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Intrathoracic extravasation of doxorubicin: treatment, evolution and literature review

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Cytotoxic drug extravasation is considered a serious adverse event that leads to an increase in morbidity. We report a case of doxorubicin intrathoracic extravasation during infusion by a central venous catheter

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A **59-year-old woman** with central osteosarcoma was treated with adjuvant (given after surgery to reduce the risk of recurrence) chemotherapy of doxorubicin 45mg/m^2 (days 1–2), methotrexate 8g/m^2 (on day 21 with leucovorin rescue) and cisplatin 120mg/m^2 (days 27–29). A central venous catheter was surgically implanted in the superior vena cava for chemotherapy administration. Chest radiography showed that the catheter was correctly positioned. Echocardiography was reported to be normal.

On the first day of the chemotherapy treatment, shortly after fluid infusion, the patient presented with dizziness, pallor and a cold sweat that resolved spontaneously. As initial symptoms resolved, doxorubicin infusion was started (four hour infusion of doxorubicin 75.15mg in 500ml 0.9 per cent sodium chloride). Half an hour after the beginning of the doxorubicin infusion, she had pain in the epigastrium, arm and right-sided hemithorax. The infusion was then stopped. Chest radiography and cardiac enzymes were normal.

An infusion of 0.9 per cent sodium chloride was restarted. A new pain episode occurred and the infusion was stopped. Chest radiography with contrast dye was performed and it showed extravasation of the radiopaque dye in the mediastinum, through the intermediate portion of the catheter. A computed tomography scan revealed incorrect positioning of the catheter, so, it was removed and high dose dexamethasone was started.

Over the next few days, the patient referred tearing chest pain that increased when she breathed and gave a cough. The auscultation (sounds from the thorax) showed crackles. On the eighth day, control chest radiography showed mild right-sided pleural effusion and 200ml fluid was drained. On the 12th day she complained of chest pain (although less than before), dyspnoea and dry cough. The auscultation showed diminished ventilation in the right-lobe.

Two months after the extravasation, the patient had some cough, mild chest pain and dyspnoea. Computed tomography scanning showed right-sided pleural effusion, although echocardiography was found to be normal.

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Discussion

Doxorubicin is a vesicant antineoplastic drug which is considered one of the most problematic cytotoxic drugs when extravasation occurs because it can produce tissue necrosis.[1,2] There are several successful measures to treat cytotoxic agent extravasation in a limb, but no consensus treatment exists on the management of intrathoracic extravasation.

Seven cases of thoracic extravasation have previously been reported (Table 1, p74).[3,4] None of these cases involved doxorubicin. In all cases, the clinical course was similar. In half the cases, radiography showed significant pleural effusion. The most frequent reason for extravasation was the perforation of the superior vena cava by the tip of the catheter. Information on these seven cases revealed that treatment was conservative in four of them (cases a,b,d,e), whereas in the other three corticosteroids were given (cases c,f,g). Additional treatment was only give in case f (open mediastinal irrigation).[3,4] The outcome of those cases was good and the patients survived.

According to the literature review, the most convenient measures for treating intrathoracic extravasation could be:

- Stop central venous infusion immediately
- Try to aspirate slowly the drug inside the catheter and then remove the catheter
- Perform appropriate screening to rule out cardiac toxicity, pneumonia or pleural effusion
- Adopt a watch-and-wait attitude and symptomatic treatment when necessary. Surgical intervention could be considered as a second-line treatment

Table 1: Cases previously reported in the literature of thoracic extravasation

Case	Cytotoxic agent	Symptoms and clinical course	Outcome
a	5-Fluorouracil	Fever, chest pain, arrhythmias, pericardial effusion	No cardiac dysfunction
b	5-Fluorouracil	Chest pain	Improvement. Fibrotic and contracted right upper lobe
c	5-Fluorouracil + epirubicin	Pain and fever for 24 hours	Mild oesophageal dysfunction
d	Vincristine	Fever, dyspnoea, swollen left neck	Improvement: minimal residual interstitial changes
e	Vinblastine	Fever, chest pain, facial oedema, thromboses	Improvement: gradual resolution of thromboses
f	Daunorubicin	Pain, cough, dysphagia, thyrotoxicosis	Pleural effusion residual changes. Recall effect*
g	Epirubicin	Pain, fever	Recurrent pleural effusion

* In this context, recall effect means that tissues that are permanently affected by chemotherapy or radiation therapy may react if chemotherapy is re-administered

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