach. Histopathological examination revealed gastric amyloidosis which was confirmed with Congo red stain and apple green birefringence under polarized light.

1. Introduction

Amyloidosis is an abnormal intercellular deposition of insoluble proteins in an abnormal fibrillar, β-pleated sheet format.[1,2] It can be caused by a wide range of disorders, resulting in impairment or even dysfunction of the organs involved.[1] The conditions involved include chronic inflammatory disorders (AA amyloidosis), hematologic malignancy (AL amyloidosis), and end-stage renal disease (Beta-2 amyloidosis).[3]

Immunoglobulin-derived light chain (AL amyloidosis), serum amyloid A (AA amyloidosis, an acute phase reactant), beta-2 microglobulin (Aβ2m, dialysis-related), and apolipoprotein E (Alzheimer's related) are the most commonly acquired amyloid precursors. The most common cause of acquired amyloidosis is a hyperproteinemic state caused by either plasma cell dyscrasia (AL) or a chronic inflammatory state (AA) but 2–4% of cases arise in the setting of a B-cell lymphoma. Acquired amyloidosis most commonly manifests later in life, between 45-64 years of age.

In the GI tract amyloid deposition occurs in the muscularis mucosae, close to vasculature, nerves, and nerve plexuses. This deposition increases the frailty of blood vessels, hinders intrinsic peristalsis and decreases the compliance of the gut wall.[3]

Amyloidosis can be localized or systemic. Organs commonly involved by amyloidosis are heart, kidney, gastrointestinal tract, and tongue. Establishing the type of amyloidosis is essential for treatment and prognosis.[2]

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Localized amyloidosis is less common. Further, localized primary gastric amyloidosis is a still rarer disorder that can be mistaken for gastrointestinal stromal tumours, gastric cancer, and ulcers during endoscopic examinations.

Here we report a rare case of a 61-year old female patient who was previously diagnosed with Hodgkin lymphoma and underwent chemotherapy, now presented with anemia and was found to have a non-healing ulcer in the body of the stomach on OGD scope. Histopathological examination of the ulcer site, revealed gastric amyloidosis which was confirmed with Congo red stain and classic green birefringence under polarized light.

2. Case Report

61 year old female patient complained with increased tiredness and breathing difficulty with facial puffiness and pedal edema. She is a known case of Hodgkin Lymphoma (post chemotherapy), hypertension, obstructive airway disease hypothyroidism, esophageal varices and Chronic liver disease. On examination vitals were stable. Laboratory findings showed Hb-7.2g/dl. Peripheral smear showed normocytic normochromic anemia. Due to her chronic liver disease she was found to have hypoalbuminemia and was sorted for gastroenterological consultation which was followed up with a OGD scope showing esophageal varices and an ulcer in the lesser curvature of body of stomach. A CECT abdomen revealed-eccentric wall thickening along the lesser curvature and anterior wall of stomach with a possibility of a neoplasm rendering the findings and was advised a histopathological examination of the ulcer site.

H&E sections (Figure 1 A) showed fragments of gastric foveolar epithelium with focal areas showing regenerative atypia along with separate fragments of tissue showing oxyntic glands and necrotic tissue. Lamina propria shows homogenous glassy eosinophilic material deposited around blood vessels. No evidence of any malignancy seen. Congo red staining (Figure 1 B&C) was done and showed apple green birefringence thus confirming the diagnosis of amyloidosis.

3. Discussion

Amyloidosis is caused by a group of heterogeneous diseases that involve the deposition of insoluble proteins in various organs and can ultimately lead to multiple organ failure. It includes six types: Primary, secondary, hemodialysis-related, hereditary, senile, and localized amyloidosis.

