“Medical follow-up and surveillance of persons following radiation emergencies”
Headquarters in Vienna, Austria, from June 15 to June 17, 2015

Follow-up programme of patients overexposed after medical interventions in Argentina

Dr. Mercedes Portas
Introduction

Based on the last radiation emergencies in the world, the need to establish a common basis / harmonized criteria to organize the medical follow-up of persons involved in a nuclear or radiological emergency has been identified.
The purpose of the meeting
To discuss the characteristics of the medical follow-up established in several radiation emergencies in the world.
- Working group

- The meeting should include participants related with the follow-up of persons involved in nuclear and radiological emergencies, from different part of the world. Including nuclear and radiological accidents; follow-up survivors from atomic bombs; follow-up of overexposed patient after medical interventions.
<table>
<thead>
<tr>
<th>Expert</th>
<th>Contact email</th>
<th>Institution</th>
<th>Country</th>
<th>Involvement</th>
</tr>
</thead>
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</tbody>
</table>

DRA MERCEDES PORTAS-HOSPITAL DE QUEMADOS
Burns Hospital

Radiopathology Lab

Nuclear Regulatory Authority

Dra. Adriana Coppola
Radiology

Dr. Juan Carlos Giongrande
Pathologist

María del Carmen De Lellis
Psychologist

Dr. Mercedes Portas
Head of Surgical Departament
Burns Hospital 1997-2015
N= 266

- 90.60%
- 8.65%
- 0.75%

- Radiotherapy
- Accidents
- Interventional Procedures
- Procedures
Burns Hospital 1997-2015
N= 266

Intervencionismo por año n=23

Interventional procedures
## Cutaneous Radiation Syndrome

<table>
<thead>
<tr>
<th>Condition</th>
<th>Dose Threshold (Gy)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Eritema</td>
<td>3-10</td>
</tr>
<tr>
<td>Transitory Hair-Loss</td>
<td>3-7</td>
</tr>
<tr>
<td>Permanent Hair-Loss</td>
<td>7-10</td>
</tr>
<tr>
<td>Dry Epithelitis</td>
<td>10-15</td>
</tr>
<tr>
<td>Wet Epithelitis</td>
<td>15-25</td>
</tr>
<tr>
<td>Radionecrosis</td>
<td>&gt;25</td>
</tr>
</tbody>
</table>
Treatment Protocol for C. R. S

- **Local debridement**
  - Collagenase: metalloproteinase which breaks peptide bonds of collagen which may be type I, II, III, IV and V

- **Antioxidants**
  - Super oxido dismutasa (SOD)
  - Vitamina E 400 U.I
  - Vía oral

- **Obliterans**
  - Endarteritis
  - Isquemia – reperfusión
  - Treatment

- **Pentoxifilin 400**
- Vía oral
Concept

- The reactions occurs in a delayed pattern

- Many times it is impossible to discriminate between a:
  - Thermal burn
  - A chemical toxic reaction
  - A radiation injury
Ultrasonography + Ecodoppler

It is a valuable tool for diagnosis and prognosis. It shows in detail the vascularization status of skin.

The presence of reperfusion constitutes a sign of improvement.
Teletermography
Burns Hospital
Detection:

- High frequency ultrasound
- Magnetic Resonance Imaging (MRI)
- Telethermography
- Clinical Record
Score:

EORTC/RTOG

European Oncology Radiation Therapy
Criteria/Radiation Therapy Oncology Group
Burns Hospital
Patients assisted
1997-2015  N= 266

ERTOG N=266

- 51.13%
- 23.31%
- 4.89%
- 18.42%
- 2.26%
- S/D
<table>
<thead>
<tr>
<th>Grades</th>
<th>Acute radiotoxicity: &lt; 90 días</th>
<th>Chronic radiotoxicity: &gt; 90 días</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Erythema Epilation itching Dry descamacion</td>
<td>Atrophy Pigmentary changes Partial loss of hair</td>
</tr>
<tr>
<td>2</td>
<td>Erythema Wet descamacion Edema</td>
<td>Moderate atrophy Telangiectasia Partial loss of hair</td>
</tr>
</tbody>
</table>
PATIENTS
Burns Hospital
- A, Julio
- Profession: radiologist
- Background: Smoker
- First visit: 02-08-2010 He refers permanent pain in the 3rd finger of left hand (used to move his patients during fluorocopy studies)
14-08-2010

