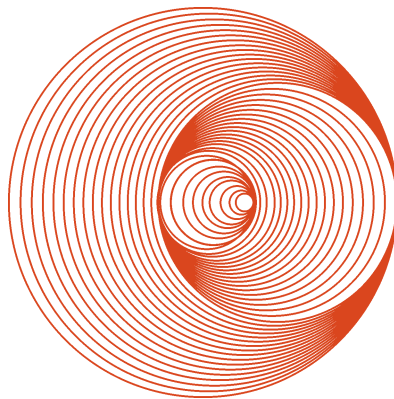


EUROPEAN JOURNAL OF ONCOLOGY

GIORNALE EUROPEO DI ONCOLOGIA

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MATTIOLI 1885 - SRL
CASA EDITRICE

Autorizzazione del Tribunale di Parma n. 14/97 del 11/6/1997 - ISSN 1128-6598

La testata fruisce dei Contributi Statali diretti di cui alla legge 7 agosto 1990, n. 250

The European Journal of Oncology is indexed by Excerpta Medica (EMBASE), the Elsevier BioBASE, Science Citation Index Expanded (SciSearch®), Journal Citation Report/Science Edition, ISI Web of Science
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CONTENTS/INDICE

VOLUME 17 - N. 1 - 2012

EDITORIAL / EDITORIALE

- Cancer risks among construction workers / Rischio di cancro tra i lavoratori edili**
 A. Englund 5

ARTICLES ON ORIGINAL STUDIES AND RESEARCH / ARTICOLI SU STUDI E RICERCHE ORIGINALI

GENERAL TOPICS / ARGOMENTI GENERALI

- Kinase inhibitors reduce 7,12-dimethylbenz[a]anthracene-induced onco-suppressor gene expression in short-term experiments / Inibitori delle chinasi riducono l'espressione genica dell'onco-soppressore indotto da 7,12- dimethylbenz[a]anthracene in esperimenti a breve termine**
 P. Gergely, F. Budán, I. Szabó, G. Mezey, Á. Németh, A. Huszár, J. Iványi, K. Gombos, Á. Knapp, L. Órfi, G. Kéri, I. Ember 11
- Targeting mitochondria for cancer treatment / Individuazione dei mitocondri per il trattamento del cancro**
 J. Pokorný, M. Cifra, A. Jandová, O. Kučera, F. Šrobár, J. Vrba, J. Vrba Jr., J. Kobilková 23

ARTICLES ON SPECIFIC TOPICS / ARTICOLI SU TEMATICHE SPECIFICHE

GENERAL TOPICS / ARGOMENTI GENERALI

- Argon plasma coagulation in the treatment of post-radiotherapy rectal bleeding / Argon plasma coagulation nel trattamento della proctite emorragica causata dalla radioterapia**
 G. Tomasello, M. Bellavia, G. Damiano, V.D. Palumbo, G. Spinelli, P. Damiani, F. Damiani, S. Buscemi, S. De Luca, S. Di Gangi, G. Buscemi, A.I. Lo Monte 37
- Cantieri navali e mesotelioma nell'area di Monfalcone. Evoluzione dell'epidemia / Shipbuilding and mesothelioma in the Monfalcone area, Italy. Trend of the epidemic**
 C. Bianchi, T. Bianchi 43

CLINICAL CASE REPORTS / RESOCONTI DI CASI CLINICI

Leukemia/*Leucemia* (C92.4)

Hepatosplenic fungal infection during induction remission therapy for acute promyelocytic leukemia: a case report / *Le infezioni epatospleniche fungine durante trattamento di induzione della remissione per leucemia acuta promielocitica: un caso clinico*

R. Liang, X.-q. Chen, Q.-x. Bai, Z. Wang, T. Zhang

49

OBITUARY / *NECROLOGIO*

Prof. Stephen Levin 1941-2012

P. Landrigan

55

Argon plasma coagulation in the treatment of post-radiotherapy rectal bleeding

Argon plasma coagulation nel trattamento della proctite emorragica causata dalla radioterapia

Giovanni Tomasello*, Maurizio Bellavia*, Giuseppe Damiano*, Vincenzo Davide Palumbo*, **, Gabriele Spinelli*, Provvidenza Damiani***, Francesco Damiani*****, Salvatore Buscemi*****, Salvatore De Luca*, Simona Di Gangi*, Giuseppe Buscemi*, ****, Attilio Ignazio Lo Monte*, **

