Extravasation of chemotherapeutic agents from a peripheral cannula is a known problem, and to prevent that, oncology units use central vein access with indwelling catheters such as port-a-cath or Hickman catheter. The intrapleural extravasation of chemotherapeutic agents is a rare event. We describe a 9-year-old girl with newly diagnosed Ewing’s sarcoma of the left upper humerus receiving neoadjuvant chemotherapy through a newly inserted port-a-cath device. The patient developed tachypnea and right-sided chest pain on day 2 of chemotherapy. The radiological investigations confirmed the extravasation of doxorubicin into the pleural space. The surgical washout with chest-drain insertion was done, and we continued flushing with normal saline until the drain fluid became clear. She has completed neoadjuvant therapy. This case report shines light into scenarios where extravasation of anthracycline into the pleural cavity or thorax can be managed conservatively and in settings where dexrazoxane is unavailable without causing much delay in restarting the chemotherapy.

Keywords: Cancer, chemoport, children, doxorubicin, extravasation, port-a-cath
with extravasation of doxorubicin into the pleural space from a newly inserted port-a-cath and successfully managed.

**Case Report**

A 9-year-old girl was referred to our center with swelling of the left upper arm, diagnosed as Ewing’s sarcoma of the left humerus. A port-a-cath was inserted through the right subclavian vein, and she was started on neoadjuvant chemotherapy as per Euro Ewing’s 12 protocol. The first course (VDC) consisted of vincristine, cyclophosphamide, and two doses of doxorubicin infusion over 24 h each. She was given 30 mg doxorubicin (37.5 mg/m²) diluted in 500 ml normal saline, which was infused over 24 h. Adequate flushing was done post insertion of port-a-cath and ensured that there was bleeding back from the line. An intraoperative fluoroscopy image confirmed the tip of the port-a-cath in the right atrium. The backflow of blood was observed from the port-a-cath on day 1 before the administration of doxorubicin.

On day 2, following little initial difficulty in withdrawing blood, bright red-colored backflow was observed, which was thought of blood, and chemotherapy was initiated [Figure 1]. Twelve hours later, she developed right-sided chest pain and tachypnea. On clinical examination, there was reduced air entry on the right side of the chest. The chest X-ray showed massive pleural effusion on the right side [Figure 2a]. The contrast dye imaging showed leakage from the tip of the port-a-cath and extravasation into the right pleural space [Figure 2b]. Immediately as the child was in respiratory distress, the port-a-cath was removed, two chest drains were placed, and the pleural space was irrigated. We drained doxorubicin-containing fluid from pleural space. IV hydrocortisone 50 mg was given every sixth hourly for 72 h. Dexrazoxane was not given as it was not available in our setting. Later, the girl started to complain of right-sided chest pain, which progressively got worse, requiring a transdermal buprenorphine patch (5 µg/h). The chest percussion physiotherapy was initiated as well. Through the intercostal drain (ICD), the doxorubicin-containing fluid continued to drain, and the pleural space was irrigated with 50 ml of normal saline every 2 h during the daytime until the drained fluid was clear. Thirteen days later, once the pleural fluid became clear and no further drain, we removed intercostal tubes sequentially. The second course of chemotherapy was administered (ifosfamide 1.8 g/m² + etoposide 100 mg/m²) for 5 days which was delayed by 2 days. Later, she was discharged home. However, 6 days later, she started to have fever spikes and worsening chest pain and suspected an extravasated right pleural space infection. The chest X-ray showed right-sided opacity suggestive of fluid, and ultrasound [Figure 2c] showed localized and partially organized right pleural effusion with thick internal Septations suggestive of infective aetiology. She was neutropenic too and commenced treatment as per febrile neutropenia protocol. Thoracoscopy under general anesthesia was performed, which showed thick adhesions and the right-sided pleura basal and lateral aspects. There was no obvious pus, but the thick fluid was noted. The pleural space was thoroughly cleaned of thick fluid and flakes. Adequate lung expansion was noted after the procedure. At the end of thoracoscopy, two ICDs were placed. The pleural fluid/tissue culture grew streptococcus pneumonia, and sensitive antibiotics were commenced. The blood

**Figure 1:** Image showing the bright red backflow obtained from the port-a-cath which was mistaken for blood

**Figure 2:** (a) massive pleural effusion on the right side, (b) The contrast dye imaging showing leakage from the tip of the port-a-cath and extravasation into the right pleural space, (c) Imaging of the chest with chest x-ray showing right sided opacity suggestive of fluid and ultrasound., (d) HRCT chest showing minimal hydropneumothorax with small locule in the right paracardiac region, patchy areas of consolidation on the right upper and middle lobes with no evidence of fungal nodules
and urine cultures were negative. Fifteen days after thoracoscopy, because of persistent fever on right antibiotics, high-resolution computed tomography of the chest [Figure 2d] was done to look for any evidence of fungal infection. It showed minimal hydropneumothorax with a small locule in the right paracardiac region, patchy areas of consolidation on the right upper and middle lobes with no evidence of fungal nodules. Her third course of chemotherapy was delayed by 1 week, and Vincristine, Doxorubicin, Cyclophosphamide (VDC) chemotherapy was administered with chest drains in situ through peripheral IV cannula. The chest tubes were removed sequentially 16 days after the thoracoscopic procedure. On subsequent follow-up, she is asymptomatic and completed a further six cycles of neoadjuvant chemotherapy.

