A Case of Post-Radiotherapy Gastritis: Radiation Does Not Explain Everything

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Abstract
Hemorrhagic gastritis is a possible late toxicity outcome after radical radiotherapy but it is nowadays a very rare condition and most likely depends on other clinical factors. We report the case of a 77-year-old woman with a symptomatic solitary extramedullary intra-abdominal plasmacytoma and multiple gastric comorbidities, treated with external beam radiotherapy. Despite the good response to radiotherapy, the patient experienced multiple gastric bleeding a few months later, with the need of multiple treatments for its control. In this paper we will discuss in detail all aspects related to the different causes of hemorrhagic gastritis.

Introduction
Primary extramedullary plasmacytoma (EMP) accounts for approximately 4% of all plasma cell neoplasms [1]. Solitary EMPs of the retroperitoneum are rare with few reports in the literature [2]. Plasma cell tumors tend to be radio- and chemosensitive; therefore, the treatment of choice for EMPs can either be surgery, chemotherapy or radiotherapy [3]. The best choice for treatment is not evident [2], but most cases are localized, and some studies have shown that radical radiotherapy offers potential local control and organ preservation associated with low toxicity [4–6]. However, post-radiotherapy gastritis is possible, and several cases of bleeding have been reported [7, 8]. We present a case of gastritis after radiotherapy treatment and analyze all possible causes in detail.
Case Presentation

A 77-year-old female was referred to our Radiotherapy Department with newly diagnosed retroperitoneal solitary EMP. By the end of January 2012, the patient presented with abdominal pain and stomach fullness. An abdominal CT scan (February 2012) revealed a 10.5 × 9.5 × 8 cm heterogeneous solid mass localized adjacent to the pancreas tail involving the aortic and renal arteries (fig. 1). A biopsy of the tumor (March 2012) was CD138+, lambda light chain positive, had normal bone marrow and no skeletal lesions, which confirmed the diagnosis. Relevant personal history included a record of gastritis from Helicobacter pylori (HP) infection treated in 2008 and hyperplastic micropolyps, atrophic gastritis and erosive gastritis in 2010, which was related to nonsteroidal anti-inflammatory drug intake. The patient was on dexamethasone (40 mg/day; 4 days/week every 2 weeks), darbopoetin (500 μg bimonthly) and pantoprazole (40 mg/day).

The patient was treated with conformal external radiotherapy and received a total dose of 48.6 Gy in 27 fractions (May 22 to June 29, 2012). The mean absorbed dose (stomach) was 45.5 Gy with a maximum of 52.1 Gy. No organs at risk were compromised. Post-radiotherapy toxicity included gastrointestinal toxicity and leucopenia grade 2. Soon after treatment, the patient experienced relief of her symptoms. A 18F-FDG PET-CT scan performed 2 months later was unremarkable for abnormal metabolic uptake.

By the end of October 2012, the patient suffered an episode of hematemesis. An endoscopic evaluation documented gastric angiectasis without active gastric bleeding. This episode was successfully treated with proton pump inhibitors. However, one month later, the patient was again admitted to the Emergency Room due to new and persistent gastric bleeding unresponsive to endoscopic treatment (fig. 2) and required hemodynamic surveillance as well as intensive transfusion support. At that time, an endoscopy with gastric biopsies exhibited mild gastritis with focal activity and reparative mucosal changes. There was HP positivity in a low concentration (fig. 3), and malignancy was excluded. A CT scan was inconclusive. The patient was submitted to an exploratory laparotomy combined with intraoperative endoscopy, and an active hemorrhagic ulcer localized on the lesser curvature was found and resolved. Despite surgical treatment, hemorrhagic emesis with clots persisted. Hyperbaric oxygen treatment was then proposed. After 20 sessions of treatment, the patient noticed a relief of symptoms and an imagiological response upon endoscopy was documented. Despite being asymptomatic for the next 5 months, in June 2013, the patient had another digestive bleeding episode. Endoscopy identified a small clot on the distal esophagus-pigmented mucosa and gastric friable mucosa with neovascularure. Hyperbaric oxygen treatment was restarted, and a remarkable improvement in symptoms was noted. On the latest follow-up (October 2013), the patient was still on hyperbaric oxygen treatment and remained asymptomatic. A good tumor response to treatment was noted upon an abdominal CT scan, and an 18F-FDG PET-CT scan detected minor metabolic expression suggesting an inflammatory pattern (fig. 4).

