IOSR Journal of Dental and Medical Sciences (IOSR-JDMS)
e-ISSN: 2279-0853, p-ISSN: 2279-0861.Volume 22, Issue 10 Ser.4 (October. 2023), PP 48-51
www.iosrjournals.org

A Rare Coexistence Of Duodenal Gastrointestinal Stromal Tumor With Hemophilia A

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Abstract:-
Introduction:-*Hemophilia is a severe bleeding disorder, primarily caused by the inactivity of factor VIII and is inherited as an X-linked recessive trait. Although most cases are hereditary, 30% result from new mutations. Gastrointestinal stromal tumors (GISTs) are most common mesenchymal tumors of gastrointestinal tract and are derived from interstitial cells of Cajal (ICC) - GI pacemaker cells. We present rare case of a 44 year old male who presented with upper GI bleed to emergency care. On evaluation he was diagnosed with hemophilia A and D2 duodenal GIST*
Case report:-*44 years old male with positive family history of hemophilia presented with malena and severe anemia. There was no past history of any bleeding episodes. Hemophilia was confirmed of factor assay*
*He was resuscitated and evaluated with UGI endoscopy which revealed antimesentric D2 submucosal lesion suggestive of GIST. There was active bleeding which was arrested with hemoclips.CECT abdomen pelvis revealed 2*2cm lesion on lateral wall of D2 with no vascular abnormality. There was no lymphadenopathy or any evidence of metastasis. Patient was transfused with blood products and replacement therapy-recombinant factor VIII. After initial stabilization patient again developed malena and had significant drop in hemoglobin. Multidisciplinary team meeting was held and decision taken to go ahead with surgical resection with peri-operative factor VIII administration. Patient underwent local resection of GIST with REY duodeno-jejunostomy. Post-operative course was uneventful.*
Discussion:-*The coexistence of hemophilia and GIST presents a challenging clinical scenario, necessitating a comprehensive and coordinated approach from a multidisciplinary team. This case emphasizes the importance of individualized management strategies to address the unique challenges posed by the combination of these rare disorders.*

Date of Submission: 08-10-2023 Date of Acceptance: 18-10-2023

I. INTRODUCTION

Hemophilia is a severe bleeding disorder, primarily caused by the inactivity of factor VIII and is inherited as an X-linked recessive trait. Although most cases are hereditary, 30% result from new mutations. Individuals with severe hemophilia A have significantly low factor VIII levels (less than 1% of normal), while milder deficiencies may only become evident during trauma or hemostatic stress. The various levels of factor VIII deficiency stem from diverse causative mutations, such as deletions, inversions, and splice junction mutations. Approximately 10% of patients exhibit normal factor VIII concentration as per immunoassay, but low coagulant activity due to a loss-of-function mutation in factor VIII. [1]

Gastrointestinal stromal tumors (GISTs) are most common mesenchymal tumors of gastrointestinal tract and are derived from Interstitial cells of Cajal (ICC)- GI pacemaker cells.(2) They are most commonly seen in

stomach (50-60%) and duodenal GIST account for only 3-5% of GIST cases. (3) 95% cases of GIST express CD 117 and immunohistochemical staining with C117(c kit), CD 34 and PDGFRA(platelet derived growth factor receptor A) are diagnostic .Approximately 5% of GISTs are associated with an underlying heritable mutation such as Familial GIST syndrome (mutation in KIT or PDGFRA), Neurofibromatosis 1, or Carney-Stratakis syndrome (GIST and paraganglioma with or without pulmonary chondroma).(2) No other consistent association has been described in literature.

We present rare case of a 44 year old male who presented with upper GI bleed to emergency care. On evaluation he was diagnosed with mild hemophilia A and D2 duodenal GIST. In the literature, there is only one

such co- existence of hemophilia A with GIST which was gastric origin, reported from Turkey [4]. So this would the first case of hemophilia A presenting with duodenal GIST.

II. CASE PRESENTATION

A 44-year-old male presented with recurrent episodes of melena and fatigue for the past over 1 week. Patient never had any history of bleeding episodes from any site in the past. He was referred to our tertiary care hospital from a peripheral hospital. Patient gave family history positive for Hemophilia in two 3rd degree relatives. On General examination patient had tachycardia, pallor however BP was maintained around 110/70 mm Hg. Per abdomen examination was normal. Digital rectal examination confirmed malena. Patient was initially resuscitated with crystalloids and blood was sent for cross-matching.

