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ESMO Clinical Practice Guidelines

Chemotherapy Extravasation Case Discussion

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Management of chemotherapy extravasation: ESMO–EONS Clinical Practice Guidelines†

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Definitions

- Chemotherapy extravasation refers to the inadvertent infiltration of chemotherapy into the subcutaneous/subdermal tissues surrounding the intravenous administration site
- Extravasated drugs are classified according to their potential for causing damage as:
  - Vesicant: DNA / Non-DNA binding
  - Irritant
  - Nonvesicant

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Classification of anticancer drugs according to their ability to cause local damage after extravasation

Vesicants

DNA binding

Alkylating agents

- Mechloretamine
- Bendamustine

Anthracyclines

- Doxorubicin / Daunorubicin
- Epirubicin / Idarubicin

Others

- Actinomycin D / Mitomycin C
- Mitoxantrone

Non-DNA binding

Vinca Alkaloids

- Vincristine
- Vindesine
- Vimblastine
- Vinorelbine

Taxanes

- Paclitaxel / Docetaxel

Others

- Trabedectin

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Classification of anticancer drugs according to their ability to cause local damage after extravasation

Irritants

Alkylating agents
- Carmustine
- Ifosfamide
- Streptozotocin
- Dacarbazine
- Melphalan

Liposomal Anthracyclines

Others
- Mitoxantrone
- Ixabepilone

Topoisomerase II inhibitors
- Etoposide / Teniposide

Antimetobolites
- 5-FU

Platin salts
- Cisplatin / Carboplatin
- Oxaliplatin

Topoisomerase I inhibitors
- Topotecan / Irinotecan

Classification of anticancer drugs according to their ability to cause local damage after extravasation

Nonvesicants

- Arsenic Trioxide
- Aparaginase
- Bleomycin
- Bortezomib
- Cladribine
- Cytarabine
- Etoposide
- Gemcitabine
- Fludarabine
- Interferons
- Interleukin 2
- Methotrexate
- Monoclonal antibodies
- Pemetrexed
- Raltitrexed
- Temsirolimus
- Thiotepa
- Cyclophosphamide

Factors associated with increased risk of extravasation: Patient-related

- Small and fragile veins
- Hard/sclerotic veins due to multiple previous CT courses
- Altered circulation (Raynaud's, Diabetes, severe peripheral vascular diseases, Lymphedema, Superior Cava syndrome, etc…)
- Bleeding predisposition or coagulation abnormalities
- Obesity
- Sensory defects
- Communication problems
- Prolonged infusions

Factors associated with increased risk of extravasation: Cannulation/Infusion procedure-related

- Untrained/unexperienced staff
- Multiple cannulation attempts
- Unfavorable cannulation sites
- Bolus injection
- High flow pressure
- Choice of equipment
- Inadequate dressings or poor cannula fixation
- Poorly implanted ports (CAVD)

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Prevention

- Most chemotherapy extravasations can be prevented with a systematic implementation of careful, standardized and evidence-based administration techniques

- The staff involved in the infusion and management of cytotoxic drugs must be trained in the implementation of several prevention protocols

Management of Chemotherapy extravasations: General measures

- Patient education
- Early start of treatment
- Trained staff to deal with extravasation
- Extravasation protocol easily available
- Multidisciplinary approach from the very beginning: nurses, medical oncologists, plastic or general surgeons, etc…

Management of Chemotherapy extravasations: Specific antidotes

- Local injections with topical corticosteroids
- Sodium Thiosulfate
- Dimethyl Sulfoxide (DMSO)
- Dexrazoxane
- Hyaluronidase

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Management of Chemotherapy extravasations: Specific antidotes

Recommendations on the use of Dexrazoxane

- Useful to reduce anthracycline-induced cardiotoxicity
- Some experimental trials show protection after anthracycline extravasation in mice
- Two phase II studies show benefit in preventing tissue damage after extravasation
- Dexrazoxane given in a three day schedule (1000/1000/500 mg/m2) starting no later than 6 hours after extravasation
- To be given in a large vein in the opposite arm from which the extravasation occurred
- To be reduced by 50% if creatinine clearance < 40 cc/min

Mouridsen et al. Ann Oncol 2007; 18:546.

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Management of Chemotherapy extravasations: Specific antidotes

Extravasated drug	Suggested antidote	Level of evidence
Anthracyclines	Dexrazoxane i.v. Start as soon as possible (no later than 6 h) at a 1000 mg/m^2 dose on day 1 and day 2 and at 500 mg/m^2 on day 3.	III-B
Anthracyclines	Topical DMSO (99%). Start as soon as possible (preferably in the first 10 min). It should be applied every 8 h for 7 days.	IV-B
Mytomicin C	Topical DMSO (99%). Start as soon as possible (preferably in the first 10 min). It should be applied every 8 h for 7 days.	IV-B

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Management of Chemotherapy extravasations: Specific antidotes

Extravasated drug	Suggested antidote	Level of evidence
Mechlorethamine	Sodium thiosulfate 0.17 M in subcutaneous injection. Start immmediately. Subcutaneous injection of 2 ml of solution made from 4 ml sodium thiosulfate + 6 ml sterile water.	V-C
Vinka alkaloids	Hyaluronidase in subcutaneous injection. Administer 150-900 IU around the area of extravasation.	V-C
Taxanes	Hyaluronidase in subcutaneous injection. Administer 150-900 IU around the area of extravasation.	V-C

Management of Chemotherapy extravasations: Surgical approaches

- Only if severe tissue damage occurs
- Surgical debridement is recommended when tissue necrosis or local pain persists after ten days
- Such a procedure should consist of:
  - a wide tridimensional excision of all involved tissue
  - temporary coverage with a biologic dressing
  - simultaneous harvesting and storage of a split-thickness skin graft
- Once the wound is clean, delayed application of the graft is performed (usually at 2–3 days)

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Management of Chemotherapy extravasations: Adequate reporting

- Patient name and chart number
- Date and time of extravasation
- Name of drug extravasated as well as the diluent used
- Signs and symptoms as reported by the patient
- Description of the iv access
- Extravasation area and volume approximated of extravasated drug
- Management steps and time
- Photographic documentation

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Steps to be taken in case of Extravasation

Step 1

Stop and disconnect infusion. Do not remove cannula.

Step 2

Identify extravasated agent.

Step 3

Leaving the cannula in place, try to gently aspirate as much as extravasated solution as possible. Record aspirated volume in patient chart. Avoid manual pressure over the extravasated area and remove cannula.

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Steps to be taken in case of Extravasation

Step 4

Mark with a pen an outline of the extravasated area.

Step 5

Notify physician and start specific measures as soon as possible.

Step 6

If non vesicant: cold dry compresses

If vesicant or irritant: Next

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Steps to be taken in case of Extravasation

Vesicant or Irritant

Localize and neutralize
- Anthracyclines
- Antibiotics
- Alkylating agents

Disperse and dilute
- Vinca alkaloids
- Taxanes
- Platinum salts

Localize
Apply dry cold compresses 20 min x 4/day 1-2 days
Avoid alcohol compresses

Disperse
Apply dry warm compresses 20 min x 4/day 1-2 days

Neutralize
For anthracyclines: dexarozane/ topical DMSO

For MMC: topical DMSO

Dilute
Administer agents increasing resorption
Vinca alkaloids and taxanes: hyaluronidase

Elevate the limb. Give analgesia.

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Conclusions

- Prevention is key by expert staff/patient information
- Multidisciplinary management
- Appropriate reporting
- Rapid intervention as earlier as possible