**DISCUSSION**

The central venous catheters are used to deliver chemotherapy in pediatric oncology units. These catheters may result in multiple complications such as fragmentation of catheter, fragment embolization, migration of the tip, and tip obstruction. Extravasation is an accidental leakage of a cytotoxic drug from the blood vessel into the adjacent tissues. The extent of tissue damage will depend on multiple factors such as type, dosage, concentration, site of infusion of chemotheapeutic agents and kind of treatment provided for extravasation. It is mandatory to check the position and function of venous catheters before accessing them. Anthracycline administration should be performed by the health-care professionals trained in handling the central venous catheters to identify alarming signs of extravasation as soon as possible. The confirmation of backflow of blood from the central venous catheter and ensuring the correct placement of an access needle into the port before connecting or administering any medicine is an excellent way to ensure the functional patency of the device. Correctly identifying blood or blood mixed with cytotoxic agents should be of paramount importance as the slightest delay in identifying the same could lead to severe complications.

Only eight cases of anthracycline extravasation into the thorax have been reported so far, with only one in the pediatric age group [Table 1]. Among the reported cytotoxic drug extravasation cases, it has been noted that anthracyclines are the most common drug to be extravasated into the tissues, which was managed in almost all cases by removing the indwelling central line. It has been observed that most of the patients immediately developed pleural effusion and complained of pain as a long-standing sequel of the extravasation. In all the reported cases, including this one, there was hardly any delay in restarting the next course of chemotherapy. Except in a few cases, all the patients with reported extravasation had good outcomes both

| Author et al. | Age of the patients (years) | Interval between chemopump insertion and extravasation (days) | Interruption to chemotherapy (days) | Management | Complications | Outcome |
|---------------|----------------------------|---------------------------------------------------------------|------------------------------------|------------|---------------|---------|
| Watterson et al. [19] | Pediatric age group | NA | NA | Central line removal and conservative management | NA | Good |
| Bozkurt et al. [12] | 34 | 1 | Yes/60 | Central line removal and pleural tapping | Pleural thickening and minimal increase of mediastinal fatty planes | Good |
| Quintanar Verdúguez et al. [4] | 48 | Few days | No | Central line removal and conservative management | No complication | Good |
| Chang and Murray [3] | 54 | 5 | NA | Surgical washout of pleural space and IV dexrazoxane | Pleural effusion | Good |
| Duhrsen [11] | 64 | NA | No | Conservative management | Pleural and pericardial effusion, irritation to esophagus and thyroid | Relapsed and deceased |
| Rodier et al. [5] | 69 | 80 | Yes | Central line removal and conservative management | NA |
| Manheimer et al. [13] | 72 | 63 | NA | Hickman line removal and conservative management | Fibrotic and contracted right upper lobe of lungs | NA |
| Anderson et al. [14] | NA | NA | NA | Central venous catheter removal and conservative management | NA | Good |

NA: Not available; IV: Intravenous
in terms of the management of the disease and the extravasation and one patient relapsed and passed away during the treatment. Watterson et al. reported two cases of mediastinal extravasation of chemotherapy drugs in the pediatric population. One among them was a case of doxorubicin extravasation, which was managed conservatively.\(^\text{[10]}\) Only four cases leading to mediastinitis have been reported due to extravasations in the last decade, among which two were due to anthracycline extravasation.\(^\text{[11,12]}\) Almost all the reported cases of anthracycline extravasation into the mediastinum completed the chemotherapy without much complications or delay in restarting. In our case, though there was backflow of apparent blood on day 1, there was some difficulty in the drawing back of blood, but because it looked red thought of blood and continued day 2 chemotherapy infusion.

Clinically, irrespective of the extravasated cytotoxic drug, all the reported cases had similar complaints, and the most common among them was pain. Hence, any patient with a central line catheter presenting with chest pain should alarm the clinician with the differential diagnosis of extravasation of the cytotoxic drug. To remove the agent as much as possible, identification of extravasation and timely surgical intervention should be made wherever possible.\(^\text{[12]}\)

**Declaration of patient consent**

The authors certify that they have obtained all appropriate patient consent forms. In the form, the patient has given her consent for her images and other clinical information to be reported in the journal. The patient understand that name and initials will not be published and due efforts will be made to conceal identity, but anonymity cannot be guaranteed.

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**Conflicts of interest**

There are no conflicts of interest.

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