INVESTIGATIONS:-

Blood investigations:

On complete blood count, the patient had a very low hemoglobin level (3.4gm/dl). The total leucocyte count and the platelet count were normal. Renal- liver function tests and electrolytes were normal.

Prothrombin time was normal (14 seconds) while activated partial thromboplastin time was raised (42 seconds). Factor VIII assay (assessed in view of positive family history) was done which showed the factor level to be 11.4%.

Endoscopy:-

Upper Gastrointestinal endoscopy revealed a 2*2cm submucosal lesion just proximal to D2-D3 junction on lateral wall of duodenum highly suggestive of GIST. Ampulla was normal. Active ooze was noted from surface of this lesion and hemo-clips were applied to restrict the blood loss. No biopsy was taken in view of active bleeding.

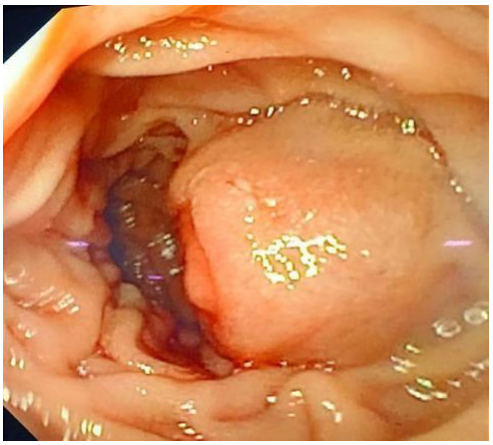

Figure 1:-Upper GI endoscopy suggestive of submuocal lesion with oozing at its inferomedial aspect, suggestive of bleeding D2 GIST

CECT Abdomen pelvis with angiography:-

Triple phase CECT of the abdomen pelvis with angiography revealed well-defined mildly enhancing oval-shaped mass measuring 2.5 x 1.8 cm over the D2 segment of the duodenum with over distended stomach without any areas of calcification or necrosis suggesting a benign etiology. There was no vascular abnormality or active blush noted.

Management:-

Patient was resuscitated with crystalloids and was given 4 pint pack red blood cell transfusion to achieve target hemoglobin of more than 8 gm/dl. Replacement therapy with recombinant Factor VIII concentrate was initiated post which the malena stopped and the patient had no pallor and hemoglobin levels were static. However after 72 hours, despite blood transfusions and factor replacement malena reappeared and his hemoglobin fell to 5.3gm/dl.

Multidisciplinary team meeting was held. Teams involved were Hematologists, Interventional

Radiologist, Transfusion medicine team, medical gastroenterologists and surgical gastroenterologists. Decision was taken to go ahead with surgical exploration and local resection with pre-operative optimization and perioperative factor replacement therapy.

Hemophilia management:-

Replacement therapy with recombinant Factor VIII concentrate was initiated and a 100 percent factor correction was given just prior to surgery and was maintained till post-operative day 3 followed by tapering to 80 percent from postoperative days 4-5, 50 percent for postoperative days 6-7, with monitoring of trough factor levels on post-operative day1 and 3 and the clinical condition of the patient. The patient required factor correction for a total of 7 days.

Surgical exploration:-

Exploratory Laparotomy was performed and as seen in figure 2 exophytic mass was noted just above D2-D3 junction was noted. Patient underwent resection of duodenal GIST with REY duodeno-jejeunostomy. Blood loss during the procedure was around 100ml.

Post-operative care:-

Patient was given recombinant factor VIII (schedule mentioned previously) post- operatively. Ryle's tube was removed after 72 hours. Orals were started on post-operative day 4. On post-operative day 5 drain was removed and by day 6 patient was tolerating oral soft diet. Patient was discharged on post- operative day 8. The patient was given factor 8 prophylaxis of 20 IU/kg twice a week for 2 weeks.

