

# SEVERE TOXICITY IN A PATIENT WITH ACUTE LYMPHOBLASTIC LEUKAEMIA RESULTING FROM SUBSTITUTION OF DAUNORUBICIN WITH DOXORUBICIN DUE TO MEDICINE SHORTAGE: A CASE REPORT

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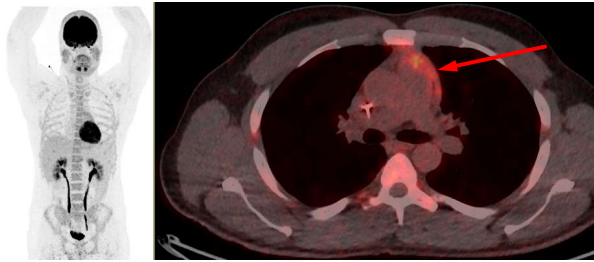
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## BACKGROUND AND IMPORTANCE

- We present the case of a young patient with T-lymphoblastic lymphoma (T-LBL) who developed severe toxicity after receiving an anthracycline-based protocol, that is generally well tolerated by fit patients.
- We assume that the substitution of daunorubicin by doxorubicin due to a nationwide shortage of daunorubicin has played a crucial role in developing severe toxicity.

## AIM AND OBJECTIVES

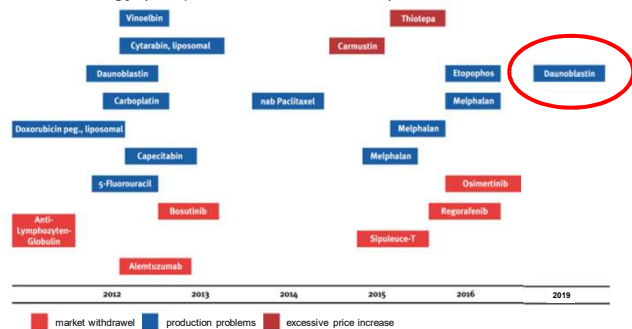
- The 19-year-old male with no previous illnesses was diagnosed in December 2019 with T-LBL - a rare, aggressive neoplasm of precursor T cells that progresses rapidly and requires prompt diagnosis and medical intervention.
- Figure 1: glucose-hypermetabolic mediastinal mass (FDG-PET/CT, December 2019)



- T-LBL shows morphological and immunophenotypical similarities to acute lymphoblastic leukemia (ALL), T-LBL treatment is the same as for ALL.

## MATERIAL AND METHODS

- The induction protocol consisted of dexamethasone, vincristine, daunorubicin, and pegasparginase.
- Due to a nationwide shortage, daunorubicin (30mg/m<sup>2</sup>) was substituted by doxorubicin (25mg/m<sup>2</sup>).
- Figure 2: exemplary illustration of drug shortages in hematology and oncology (adapted from reference 1)



## RESULTS

- Chemotherapy was initially well-tolerated, but beginning on day 15, the patient developed pronounced mucositis and increased skin toxicity (hand-foot-syndrome, grade IV). Moreover, coagulation parameters deteriorate, and repeated transfusions with erythrocytes and platelet concentrates were needed.
- After administration of pegasparginase on day 31, liver values increased, and finally, the patient had to be transferred to the intensive care unit due to fulminant pancreatitis.
- After three days, the patient could be transferred back to our ward. Still, within two weeks, the patient developed sensory disturbances in all extremities, which was classified as chemotherapy-associated polyneuropathy.
- In the further clinical course, the patient's general condition improved, and a PET-CT showed complete metabolic remission.
- Figure 2: complete metabolic remission (FDG-PET/CT, January 2020)



- Due to the severe chemotherapy-associated side effects, intensive consolidation treatment, according to the protocol was canceled. Instead, a consolidating therapy with nelarabine was carried out without complications. Until now (February 2021), the patient is in good clinical condition and has neither developed a disease recurrence.
- Probability assessment using the Naranjo algorithm (reference 2) resulted in "probable adverse drug reaction" (score=6).

| Question  | Score    |
|---|----------|
| Are there previous conclusive reports on this reaction? (reference 3)                                       | +1       |
| Did the adverse event appear after the suspected drug was administered?                                     | +1       |
| Did the adverse reaction improve when the drug was discontinued, or a specific antagonist was administered? | +1       |
| Did the adverse event reappear when the drug was re-administered?   | -        |
| Are there alternative causes (other than the drug) that could on their own have caused the reaction?        | +2       |
| Did the reaction reappear when a placebo was given?   | -        |
| Was the drug detected in blood (or other fluids) in concentrations known to be toxic?                       | -        |
| Was the reaction more severe when the dose was increased or less severe when the dose was decreased?        | -        |
| Did the patient have a similar reaction to the same or similar drugs in any previous exposure?              | -        |
| Was the adverse event confirmed by any objective evidence?  | +1       |
| <b>TOTAL SCORE:</b>   | <b>6</b> |

## CONCLUSION AND RELEVANCE

Our case report underlines that shortages of essential anticancer drugs have a particular impact on established chemotherapy regimens' efficacy and safety, as these medicines often have few or no proven effective alternatives.

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