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Case report

External-beam radiotherapy: A realistic therapeutic option for the gastric antral vascular ectasia

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ABSTRACT

The gastric antral vascular ectasia (GAVE) is a well recognizable endoscopic entity characterized by the presence of multiple linear angioectatic vessels predominantly located in the antrum, with a typical appearance of "watermelon stomach". This condition typically affects elderly females presenting as iron-deficiency anaemia due to chronic gastric bleeding. Standard treatment is endoscopic ablation of the gastric mucosa. For non-responders, radical surgery is considered a curative treatment but with considerable morbidity and mortality. Radiation therapy is a well-known alternative for many benign diseases, including anomalous vascular hyperproliferative diseases, although its role has not been defined for GAVE. The present case illustrates the efficacy and tolerance of radiotherapy in the treatment of symptomatic gastric watermelon.

1. Background

Gastric antral vascular ectasia (GAVE) is a rare but well described cause of recurrent upper gastrointestinal bleeding in the elderly manifested clinically as iron-deficiency anaemia. Its prevalence varies between less than 0.3% of cases in large endoscopic series and up to 4% in selected series with patients being studied for upper gastrointestinal bleeding of uncertain origin.[1] GAVE prevalence is higher among elderly females, with a 5:1 female preponderance. Patients are usually transfusion dependent with average requirements as high as 50–100 units of blood per year in severe cases.[2–4]

GAVE's etiology is unclear. Immunological disturbances such as systemic lupus, scleroderma, systemic sclerosis, pernicious anemia or primary biliary cirrhosis have been associated to this disease. Also, GAVE has been related to non-immunitary disorders, such as chronic renal dysfunction, hepatic cirrhosis, ischemic cardiomyopathy, diabetes mellitus, familiar Mediterranean fever or after haematopoietic cell transplantation.[2,5]

GAVE was initially reported in 1953 by Ryder et al. in a gastrectomy specimen from an old woman. It was described as "erosive atrophic gastritis with remarkable venous capillaries ectasia".[6] In 1984, Jabbari et al. coined the expression "*watermelon stomach*", describing a typical endoscopic appearance

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with red stripes and/or erythematous areas corresponding to dilated blood vessels.[7]

GAVE's treatment aims to minimize, or even eliminate, blood transfusion requirements. Therapeutic approaches have included endoscopic ablation techniques, pharmacological treatments and surgery, but with variable results.

Radiotherapy has been employed for treatment of different vascular disorders, not necessarily of malignant etiology. In the past, low dose radiotherapy was used for treatment of peptic ulcer disease and associated gastric or duodenal bleeding with good results.[8]

2. Aim

We present an own clinical case of a woman treated with radiotherapy for persistent GAVE after other therapies, which highlights the effectiveness and well tolerance of radiation therapy, supporting its consideration after failure of other standard treatments.

3. Case report

A 77 year-old woman, with a previous medical history of type II diabetes mellitus and hypertension, had been diagnosed 3 years before her attendance of GAVE. She was consulted because of iron-deficiency anaemia due to chronic gastric bleeding leading to weekly blood transfusions. Oral gastroscopy evidenced the presence of an antral vascular ectasia with typical red stripes found in watermelon stomach. The patient began to be treated with oral iron-supplements and estrogens. By the time of the diagnosis, no signs or symptoms of hepatopathy were manifested. For the next two years, the patient was treated with several argon-plasma coagulations (APC) of GAVE lesions localized in the gastric antrum. One year after the initial diagnosis she developed signs of chronic hepatopathy and portal hypertension without hydropic decompensation, persisting the GAVE lesions in the antrum. Despite sequential endoluminal APC, the patient continued with refractory anaemia, requiring 1–2 blood transfusions per week. An oral endoscopy showed grade II oesophageal varicose veins without evidence of active bleeding, as well as multiple aberrant vascular formations located mainly in the antrum and occasionally in the fundus and stomach body, with classic aspect of GAVE (Fig. 1A and B). Due to the persistence of the GAVE lesions despite the treatments administered, other therapeutic options were considered. The patient refused surgical treatment and was remitted to our department. At her attendances, laboratory findings showed haemoglobin of 8.2 g/dl, hematocrit of 30% and normal hepatic function, platelet count, prothrombin time and INR. A radiation treatment was proposed and the patient signed an informed consent. After patient immobilization using an individualized alpha-cradle to ensure daily repositioning, we performed a CT-scan acquisition of the thorax and abdomen at 5-mm-thin intervals. The clinical target volume (CTV), involving all GAVE lesions along with the surrounding organs at risk (spine, lungs, heart, kidneys, liver and spleen) were contoured on CT slices. A security margin was added to the CTV to compensate the physiological organ movements and potential inaccuracies in the daily positioning of the patient, establishing the planning target volume (PTV). A total dose of 20 Gy for the PTV, with conventional 2 Gy-daily fractionation, five days a week, was prescribed. The treatment was carried out by a linear accelerator using multiple conformed fields with 6 MV photons. Oral antiemetic prophylaxis with a 5-HT3 receptor antagonist was given to the patient to avoid radio-induced emesis.

