ACUTE LYMPHOCYTIC LEUKEMIA IN PREGNANCY: CASE REPORT AND REVIEW OF THE LITERATURE

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INTRODUCTION

Leukemia occurs in about 1 in 1000 pregnancies and of these only 28% have acute lymphocytic leukemia (ALL). A 28-year-old woman, G2P1 was diagnosed with Philadelphia negative B-ALL at 24 weeks' gestation at our center. She was induced with UKALL14 and achieved a flow negative complete remission post-induction. During induction chemotherapy, the fetus remained at the 50th percentile. The patient was kept on weekly vincristine and prednisone and had an elective repeat c-section at 31+3 weeks for her to safely resume chemotherapy. Baby girl had an uneventful course and was discharged from hospital on Day 29.

AIM

Given the sparse data on this challenging topic, we decided to review the literature for all reported cases of ALL in pregnancy.

METHODS

We reviewed the literature for all reported cases of ALL from 2010 to 2023. We collected available data on the patient, pregnancy, and fetal outcome as well as leukemia characteristics and chemotherapy received.

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Table 1: Characteristics and Outcomes of Individually Reported Cases of ALL Presenting in T2/T3

Pt #	Reference	Maternal Age (years)	B / T cell	GA at Dx (weeks)	Pregnancy outcome	GA at delivery	Fetal outcome	Chemotherapy	Response
1	Kobayashi, Shuhei et al.	33	Ph+ B ALL	33	Delivery - CS	34+1 wk	live birth	Dasatinib + steroid	CR
2		36		15 (relapse)	Delivery - SVD	34+6 wk	live birth	HyperCVAD (CPM, VCR, ADR, DEXA)	CR
3	Zhu, D et al	33	B ALL	34	Delivery - CS	term	live birth	DNR + VCR + CPM + PRED	CR
4		41	B ALL	27	Delivery - SVD	premature	live birth	DNR + VCR + CPM + PRED	CR
5		19	B ALL	<4	-	-	-	Declined	
6	Vlijm-Kievit A, Jorna NGE, Moll E, et al.	37	T ALL	36	Delivery - SVD	37+2 wk	live birth	PRED prephase	CR
7	Farhadfar N., et a	19	ALL L1	16	stillbirth	22 wks	dead	DNR + PRED + VCR	CR
8		28	B ALL	35	Delivery - SVD	38 wk	live birth	DNR + PRED + VCR	CR
9	Mainor C, et al.	38	Ph +B ALL	24	Delivery - CS	30 wk	live birth , low birth weight	HyperCVAD (CPM, DEXA, ADR, VCR) , CTR, imatinib mesylate)	Not reported
10	Saleh AJ., et al	23	Pre B ALL	38	Delivery	38 WK	live birth	None	
11		26	Pre B ALL	28	Spontaneous abortion		miscarriage	VCR, ADR, PRED, CPM, L-ASP	CR
12		23	pre B ALL	13	Spontaneous abortion	14 wk	miscarriage	none	
13		37	pre B ALL	29	Delivery	38 wk	live birth	VCR, ADR, PRED, CPM, L-ASP	CR
14		20	T ALL	31	Delivery	33 wk	live birth	VCR, PRED	CR
15	Khandaker S, Munshi S.	25		26	Delivery - CS	34 wk	live birth	DEXA, PRED, MTX (IT), VCR, L-ASP	CR
16	Ticku, J et al	22	Ph+ B ALL	26	Delivery - CS	30 wk	live birth	HyperCVAD (CPM, VCR, ADR, DEXA)	CR
17	Nakajima Y, et all	36	Ph+ B ALL	27	Delivery - CS	32+1 wk	live birth	DNR, VCR, CPM, PRED	CR
18	Bottsford-Miller J, et al.	27	pre B ALL	24	Delivery - CS	30 wk	live birth	VCR, DNR, pegaspargase, PRED, CTR (IT) , MTX (IT)	CR
19	Aljurf, M et al.	37	pre B ALL	29	Delivery - SVD		live birth , anemia	VCR, DEXA, IDR, ASP	CR
20		25	pre B ALL	14	Spontaneous abortion	-	miscarriage	VCR, DEXA, IDR, ASP	refractory
21		21	pre T ALL	30	Delivery		live birth , anemia	VCR, DEXA, IDR, ASP	CR
22		27	pre B ALL	13	Spontaneous abortion	14 wk	Miscarriage	not indicated	CR
23	Parovichnikova EN, et al	23	T ALL	35	Delivery - CS	35 wk	live birth , IVH, NCI	PRED, DEXA, DNR,VCR	CR
24		18	B ALL	36	Delivery - CS	36 wk	live birth	PRED, DEXA, DNR,VCR	refractory
25		24	B ALL	40	Delivery - SVD	40 wk	live birth	PRED, DEXA, DNR,VCR	CR
26		25	T ALL	15	Delivery - CS	35 wk	live birth , Intestinal obstruction at +2 wks	PRED, DEXA, DNR, VCR, CPM, CTR, 6MP	CR after 2nd induction
27		29	T ALL	20	Delivery - CS	35 wk	live birth , SGA	PRED, DEXA, DNR, VCR, CPM, CTR, 6MP	refractory
28		35	B ALL	20	Delivery - CS	35 wk	live birth	PRED, DEXA, DNR, VCR, CPM, CTR, 6MP	CR after pred-phase
29		32	T ALL	25	Delivery - CS	34 wk	live birth, NCI	PRED, DEXA, DNR, VCR, CPM, CTR, 6MP	CR after extended 2nd induction
30		21	B ALL	26	Delivery - SVD	36 wk	live birth	PRED, DEXA, DNR,VCR	CR
31		26	B ALL	28	Delivery - CS	34 wk	live birth	PRED, DEXA, DNR,VCR	CR
32		29	B ALL	29	Delivery - CS	36 wk	live birth , SGA, NCI	PRED, DEXA, DNR, VCR, CPM, CTR, 6MP	CR
33		29	T ALL	31	Delivery - SVD	36 wk	live birth	PRED, DEXA, DNR,VCR	CR
34		41	T ALL	31	Delivery - CS	38 wk	live birth, NCI	PRED, DEXA, DNR,VCR	CR
35	Papantoniou N, et al	16	B ALL	26	Delivery - CS	32+4 wk	live birth , SGA	German ALL-BFM 95 protocol Ia (PRED, VCR, DNR, ASP, MTX (IT))	CR after phase 2
36	Matsouka, C et al.	16	B ALL	26	Delivery - CS	32 wk	live birth , SGA	DNR, VCR, ASP, PRED, MTX	CR
37	Molkenboer, J et all	37	Ph+ B ALL	15	Spontaneous abortion	22 wks	miscarriage	PRED, VCR, ASP, DNR, MTX. After 3 wks CTR	Refractory
38	Chelghoum Y., et al	25	T ALL	27	Delivery - SVD		preterm	DNR, VCR, CPM, PRED	Refractory
39		33	pre B ALL	26	Delivery - CS		preterm	DNR, VCR, ASP, PRED	CR
40		21	pre B ALL	28	Delivery - CS		preterm	DNR, VCR, CPM, L-ASP, PRED	CR
41	Terek MC., et al	21	B ALL	30-31	Delivery - CS	30-31	live birth	VCR, DNR, PED, L-ASP	died
42	Greenlund LJ., et al	19	-	18	maternal death	-	-	DNR, VCR, Ara-C, PRED	CR
43		28	-	33	Delivery	38 wk	live birth	unspecified	CR
44	Hansen WF., et al	24	B ALL	24	Delivery - SVD	36+2 wk	live birth	CALGB Study 9111 (INDUCTION: CPM, VCR, PRED, DNR, L-ASP. Followed by 2 cycles of MTX (IT), CPM, 6MP, CTR, VCR, L-ASP)	CR