Trophic nail disorders in the MIDDLE FINGER
distal hyperkeratosis
Signs of cutaneous peri-nail hipotrofia

We prescribed treatment protocol

- Pentoxifilin 400 mgrs
- E vitamin 400 I.U.
- Locally: SOD
The patient expressed a marked improvement on the issue of consultation; Middle finger pain. He felt content because he did not know of the existence of our team and more confident at being included in a protocol of radiation injuries we have recommended not continue with the activity as a radiologist, only can do ultrasound studies of his patients.
S.M – Female – 72 years old

Patient with a mastectomy due to Breast Carcinoma. After receiving 5000 cGy as radiotherapy, exudative epithelitis appeared.
D.S – Female – 46 years old

Patient with a tumorectomy due to in situ ductal carcinoma. After receiving 5000 cGy as radiotherapy, dry epithelitis appeared.
<table>
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<tr>
<th>Grado</th>
<th>Acute Radiotoxicity</th>
<th>Chronic Radiotoxicity</th>
</tr>
</thead>
<tbody>
<tr>
<td>3</td>
<td>Confluent moist desquamation Severe edema</td>
<td>Confluent areas of marked atrophy Telangiectasias</td>
</tr>
<tr>
<td>4</td>
<td>Bleeding Ulceration Necrosis</td>
<td>Ulceration Bleeding</td>
</tr>
</tbody>
</table>
ERTOG 1/2

Ultrasound Ecodoppler

NO Deep muscular compromised
NOT compromised vascularization

Evolution

Good evolution in 6 to 12 months

Local evolution

Remission of symptoms
Response to treatment
Aparent healing

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A 57 year old female patient with heart disease, heavy smoker, who was exposed to X rays during an interventional procedure(stent) in 2005/September.
Early manifestations were blisters, which were diagnosed by a dermatologist as Herpes Zoster. Few months later, in the same localization, a deep ulcer with severe pain appeared. During 2006, the patient underwent a surgical plastic procedure: two rotation flaps were performed to close the wound. Total necrosis of the rotation flaps, leaving a large ulcer near 20 by 20 cm, occurred. The chronic ulcer was treated with sugar and prone position by general surgeons. Non specific treatment was installed due to lack of knowledge of this particular entity (CRS).
Five months later, in her first medical appointment within the Burn Hospital:

conservative treatment of late radiation skin lesions was performed according to our protocol as follows:

Cleaning of erosive-ulcerous defect
Antibacterial procedure
Anti-inflammatory prevention
Acceleration of epithelium recovery
Improvement of microcirculation and blood rheological features
Following overexposure, the main directions of medical management for persons under care are:

Monitoring the health status of patients in order to early diagnose the stochastic and deterministic radiation effects, and preventing the appearance and progression of local complications. Treatment of somatic diseases already present in the exposed patients.
Serial Eco-Doppler studies showed:
progressive vascularization

This success was attributed to:

hyperbaric oxygen procedures
and pentoxifylline treatment
Eco-Doppler studies showed:
progressive vascularization
progressive closure of the wound:

using allograft, porcine dermis as temporary skin substitute avoiding bacterial infection

We observed:

The good quality of the new epidermis,
A.C – Male – 47 years old

Patient irradiated with $\beta$-therapy for keloid scar after cholecistectomy. He showed recurrent radionecrotic ulcers until treatment was started.

Initial status

After 15 days of treatment

After 1 month of treatment
Radionecrosis: a large inflammatory foci are seen around the lesion

27-12-2005

Estocastic efects: carcinoma de Ackerman

Flaps de avance with an autograph
C,N- HC 759455 Age: 74 years Female patient

Background:
Diabetes, venous insufficiency, and hypothyroidism.