At discharge, the patient was in a stable condition. A repeated oral endoscopy three months after radiotherapy finalization only showed isolated petequial dotted in the antrum, fundus and body of the stomach, suggestive of chronic pangastritis. No endoluminal therapy was necessary at that time (Fig. 2A and B). No more blood transfusions were needed.

4. Discussion

Although GAVE is a relatively infrequent disorder, it has to be considered in the context of a chronic or acute gastrointestinal bleeding in older patients. The most common clinical presentation is a chronic occult gastrointestinal bleeding that leads to the establishment of symptomatic anaemia, although it has also been described as an acute massive gastrointestinal bleeding. Frequently, the patient does not respond to iron replacement therapy and becomes highly dependent

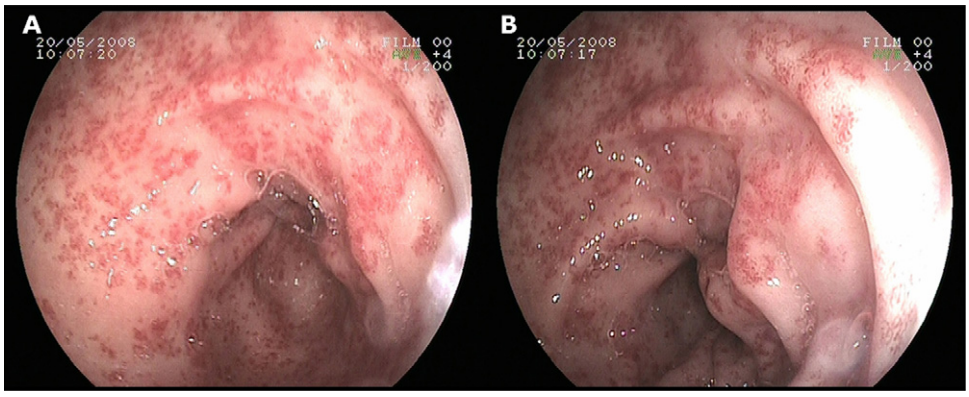

Fig. 1 – (A and B) Endoscopic view from gastric mucosae, showing lesions with vascular aspect, congestive, with lineal disposition and antral predominance typical of GAVE.

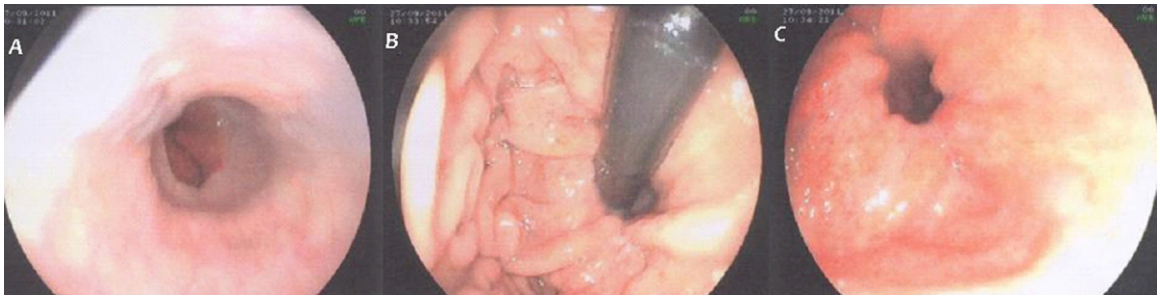

Fig. 2 – (A–C) Endoscopic view of antral mucosa 3-months after radiotherapy showing images with petequial aspect, patched disposition, non-congestive, according to petequial gastritis.