RESULTS

We found 57 patients across 20 studies. The median age at diagnosis was 26 years (range 16-41 years). Most affected pregnancies were during the second trimester (T2) (n 23/57) and third trimester (T3) (n 20/57). B ALL was the most common in reported cases (n 35/49. A total of 53 patients received chemotherapy, of those 33 patients were received during pregnancy, while 13 were after pregnancy, and the remaining 7 had unclear timing. Patients received different combinations of standard ALL chemotherapy agents. Dasatinib and imatinib were given to two patients at 33 and 24 weeks respectively. There were no reports of patients who were treated with immune therapy while pregnant.

All four patients who did not receive any treatment died from progressive disease. Complete remission (CR) was reported in 45 patients. One patient died during induction from septicaemia, five were refractory to induction chemotherapy and 2 did not have induction outcome reported.

T1 Pregnancies

Among the 14 T1 pregnancies, 10 were terminated electively, 3 spontaneously, and there was one maternal death due to declining treatment. Three patients received chemotherapy during T1, two suffered a spontaneous abortion and one had a missed miscarriage.

T2 Pregnancies (See Table 1)

Among the 23 T2 pregnancies, 17 resulted in live deliveries, one stillbirth during chemotherapy, one maternal death and 4 spontaneous abortions; 2 of which received chemotherapy during pregnancy, one did not receive treatment and one abortion with unclear timing of chemotherapy initiation.

T3 Pregnancies (See Table 1)

Among the 20 T3 pregnancies, 19 had successful deliveries and one stillbirth at an unindicated gestational age after receiving chemotherapy.

Foetal Outcomes:

Five babies were reported to have low birth weight, four had neonatal cerebral ischemia, one had intraventricular hemorrhage and one suffered from intestinal obstruction 2 weeks after delivery. All babies were discharged from hospital with no adverse congenital or developmental complications

CONCLUSION

Treatment of women presenting with ALL at or beyond T2 is possible with high remission rates for the mothers and delivery of healthy babies. It is important that more cases are reported on this topic due to its challenging and multidisciplinary nature, especially given the sparse data available.