Diagnosis:
Mixed parotid tumor.
Surgical procedure + radiation treatment for 1 year, one session per month

21-11-06 First visit to the hospital. We observed
Necrosis of the mastoid area 1.5 x 5.7 cm, an ulcerated lesion 2 mm depth
Thickness (depth) of the ulcerated lesion is measured, reaching 9 mm. It is observed that the loss of differentiation of plans involving the skin, subcutaneous tissues, and underlying tissue muscular plane.
V, Carmelo   HC 699996   50 years old male

Angioplasty  5 hs  in 2003
There is a discrepancy between the clinical signs and the thermography and ultrasonography studies.
We can observe the superficial aponeurosis and part of the superficial muscular fibers affected.
Serial Eco-Doppler studies showed:
progressive vascularization

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We observed:

The good quality of the new epidermis.
B, Angel 81 y.o – Angioplasty: 2012 / 3 biopsies
Ultrasound: Deep muscular compromise
C, José - 75 y.o. Underwent Angioplasty : 5 stents / 8 hs
• January 28 2010 punch for diagnosis
• February 1st 2011 punch for diagnosis
• March 27 2013 punch for diagnosis
• April 11 2014: underwent surgery for simple closing

45 sessions of Hyperbaric Oxigen were performed

4/2014

4/2015
MRI: Ulcerated injury involving skin, T.C.S, the underlying muscle structures and the rib cage. Measures 56.6 mm x 19.7 mm. Rib fracture without displacement. Post radiotherapy inflammatory process.
ERTOG 3/4

Ultrasound Ecodoppler

Deep muscular compromised

Evident signs of compromised vascularization

Uncertain

Local evolution

Repetitive crisis:
Partial response to treatment
Pain- Bleeding

DRA MERCEDES PORTAS-
HOSPITAL DE QUEMADOS
Summary
Groups 1 and 2:

1. Presented favorable evolution and complete local remission between 5 and 12 months of treatment.

2. Ultrasound does not show muscle involvement. Interfaces are thickened.

3. There is a good vascular response to treatment particularly in the perilesional areas showing centripetal healing.
1. ERTOG Groups 3 and 4
2. when the protocol is interrupted radiation injuries, decreases the latency period.
3. Recurrent exacerbation crisis due to inflammatory waves.
4. Pain related to Ischemia phenomena is manifested
5. Tissue damage by oxidative stress occurs
Our Cell Therapy Unit that provides acellular matrices is basic. It is desirable the development of a more complex Cell Therapy Unit for regenerative medicine applications, designed to work with the Good Manufacturing Practices under ISO 9001 standards. Mesenchymal stem cells are obtained, processed and expanded in another laboratory, Hospital San Martín in La Plata city, about 40 km far from the Burns Centre.
Informed Consent for fluoroscopic guided procedures

The possibility that a cutaneous radiation syndrome appears depends on the difficulty of the procedure and their sensitivity to radiation due to previous procedures, disease or genetic predisposition. You and your family will be warned if we used high levels of radiation during the procedure. If this happens you will receive instructions so that you or a family check the possible occurrence of these effects.
Cell therapy Unit:

- produces porcine acellular matrices for temporary coverage.
- Research and development protocol: “Translational Clinical Trial phase I / II to evaluate the safety and efficacy of adult mesenchymal stem cells from bone marrow for the treatment of large burns and radiological lesions”, approved by INCUCAI that is National Institute for Organ Donation and Transplantation, which is the competent authority for the production and administration of stem cells.
Case: A 66 year old male patient, heavy smoker and with high blood pressure treated with radiotherapy at the 36 years due to a right leg angioma.

Ulcers appeared approximately each 10 years, as a result of repetitive inflammatory waves, with remission after local treatment. Then, acute exacerbation crisis became more frequent (shorter intervals between ulcers expression).

On May 30th 2011 the patient consulted our hospital (Burns Hospital) for the first time exhibiting a deep necrotic ulcer on the right leg.
Proposals:

Radiation Protection Program:

Monitoring of patients who underwent these treatments. If any case appears signs of: itching, redness, pain, color changes, blisters, etc. . . . . . . is due to exposure. First think that is a radiation injury. Contact with Radiopathology Committee (experts). Indicate the treatment protocol quickly.
Recommendations, patient follow-up

Approach to patients

• Complete medical history, assess comorbidities and preexisting clinical conditions. Complete physical examination

• Previous treatments performed by other professionals indicated, where possible if the patient brings the written information, enter it in the history, but order it through to professionals working

• Interview with a psychologist
**Recommendations, patient follow-up**


II. Give the patient alarm patterns in relation to color changes, blistering, itching sensation and / or pain, etc in the compromised area.

