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Case Report

Relapsed and Resistant Bulbar Ulcer Inaugural of Polycythemia Vera

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Abstract

Digestive complications are not rare during Polycythemia Vera (PV)'s evolution. They are dominated by gastrointestinal bleeding, thromboembolic events of the mesenteric vessels, Budd-Chiari syndrome and portal hypertension. Peptic ulcers are generally considered as late symptoms or complications of the PV occurring during the second stage of this disease named "postpolycythemic phase", and inaugural forms are exceptional and unusual.

We report the case of a relapsed and resistant bulbar ulcer as a first manifestation inaugural of PV in a 39-year-old man in spite of well-conducted anti-ulcer treatment with several anti-*Helicobacter pylori*-eradication cures.

To the best of our knowledge, this situation was previously illustrated only once.

Keywords: *Peptic Ulcer; Polycythemia Vera; Essential Polyglobulia; Microthrombosis*

Introduction

Polycythemia Vera (PV) or essential polyglobulia is a genetically determined myeloproliferative disorder. It is frequently complicated by anoxia at the microcirculatory level with its cutaneous and/or visceral ischemic manifestations [1].

Digestive complications are not rare during PV's evolution. They are dominated by gastrointestinal bleeding, thromboembolic events of the mesenteric vessels, Budd-Chiari syndrome and portal hypertension [2-5].

The gastric and/or duodenal ulcers are far less common and the inaugural forms are exceptional and unusual [2,6].

We report herein the case of a relapsed and resistant bulbar ulcer as a first manifestation inaugural of Polycythemia Vera.

Case Report

A 39-year-old man without medical history and non-smoker was explored for persistent epigastralgia. Gastroduodenal endoscopy demonstrated a duodenal ulcer on the bulbar anterior face and the detection of *Helicobacter pylori* (Hp) was positive.

The Patient received a well-conducted Hp-eradication therapy as well as a proton pump inhibitor (PPI) treatment for one month but did not report any clinical improvement.

A check-up endoscopy showed that his ulcer did not totally scar. The biopsy objectified a simple duodenal ulcer with no specific histological signs and the Hp's detection was negative.

A new PPI cure was initiated and prolonged for two months with satisfactory clinical evolution.

The subsequent evolution was marked by recurrence of abdominal pain and check-up endoscopy showed the reappearance of bulbar ulceration.

Despite a well-conducted anti-ulcer treatment with several anti-Hp eradication cures, the duodenal ulceration was resistant and relapsed with a recurrence endoscopically documented eight times in two years.

Complementary investigations excluded an underlying ulcerogenic disease, in particular Zollinger-Ellison syndrome, hypercalcemia or hyperparathyroidism. Similarly, there have been no reported drug intakes, in particular non-steroidal anti-inflammatory drugs, corticosteroids or aspirin.

The last check-up endoscopy showed multiple ulcerations of the anterior face of the duodenal bulb with multiple necrotic areas.

Investigations for underlying cancer, systemic disease, necrosing vasculitis, cryoglobulinemia, anti-phospholipid antibody syndrome, hyperhomocysteinemia, and inherited thrombophilia were negative.

Blood count demonstrated some specific abnormalities: hemoglobin at 19.7 g/dL and an hematocrit level of 59.7% suggestive of PV.

The resumption of the anamnesis revealed the existence in recent months of headache, dizziness, itching triggered by contact with hot water and a facial reddening. The final diagnosis of PV was confirmed with laboratory tests: high total cell volume and positive JAK2 mutation.

The patient was initially treated with bloodletting and antiplatelet agents in preventive doses and subsequently with hydroxyurea.

After specific treatment of PV, the evolution was favorable: endoscopic check-up after one month objectified a total healing of bulbar ulcerations and the patient did not recidivated his ulcerative pathology during five years of follow-up.

Discussion

First described by Vaquez in 1892 [7], Polycythemia Vera or Vaquez-Osler syndrome is a relatively common malignant haemopathy, particularly in the elderly Caucasian. Its diagnosis is based on the international criteria of the "Polycythemia Vera Study Group". Recently the Janus Kinase 2 (JAK2) mutation was strongly associated with this disease as a specific marker [1,5,8]. This mutation conduct to an abnormal activation of the "JAK/STAT pathway" resulting in an uncontrolled clonal myeloproliferative disease predominant on the precursor cells of the erythroid line [1,5,8].

As gout and thrombosis, peptic ulcers are generally considered as late symptoms or complications of the PV occurring during the second stage of this disease named "postpolycythemic phase" [5].

The apparent frequency of peptic ulcers in Polycythemia Vera is estimated at 7 to 15% but it appears to be largely underestimated since they are often subclinical and spontaneously resolutive. Indeed, asymptomatic gastroduodenal damage was revealed by routine endoscopy in 70% of patients with PV [2].

The peptic ulcer pathophysiology in this myeloproliferative disorder remains controversial. It typically involves micro-thromboses of the gastric vessels [3,9]. These micro-thromboses, frequent during PV, are caused by: circulatory slowdown and hyperviscosity, thrombocytosis, hypercalcemia, lesions of the intima caused by circulatory turbulence and hyperviscosity [3].

Other hypothetical factors may play a role in the genesis of these ulcerations, particularly changes in gastric secretions and infection with *Helicobacter pylori* that appear to be favoured by PV [2,10]. Indeed, systemic endoscopic investigation demonstrated that 83% of patients with PV are infected by the *Helicobacter pylori* compared with only 57% of the general matched population [2].

All these findings explain the particularly increased frequency of gastrointestinal lesions during PV. In systemic endoscopic investigation, these lesions are significantly higher in patients with PV compared to the general population: 75% versus 19%, $p < 0.0001$; gastric erosions and peptic ulcers are also significantly more frequent: 46% versus 12% and 29% versus 7%, $p < 0.01$ [2].

The frequency of peptic ulcers in PV reinforces the "gastrogeneous" theory of this disease. The arguments supporting this theory are: a very high level of pepsinogen, a higher than normal erythropoietic effect in the gastric juice, and a high intrinsic factor level [3,6]. It is thus that most recent studies tend to consider the PV and the ulcerative disease as two different presentations of hyperacidity [2].

Moreover, some authors consider PV as an independent risk factor for peptic ulcer just as the *Helicobacter pylori* infection [2].

Smoking can be an additive hypothetical factor for these two diseases. In fact, the role of smoking as a contributing factor for Polycythemia Vera was demonstrated [11] as well as for peptic ulcers [12].

In our observation, the absence of other underlying disease and drug intake that may be at the origin of such a disorder as well as the frequent recurrences before the specific treatment of the PV, the absence of infection by *Helicobacter pylori* and the necrotic character of the ulcerations are arguments to link this manifestation to the PV.

As reported in our observation, gastrointestinal manifestations may be the first signs revealing PV. This situation was previously illustrated only once by the observation of El khattabi A., *et al*. in which the gastrointestinal bleeding related to a bulbar ulcer was the inaugural manifestation of PV [6].

This increased frequency of gastric ulcers during PV requires a special monitoring since gastric cancers also appear to be frequent during this condition [13,14]. These ulcerations are thus at a very high risk of malignant transformation.

Conclusion

The susceptibility to infection with *Helicobacter pylori* and the particularly high frequency of asymptomatic gastroduodenal lesions impose a particular endoscopic monitoring in subjects with PV. Similarly, a Polycythemia Vera should be considered in case of a recurrent or resistant peptic ulcer; especially in the elderly.

Conflicts of Interest

No conflicts.

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