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Summary

Introduction: Chronic radiation proctitis is often associated to radiotherapy for treatment of pelvic cancer. The most common side effect of this pathological condition is rectal bleeding but despite the great number of clinical approaches and techniques that have been employed no consensus for the management of it is available. Although prospective randomized trials about hemorrhagic radiation proctitis are still lacking, endoscopic approach delivering an Argon Plasma Coagulation (APC) seems to be a successful and available option. **Patients and Methods:** Sixteen patients suffering from post-radiotherapy rectal bleeding were followed. In the nine cases presenting a rectum ulcerative colitis (RUC) like endoscopic picture a 5-ASA therapeutic approach was chosen initially, followed by an

Riassunto

Introduzione: La proctite cronica è spesso associata a terapia radiante per il trattamento dei tumori della zona pelvica. La complicanza più comune della proctite è il sanguinamento rettale ma, nonostante le numerose tecniche utilizzate nel trattamento di tale patologia, nessuna di esse viene universalmente ritenuta la migliore. Sebbene non esistano ancora trials randomizzati sulla proctite associata a radioterapia, l'Argon Plasma Coagulation (APC) per via endoscopica sembra un'alternativa di facile realizzazione e successo. **Pazienti e Metodi:** Dei sedici pazienti affetti da sanguinamento rettale conseguente a radioterapia oggetto dello studio, nove manifestavano un quadro endoscopico caratteristico della rettocolite ulcerosa (RCU), sette presentavano un quadro clinico più lieve con sole aree di telangectasia. I

Received/Pervenuto 9.12.2011 - Accepted/Accettato 20.1.2012

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APC treatment of areas of telangectasias. The other cases, presenting only areas of telangectasias, were treated only with APC. *Results:* 5-ASA therapy led to an improvement of inflammation state related to RUC but recurrence of rectal bleeding caused by telangectasias was observed. In these cases an additional APC treatment gave a total remission of the problem. Also in the other cases, presenting only areas of telangectasias, a remission of rectal bleeding was achieved through APC application. *Conclusions:* In the cases of radiation proctitis characterized by a severe compromission of rectal mucosa integrity an anti-inflammatory pharmacological therapy is necessary but not sufficient to abrogate rectal bleeding which is often caused by the presence of areas of telangectasias. In these cases a remission of the problem could be achieved through a combination of anti-inflammatory therapy (5-ASA) and APC. *Eur. J. Oncol.*, 17 (1), 37-41, 2012

Key words: Argon Plasma Coagulation, hemorrhagic radiation proctitis, anti-inflammatory therapy in ulcerative colitis

Introduction

The treatment of pelvic malignancies, including prostate cancer and cancer of cervix and uterus, is based on ionizing radiations which cause submucosal tissue injury to the rectal wall leading to chronic radiation proctitis (Fig. 1). Its development depends on the modalities of radiotherapy administration as well as other factors including previous proctocolitis, history of smoking, diabetes mellitus. There is no agreement about the exact pathophysiology of radiation proctitis but the currently accepted hypothesis proposes a combination of radiation-induced ischemia and fibrosis (1).

Rectal bleeding is the main sign of radiation proctitis and it is generally moderate but it may also be severe causing hemodynamic disturbances which need specific therapeutic management (blood transfusion). Other side effects such as diarrhea, inconti-

nence, pain, tenesmus, rectovaginal fistula, may also occur compromising the quality of life. The endoscopic aspect of radiation proctitis is characterized by the presence of more or less dense telangiectasia dispersed locally or in a diffuse manner over the rectal mucosa which bleeds easily, particularly at introduction of the endoscope. The lesion begins at the dentate line and it may localize to one part of the rectum or may extend to the sigmoid. Interestingly it has been proposed that this chronic microvasculature injury could be partially determined by an alteration of the thrombomodulin expression in endothelial cells which is a consequence of radiotherapy (2). A large number of treatment has been proposed for hemorrhagic radiation proctitis. Pharmacological agents used for this purpose (oral, topic or mixed) are often unsatisfactory, with partial recovery and short term relapses. Several case series have proved

Parole chiave: Argon Plasma Coagulation, proctite emorragica dopo radioterapia, terapia antinfiammatoria nella retto colite ulcerosa