III. Involve the patient in their monitoring.

IV. Implement the use of superoxide dismutase local cream as antifibrotic.

V. Advise patient of potential risks from the application of radiation.

VI. Let the patient know that, if a complication occurs, it can be treated by a team of experts and that there is a protocol for treatment of radiation injuries proved scientifically and approved internationally.
VII. Implement a database containing the following information: name, surname, medical record number, exposition to radiation, time to the onset of symptoms and first consultation at the hospital, the report of previous studies and treatments, to analyze the tissue compromise, dose received, reports from studies.

It’s better to record this information at the beginning ideally prior to the implementation of the protocol, and to be repeated at 2, 4 or 6 months, according to evolution, to corroborate the revascularization process.

VIII. Important contact with colleagues involved, radiotherapist, oncologist, dermatologist etc. to combine efforts for the patient treatment.
• Prognosis is always serious. In those who interrupted treatment, severe lesions and pain reappeared.

• The chronic and cyclic evolution of these patients makes long term follow-up, including both clinical and psychological aspects mandatory.

• Increased vulnerability to trauma of the affected areas was observed.

• In all cutaneous lesions occurring within a few weeks/months after fluoroscopically guided procedures or after radiotherapy a radiation origin should be considered.

• Team intervention must include radiologist, oncologist.

• Important contact with colleagues involved, radiotherapist, oncologist, dermatologist etc. to combine efforts for the patient treatment.
Stressing the importance of the creation of specialized committees for the diagnosis and treatment of CRS with a multidisciplinary approach of such peculiar patients
description of the organization at our Burn Hospital: the multidisciplinary professional group, the therapeutic protocol and adjunctive treatments and tools employed for diagnosis and follow-up.
We did initial evaluation of patients, in compliance with standard protocols, applying diagnostic methods and therapeutic methods.
In all admitted cases, both acute and chronic, the patients underwent our therapeutic protocol according to the pathogenesis of the CRS:

- Free radical treatment: oral antioxidants (E vitamin)
- Endarteritis Obliterans: oral pentoxiphylline
- Local Treatment:
Local Treatment:

- **Open wound**: collagenase ointment (enzimatic debridment)
- Silver sulfadiazine + lidocaine + A vitamin (bacteriostatic)
- **Closed lesions**: SOD cream
Monthly evaluation of the therapeutic response (more frequently when necessary), telethermography, ultrasound and clinical follow-up; Pain management, and psychopathologic support
Approach to patients

- Complete medical history; assess comorbidities and preexisting clinical conditions. Complete physical examination
- Previous treatments performed by other professionals indicated, where possible if the patient brings the written information, enter it in the history, but order it through to professionals working
- Interview with a psychologist
Prescription of complementary studies:

- High-resolution ultrasonography
- Soft tissue Doppler
- Telethermography
- Radiosensitivity tests
Study of markers of chronic inflammation.

Recommendations: patient follow-up

Inspection of the skin: It’s recommended photography registry, pre- and post-treatment.

We give the patient alarm patterns in relation to color changes, blistering, itching sensation and / or pain, etc in the compromised area.

Involve the patient in their monitoring.

Implement the use of superoxide dismutase local cream as antifibrotic
Advise patient of potential risks from the application of radiation.

Let the patient know that, if a complication occurs, it can be treated by a team of experts and that there is a protocol for treatment of radiation injuries proved scientifically and approved internationally.
Implement a database containing the following information:

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Conclusions

Prognosis is always serious.

In those who interrupted treatment, severe lesions and pain reappeared.
The chronic and cyclic evolution of these patients makes long term follow-up, including both clinical and psychological aspects mandatory,

• Increased vulnerability to trauma of the affected areas was observed.
• In all cutaneous lesions occurring within a few weeks/months after fluoroscopically guided procedures or after radiotherapy a radiation origin should be considered.
• Team intervention must include radiologist, oncologist
• Important contact with colleagues involved, radiotherapist, oncologist, dermatologist etc. to combine efforts for the patient treatment
Buenos Aires, Argentina

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