Differentiation Syndrome in a Cohort of Egyptian Acute Promyelocytic Leukemia

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Acute promyelocytic leukemia (APL) differentiation syndrome (DS) is a common complication in APL treated with the differentiating agent All-trans retinoic acid (ATRA).

Herein, we present an observational retrospective single- center study of 110 APL patients diagnosed between 2011 and 2024. The study was carried out at Oncology Center, Mansoura University. The mean age 37.18 (±13.69 SD) years, M/F: 48/62 (43.64%/56.36%). APL patients risk stratification was 80 (72.73%) and 30 (27.27%) patients as low- and high-risk groups, respectively. All patients received ATRA-based therapy, either ATRA-monotherapy, ATRA + 3-days anthracycline, or ATRA in combination with 3+7 protocol for induction of remission in 14 (12.73%), 58 (52.73%) and 39 (35.45%) patients, respectively [Table 1]. Prophylactic oral corticosteroids were administrated with ATRA to guard against DS and were shifted to I.V dexamethasone 10mg BID upon development of DS.

The objective of this study is to determine the incidence of APL DS and its impact on overall survival (OS). Forty (36.36%) of patients experienced DS during induction therapy. Symptoms and signs of DS include fever, weight gain, rising WBC count, rising serum creatinine, and/or development of respiratory distress manifestations. Lung affection was observed in 77.5% of APL DS patients. Most common radiological features detected on CT-scans were pulmonary infiltrations and pleural effusion [Figure 1]. The median duration to development of DS from the initiation of ATRA was 10 days (range, 1-35). APL DS and pulmonary affection during the syndrome appeared to compromise overall survival (OS) outcomes in comparison to APL patients without DS and DS without pulmonary insult (2.7 vs 32.2 months, *P =0.00063*) and (9.1 vs 107 months, *P =0.0073*), respectively [Figures 2 and 3, respectively]. DS represented 50% of APL early death (ED) cases within the first 30 days of diagnosis.

In conclusion, DS represents a significant therapy-related adverse event (TAE) during the management of APL patients. It remains one of the primary contributors to ED in APL, posing an unresolved challenge in disease management despite the considerable therapeutic advancements achieved.

Therefore, the anticipation and prompt management of DS are crucial to improving survival outcomes and mitigating its detrimental impact on prognosis.

Variables	Number	Percentage
Total patients	110	100%
Males	48	43.64%
Females	62	56.36%
NCCN risk score		
Low	80	72.73%
High	30	27.27%
Differentiation Syndrome		
At all time-points	41	37.27%
At Induction	40	36.36%
At consolidation	1	0.9%
Forms of pulmonary affection in DS	31	75.61% (31/41)
Pleural effusion	10	32.26%
Pleural thickening	1	3.23%
Pulmonary opacities or consolidation	25	80.65%
Pulmonary nodules	12	38.71%
Pulmonary infiltrates	11	35.48%
Attenuated BVM	7	22.58%
Cavitary lesions	3	9.68%
Basal Atelectatic bands	3	9.68%
Lung collapse	3	9.68%
Mediastinal shift	1	3.23%
Induction and response to induction		
ATRA single agent at induction	14	12.73%
ATRA + chemotherapy at induction	96	87.27%
Anthracycline single agent with ATRA at induction	58	52.73%
Anthracycline + Cytarabine +ATRA at induction	39	35.45%
CR1	74	67.26%
Survival		
Alive at last visit	61	55.45%
Dead at last visit	49	44.55%
Early Death (ED)	26	26.64%
Due to DS	13	50%

Table 1. Characteristics of studied cohort of APL patients

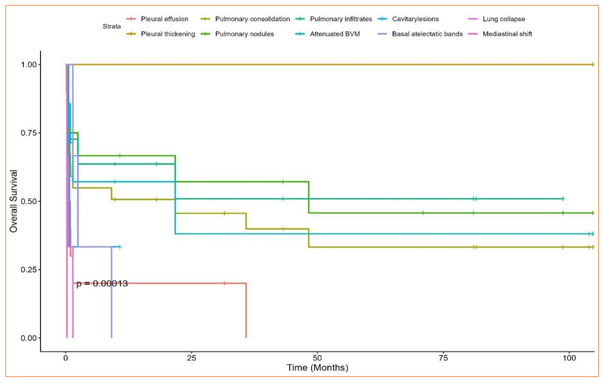


Figure 1. Different pulmonary affections detected during DS on CT-scans

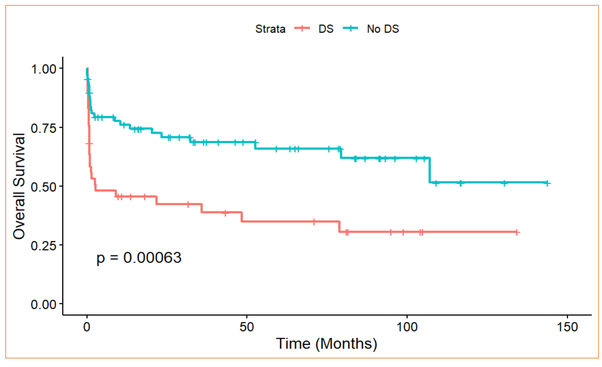


Figure 2. Overall survival in APL patients with DS vs. APL patients without DS

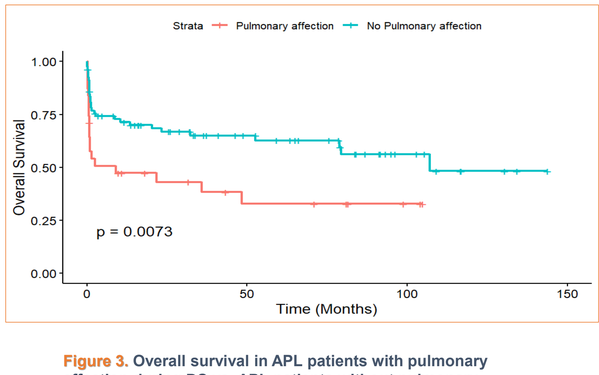


Figure 3. Overall survival in APL patients with pulmonary affection during DS vs. APL patients without pulmonary affection during DS

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