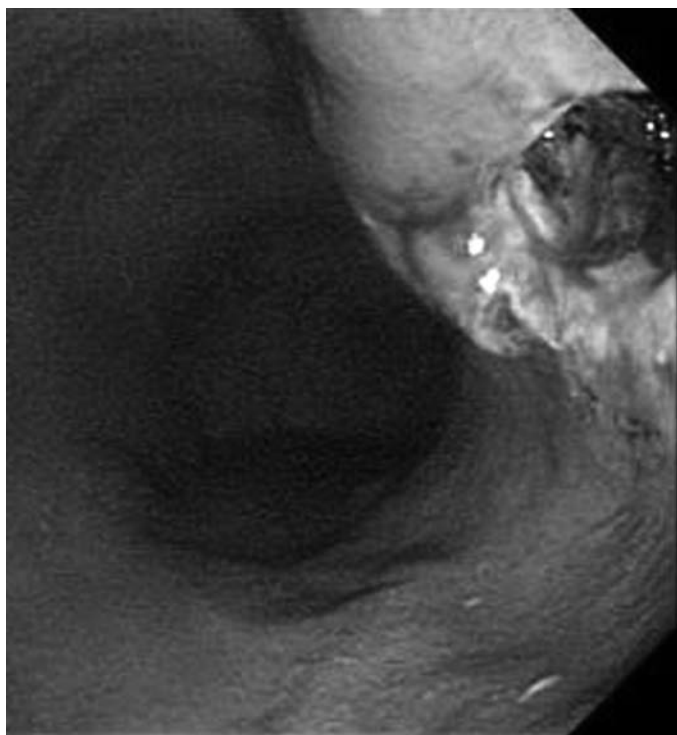


Fig. 1. Ulceration of anterior rectal wall following radiotherapy

disappointing results with topical or oral sulfasalazine, 5-aminosalicylic acid (5-ASA) and corticosteroids (3-5).

A certain degree of efficacy has been reported with topical formaldehyde and topical or oral sucral-fate (6-8).

Development of new endoscopic procedures has led to a higher rate of therapeutic success and longer period of symptomatic control. The goal of endoscopic therapy is to ablate the angioectasia with a resultant improvement in the severity and frequency of rectal bleeding. Both laser and mono or bipolar electrocoagulation have been considered to be the most effective methods of treatment for these patients. However both techniques are associated with potential morbidity derived from the difficulty of assessing the depth of the thermal effect on the rectal wall.

APC is a relatively new method of non-contact electrocoagulation well suited for hemostasis of large bleeding areas. In this paper we describe our experience in the treatment of patients suffering from radiation-induced proctitis with both pharmacological therapy (5-ASA) and APC.

Patients and Methods

From January 2005 to March 2008 we followed, at the service of our Endoscopy Unit within the Department of Oncology, sixteen patients, eleven males and five females aged between 41 and 78 years (range 62.3) who suffer from post-radiotherapy rectal bleeding. Eleven out of the sixteen patients suffer from prostate cancer, three from endometrial cancer and two from cervical cancer.

All patients underwent total colonoscopy to exclude other causes of bleeding. The equipment used were standard colonoscopes: Olympus CF 100 videoendoscope, connected to Olympus CV 100 videoprocessor, an APC equipment with APC probe with external diameter of 2 mm and internal diameter of 1.5 mm, argon delivery unit (ERBE Argon Plasma Coagulator ICC 200, ERBE Electromedizin, Tubingen, Germany). The argon gas flow was set between 1.5 and 2 l/min at 40-60 W power.

Five patients had been treated at other divisions and eleven were at the first observation. Nine out of other eleven patients showed a RUC-like endoscopic picture with intensely hyperemic mucosa, rough, crumbly bleeding involving the entire wall and not extending more than 25-30 cm from the anal. In the remaining two cases there was a similar picture to that found in the other, but more nuanced, and presence of numerous telangiectasias in areas free from erosion was observed.

The first nine cases were treated with 5-ASA, in the other two cases APC therapy was started immediately. The nine patients initially treated with 5-ASA were examined after two weeks. The RCU-like picture disappeared but we observed areas of telangiectasia which were treated with APC.

In the five cases showing recurrent episodes and which involve other treatments at other centers, we found endoscopically areas of telangiectasia which were treated with APC.

Results

All patients underwent a careful follow-up every three months. Patients who began treatment with 5-ASA had a rapid remission of symptoms and improvement in the inflammation state. Some of

these, however, during the follow-up showed a new bleeding associated to telangiectasias (Fig. 2) without mucosal inflammation. In these cases APC was the therapeutic approach (Fig. 3).