With an estimated incidence of 9 cases per million inhabitants per year, AL amyloidosis is the most common type of systemic amyloidosis in developed countries. The average age of diagnosed patients is 65 years, and less than 10% of patients are under the age of 50.[4]

Primary AL amyloidosis is associated with the presence of monoclonal light chains in the serum and / or urine,

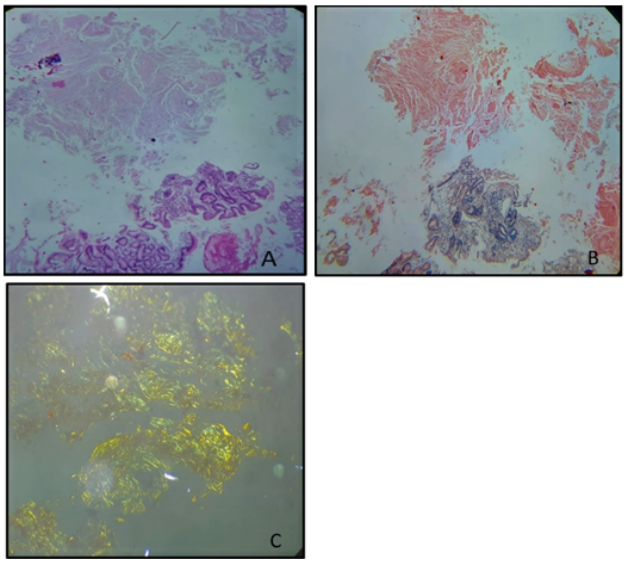

Fig. 1: A: H&E sections(10x); **B:** Congo red stain(10x); **C:** Apple green birefringence under polarised light(40x)

and it was found to be associated with multiple myeloma. The prevalence of AL amyloidosis rises with age. It is frequently associated with proteinuria, cardiac amyloidosis, and peripheral neuropathy.[5]

Hodgkin's disease has frequently been linked to hyperimmunoglobulinemia which was validated by Arends et al.[6] Hematological malignancies most often result in secondary amyloidosis and has a systemic involvement. According to a study conducted by Champion and Richards they found an association with Hodgkin and systemic amyloidosis.[7] In a study conducted by Falkson et al. only 53 cases of Hodgkin's disease in which the concurrent existence of amyloidosis was found.[8] Much literature about localized amyloidosis in association with hematological malignancies, particularly Hodgkin lymphoma was not elucidated.

The gastrointestinal tract is one of the most commonly involved regions in systemic amyloidosis[1] with the duodenum and stomach being commonly involved sites. The gastrointestinal tract is frequently involved in patients with systemic amyloidosis. In a 13-year single-center referral study including 2334 patients with all types of amyloidosis, Cowan et al. reported that 75 patients (3.2%) had biopsy-proven amyloid with gastrointestinal involvement.[9]

Localized gastric amyloidosis present with a clinical picture of epigastric pain, nausea, vomiting hematemesis, non-healing ulcers, and even perforation because of involvement of local autonomic nervous system and gastric wall structure damage.[10,11]

Diagnosis is made with the combination of endoscopic findings that include thickened irregular gastric folds,

gastric outlet obstruction, loss of rugal folds, gastric ulcers with clean bases or irregular edges, granular-appearing mucosa, plaque-like lesions ulcerative gastritis, healing gastric ulcer and gastroparesis have been reported. [12]

Pathological analysis is the gold standard for the diagnosis of gastric amyloidosis. In AL amyloidosis, there is greater amyloid deposition in the muscularis mucosa, submucosa, and muscularis propria close to vasculature, nerves, and nerve plexuses. This deposition increases the frailty of blood vessels, impairs intrinsic peristalsis and decreases the compliance of the gut wall. [3,13] H&E staining reveals extensive amyloid deposition in the mucosal or submucosal layers. Congo red staining and polarised light microscopy confirmation of apple-green birefringence in the lesions provide a sufficient diagnosis for AL amyloidosis.

Our case was confirmed for a localized amyloidosis with comparable findings on pathological examination. With the available literature search, an association could be formulated between amyloid deposition, with propensity for the gastrointestinal system, particularly the stomach and lymphoproliferative disease.

4. Conclusion

Localized gastric amyloidosis is a rare disease when compared to systemic amyloidosis and its potential to mimic a carcinoma warrants a thorough examination which should be collaborated with clinical history and laboratory investigations to find any predisposing causes for the same. Further, localized amyloidosis in conjunction with a lymphoproliferative disorder is a still rarer finding and so patient should be counselled and followed up for relevant signs and symptoms caused by deposition of these insoluble proteins amounting to any organ damage.

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6. Conflicts of Interest

There are no conflicts of interest.

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