on blood transfusions.[2–4] Several immunological as well as non-immunological diseases have been associated to GAVE development. Nevertheless, the most frequently comorbidity associated with GAVE is hepatic cirrhosis that can be found in 30–66% of the patients with a diagnosis of GAVE. In those cases, differential diagnosis between portal hypertension gastropathy (PHG), typically present in hepatic cirrhosis, and GAVE might be quite difficult. However, GAVE affects mainly the gastric antrum while PHG is more prevailing in the body and fundus. In this case we present, the patient has chronic hepatopathy signs but she has not required any specific treatment so far.[5]

The pathogeny for GAVE has not been well established. Different hypotheses have been proposed: (1) mechanical stress caused by elevated gastric peristalsis; (2) fusiform cells proliferation, due to hypergastrimenia, frequently observed in patients with GAVE, causing high venous pressure, and (3) local neuroendocrine cells proliferation, achieving high levels of vasoactive substances, such as VIP and serotonin, directly implicated in vascular dilatation.[5] The endoscopic aspect is diagnostic. The presence of the characteristically red stripes with a watermelon appearance is considered pathognomonic for this entity. Gastric biopsies offer a valuable tool with high sensitivity for GAVE, but the bleeding risk is far from negligible. Angiography shows antral hypervascularisation and ecoendoscopy allows to observe vascular ectasia in mucosae and submucosae, but although usefully, they are not considered necessary for the diagnosis of GAVE.[2,4]

The objective of the treatment is to eliminate or minimise blood transfusion needs. The therapeutic options for GAVE rely on three categories: surgical, endoluminal and pharmacological. Endoscopic treatments are considered the first option. Nd:YAG laser has been widely used but it rarely provides a complete cure. Most patients need several sessions and between 14% and 50% continue with the need of transfusion during follow-up.[2,5,9] Endoscopic argon-plasma coagulation (APC) also offers similar clinical results to those achieved with Nd:YAG laser with a limited penetration, which reduces ulceration and perforation.[10] Other endoscopic modalities used occasionally have been contact termocoagulation with thermal catheter, bipolar electrocoagulation and sclerotherapy with alcohol or polidocanol injections.[2,5]

Surgical antrectomy is the most curative option for GAVE, as evidenced by the fact that none of the patients suffered anaemia or gastrointestinal bleeding after surgery.[6,8] However, it is still the last option because of its high morbidity–mortality rates (5–10%), and its use must be limited to patients refractory to conservative treatments.[1,2,5]

Finally, pharmacological treatment for GAVE employing beta blockers, corticosteroids, hormonal treatments with estrogens and progesterone, octreotide, tranexamic acid, thalidomide or ciproheptadine have been tested by several authors in small series with no conclusive results.[2,5]

Radiotherapy effectiveness for benign diseases is supported by a broad evidence of scientific publications.[11,12] Moderate dose radiotherapy has proved its value in the treatment of many disorders characterized by anomalous vascular proliferation, including angiomas, arteriovenous malformations, Rendu–Osler–Weber syndrome or age-related macular degeneration. The benefit of radiotherapy in these pathologies is based on its apparent ability to prevent the proliferation of neovascular endothelium, stimulating apoptosis phenomenon in the endothelial cells, and its capacity to induce the regression of this neovascularisation as well as inhibiting the new vessels array.[13,14] Risk of development of radiation-induced tumours has raised concerns about radiotherapy for non-malignant diseases. However, according to the most recent reviews, this risk appears almost negligible in elderly patients, as occurs in patients with GAVE.[15]

5. Results

In our patient, not only the final dose but also the fractionation scheme was chosen with the objective of limiting the risk of acute and late radiation toxicity. Although, the final dose was empirically fixed at 20 Gy, there is enough experience in other benign diseases characterized by vascular hyperproliferation with radiation doses ranging between 20 and 30 Gy.[11–14] Radiation tolerance was excellent, allowing outpatient treatment without hospitalization or blood transfusions during the procedure. Although follow-up is still not too long, 3 months after radiotherapy ending, the patient is free of new blood-transfusion requirements.

6. Conclusion

In conclusion, despite few data in the literature, radiotherapy can be an effective and well tolerated treatment for GAVE, and

could be considered as an alternative when the conventional treatments have failed.

Conflict of interest

None declared.

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