Rapid disappearance of rectal bleeding was achieved in patients who underwent APC therapy since the first session of treatment. The endoscopic coagulation performed every 6-12 months was able to easily treat other telangiectasias eventually arisen.

All patients showed no symptoms and negative endoscopic picture during a two years follow-up and six months after the last control.

Discussion

APC shows many advantages (9). The unit is compact, mobile and easy to maintain, it is simple to perform and easily learnt. The non-contact nature of application allows large areas to be treated rapidly, in contrast to contact thermal techniques such as heater probe or multipolar diathermy. The technique creates less smoke than laser therapy, allowing better views and shorter treatment time. The favourable features of APC are related to its predictable depth of

tissue destruction and preferential arcing to areas of non desiccated tissue when it is utilized in a non-contact fashion (10).

APC has been used in gastrointestinal endoscopy since 1994 (11). Three years later were reported preliminary results about APC treatment of radiation-induced proctitis (12).

From this preliminary experience the efficacy and safety of APC have been suggested in several case series (13-17).

The results in this study provide further data about the efficacy, safety and well-tolerance of APC in chronic rectal bleeding related to radiation proctopathy; another interesting approach, reported in literature, consists of bipolar coagulation (18).

No complications were encountered in this series. All the patients were without disease after two years of follow-up.

In the patients with an endoscopic presentation like-RUC the initial use of oral 5-ASA obtained a rapid remission of the clinical manifestation and the endoscopic aspect. The subsequent use of APC over rectal telangiectasia led to a complete and persistent clinical remission.

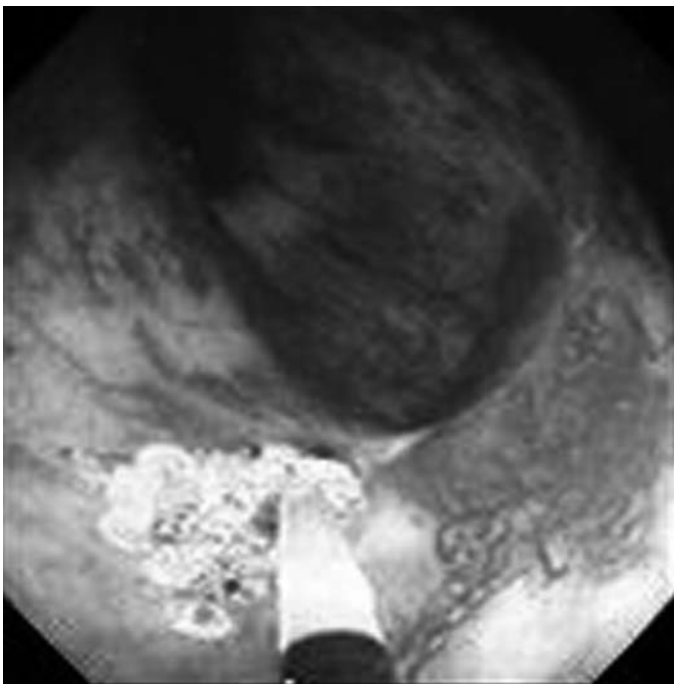


Fig. 2. Post-radiotherapy proctitis. Rectal bleeding was treated with APC. During the procedure the probe is not in close contact with the mucosa allowing the argon gas to perform its cauterizing effect when burned

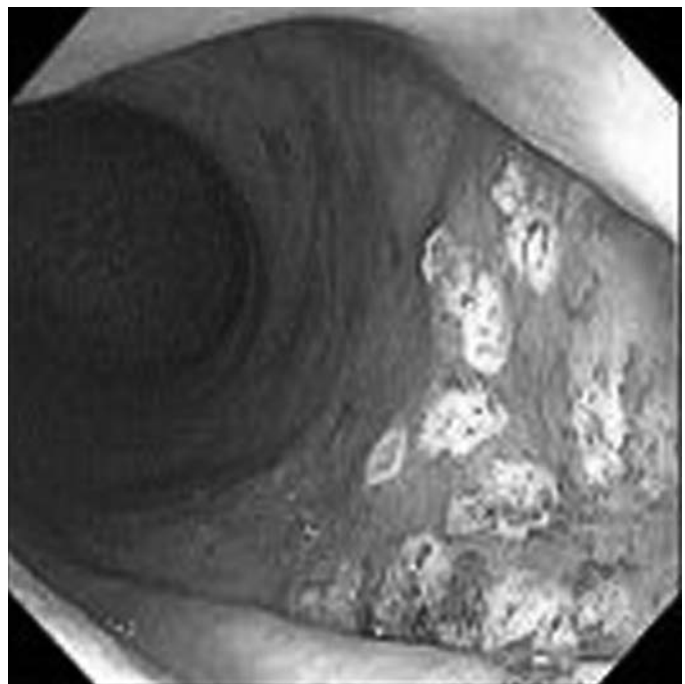


Fig. 3. Post-radiotherapy proctitis with rectal bleeding. Cauterization of bleeding lesions was achieved through APC treatment