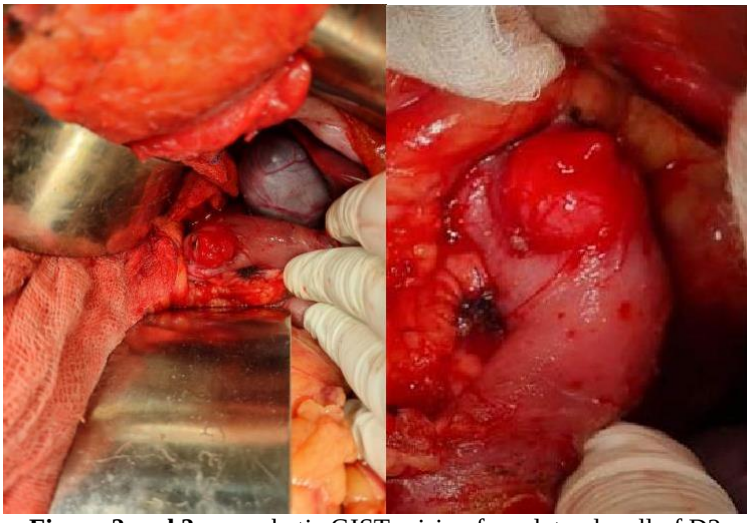

Figure 2 and 3:- exophytic GIST arising from lateral wall of D2

Histopathology:- The resected mass was confirmed as a Gastro-intestinal stromal tumor on histopathological examination. Immunohistochemistry was positive for CD117 and DOG1 and negative for CD34, SMA, desmin, S100 and a MIB1 index of 5 percent.

III. DISCUSSION

Duodenal GIST accounts for 3-5% of cases of GIST; has male preponderance and usually diagnosed in 5th decade of life. [3] Patients present with hemorrhage in more than one third patients and malena occurs more frequently than hematemesis. It commonly seen in D2 (51%) and D3 (31%) and around 53% patients on anti-mesenteric wall as was in our case.[2, 3]

One of the most common clinical manifestations of hemophilia is gastrointestinal bleeding. In a study conducted by Forbes et al., the commonest cause of GI bleed in hemophilia patients was peptic ulcer disease. [5]

Duodenal GIST is usually diagnosed with UGI endoscopy and biopsy. They are smooth appearing rounded submuosal lesions with central ulceration. UGI biopsy yield is poor and hence EUS guided biopsy may be considered for pre-operative diagnosis in stable patients. EUS guided FNA biopsy has sensitivity of 80% and specificity of 100%. As expertise is not available at all centers, EUS-biopsy is not routinely recommended in otherwise operable lesions. EUS-biopsy is of value in patients who are unresectable and would require neoadjuvant Imatinib therapy. CECT abdomen with negative oral contrast also essential to assess extramural extent, degree of necrosis and evidence of metastasis.[2]

Complete surgical excision remains mainstay of treatment and lymphadenectomy is not routinely recommended. One has to be very careful to avoid intra-operative tumor rupture.[2] Tumor size, location and involvement of adjacent organs would dictate the type of surgery in duodenal GIST. Local resection versus standard pancreaticoduodenectomy has always been discussed. Retrospective analysis performed by Lui et al

revealed that local resection is more commonly performed for Duodenal GIST and pancreaticoduodenectomy is considered for descending lesions and those with larger diameter. However type of surgery performed had no bearing on prognosis. [(6)] The independent negative prognostic factors are mitotic index >5/50, primary tumor size >5 cm, male sex, R1 resection/tumor rupture, and nongastric primary tumor location.[(7)]

In our case the situation was made complex by presence of mild hemophilia A. With coordinated efforts between the teams, patient was resuscitated and was planned for surgery. He was given 100% replacement of recombinant factor VIII just before induction and standard protocol for post-operative replacement was followed. The timely administration of Factor VIII with monitoring of Factor VIII levels remains Achilles heel in post-operative care of such patients.

The management of surgical procedures for individuals with hemophilia has consistently raised significant concerns. Inadequate control of hemostasis could lead to considerable illness and death. However, the outcome of surgical procedures is not solely reliant on the proper replacement of the deficient factor. Interventions before and after the operation, continuous monitoring in laboratories, patient care, and rehabilitation are crucial aspects.[(8)] Surgery should be planned early in the week and early in the day to acquire optimal support from the laboratory as well as the blood bank. [9]Hence, it is essential that surgical procedures for hemophilia patients be conducted in well-equipped hospitals capable of offering a comprehensive approach, often referred to as a "Comprehensive Hemophilia Treatment Center." [8]

The coexistence of hemophilia and GIST presents a challenging clinical scenario, necessitating a comprehensive and coordinated approach from a multidisciplinary team. This case emphasizes the importance of individualized management strategies to address the unique challenges posed by the combination of these rare disorders.

Conflict of interest:-
There are no conflicts of interest.

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