Discussion

Radiotherapy is considered a plausible option for treating non-head-and-neck EMP as it achieves symptomatic control and is likely to be less toxic compared with surgery and chemotherapy [6]. Evidence of this fact is supported by individual cases in the literature although there are no clinical studies categorically confirming it [1–5]. In some cases, radiotherapy is given after the failure of previous treatments, but in those cases, cumulative tox-
icity may be expected. In the present case, the treatment was radiotherapy based, and repeated hemorrhagic episodes were linked to radiotherapy. In fact, our patient experienced two gastric bleeding episodes with the first occurring 4 months after radiotherapy, which may be interpreted as an expected late toxicity. However, this event is rare and was only reported in 5–7% of cases, which had higher doses. The absorbed dose in the whole stomach was 45 Gy based on updated recommendations [9]. The maximum point dose has been suggested to be a good predictor for late toxicity [9]. Unfortunately, most studies evaluate doses between 40 and 50 Gy and do not take into account organ position variability [7, 9]. The initial injury from radiation is acute inflammation of the gastric mucosa. If the injury progresses, it may evolve to progressive vasculopathy, leading to mucosal ischemia, ulceration, and telangiectasia. The characteristic endoscopic finding is the presence of telangiectasia, which was observed during the first bleeding event. Bleeding is a diffuse process with multiple bleeding sites [10]. Other findings may include diffuse erythema of the mucosa, shallow or deep ulcers, and scar formation. Although the morphological aspects observed in the most recent biopsies might be related to HP gastritis, reparative changes may also be related to radiation gastritis recovery.

In contrast, HP presence after eradication may contribute to the reappearance of gastric ulcers and hemorrhaging and may be correlated with chronic gastritis activity independent from radiation injury [11, 12]. Unfortunately, few biopsies were performed during the last endoscopic examination [12, 13]. Only the examination of gastric vessels at some distance from the ulcers can be helpful in defining radiation as the cause because these will have radiation-vasculopathy characteristics (neovascularization, telangiectasia, and obliterator intimal lesions) [13]. Moreover, in our patient, these vasculopathic features were not observed, and only minor fibrosis was documented.

Although the final histological diagnosis may be uncertain due to the lack of criteria, it is suggested that there may be an overlap of several causes. The patient’s previous stomach-related disease, the presence of HP, and multiple endoscopic interventions (visible scars from multiple biopsies) are factors for potential gastric complications, which may be independent from radiation effects or can alter the threshold for toxicity. Recognizing these factors in a particular patient increases the ability to predict potential radiotherapy-related toxicity as bleeding. To the best of our knowledge, no radiotherapy recommendations have addressed this question yet [7, 9].

In conclusion, radiotherapy is an option for the treatment of EMPs, offering an opportunity for the local control and relief of such a large tumor.

Frequent complications such as hemorrhagic episodes secondary to HP gastritis may also occur in patients with unusual diseases and comorbidities, highlighting the importance of clinical suspicion.

References


Fig. 1. CT scan performed in February 2012, revealed a retroperitoneal mass.
Fig. 2. Low-debit hemorrhage on the upper portion of the lesser curvature documented by endoscopy on November 27, 2012 between the endoscopic treatments.

Fig. 3. HP identification (red circle) on gastric biopsy on December 7, 2012. Modified Giemsa staining. ×900.
Fig. 4. Documentation of radiotherapy response between by comparing the ^18F-FDG PET-CT scans from October 2012 (left panel) and July 2013 (right panel).