Conclusions

The authors believe that the post-radiotherapy rectal bleeding is caused initially by inflammation but, in the later steps, the formation of areas of telangiectasia reminiscent of angiodysplasia of the colon plays a crucial rôle; therefore elimination of areas of telangiectasia, using APC therapy, seems to be successful and free of complications in the treatment and prevention of recurrent episodes of rectal bleeding.

References

- Kennedy GD, Heise CP. Radiation colitis and proctitis. *Clin Colon Rectal Surg* 2007; 20: 64-72.
- Konrad K, Richter MD, Louis M, *et al.* Differential effect of radiation on endothelial cell function in rectal cancer and normal rectum. *Am J Surg* 1998; 176: 642-7.
- Bonis PA, Nostrant TT. Diagnosis and treatment of chronic radiation proctitis. *UptoDate* 2003; 11.
- Baum CA, Biddle WL, Minner PB. Failure of 5-aminosalicylic acid enemas to improve chronic radiation proctitis. *Dig Dis Sci* 1989; 34: 758-69.
- Baughan CA, Canney PA, Buchanan RB, *et al.* A randomized trial to assess the efficacy of 5-aminosalicylic acid for the prevention of radiation enteritis. *Clin Oncol* 1993; 5: 19-24.
- Seow-Choen F, Goh HS, Ew KW. A simple and effective treatment for hemorrhagic radiation proctitis using formalin. *Dis Colon Rectum* 1993; 36: 135-8.
- Luna-Perez P, Rodriguez-Ramirez SE. Formalin instillation for refractory radiation-induced hemorrhagic proctitis. *J Surg Oncol* 2002; 80: 41-4.
- Kochar R, Sharma SC, Gupta BB, *et al.* Rectal sucralfate in radiation proctitis. *Lancet* 1988; 2: 400.
- Rustagi T, Mashimo H. Endoscopic management of chronic radiation proctitis. *World J Gastroenterol* 2011; 17(41): 4554-62.
- Kwan V, Bourke MJ, Williams SJ, *et al.* Argon plasma coagulation in the management of symptomatic gastrointestinal vascular lesions: experience in 100 consecutive patients with long-term follow-up. *Am J Gastroenterol* 2006; 101: 58-63.
- Farin G, Grund KE. Technology of argon plasma coagulation with particular regard to endoscopic application. *Endosc Surg* 1994; 2: 71-7.
- Chutkan R, Lipp A, Wayne J. The plasma argon coagulator: a new and effective modality for treatment of radiation proctitis. *Gastrointest Endosc* 1997; 45: AB 27.
- De La Serna Higuera C, Martin Arribas MI, Rodriguez Gomez SJ, *et al.* Efficacy and safety of argon plasma coagulation for the treatment of hemorrhagic radiation proctitis. *Rev Esp Enferm Dig* 2004; 96 (11): 758-64.
- Silva RA, Correia AJ, Dias LM, *et al.* Argon plasma coagulation therapy for hemorrhagic radiation proctosigmoiditis. *Gastrointest Endosc* 1999; 50 (2): 221-4.
- Smith S, Wallner K, Dominitz JA, *et al.* Argon plasma coagulation for rectal bleeding after prostate brachytherapy. *Int J Radiat Oncol Biol Phys* 2001; 51(3): 636-42.
- Taieb S, Rolachon A, Cenni JC, *et al.* Effective use of argon plasma coagulation in the treatment of severe radiation proctitis. *Dis Colon Rectum* 2001; 44(12): 1766-71.
- Tjandra JJ, Sengupta S. Argon plasma coagulation is an effective treatment for refractory hemorrhagic radiation proctitis. *Dis Colon Rectum* 2001; 44(12): 1759-65.
- Lenz L, Tafarel J, Correia L, *et al.* Comparative study of bipolar electrocoagulation versus argon plasma coagulation for rectal bleeding due to chronic radiation coloproctopathy. *Endoscopy* 2011; 43(8): 697-701.

