BURKITT'S LYMPHOMA DURING PREGNANCY: A CASE REPORT AND REVIEW

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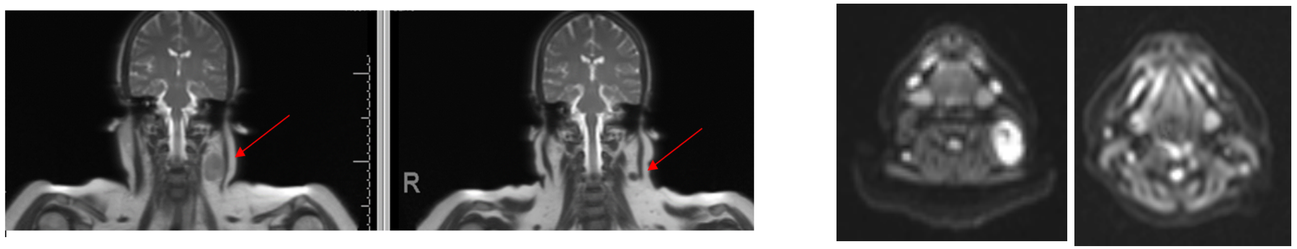
BACKGROUND

- Burkitt's Lymphoma (BL) is an aggressive B-cell non-Hodgkin's lymphoma characterized by a high proliferation rate and dysregulation of c-myc gene
- BL during pregnancy is extremely rare with 40 cases reported since 1900 .
- Due to its aggressive nature, it can be fatal if left untreated to both mother and fetus
- Several variants of BL exist: endemic, sporadic, and HIV- associated BL
  - Sporadic variant is most commonly seen in United States and Western Europe
- BL comprises 30% of pediatric lymphomas and <1 percent of adult NHL in US
- We present a case of stage II extranodal BL during pregnancy diagnosed at 16 weeks gestational age (GA)

CASE REPORT

- 31-year-old woman diagnosed with BL at 16 weeks GA by core needle biopsy
- Immunohistochemistry demonstrated neoplastic cells positive for CD43, CD79a, C-MYC (>90%), BCL6 and negative for CD3, CD34, BCL2, MUM1, TDT, and CyclinD1; Ki-67 was 100%.
- Bone marrow biopsy negative for lymphoma, but positive for Epstein Barr Virus by PCR.
- Due to pregnancy, staging with MRI whole body without gadolinium contrast and baseline echocardiogram was normal
- At diagnosis, had stage IIB disease, elevated lactate dehydrogenase and B symptoms
- Due to the teratogenic nature of methotrexate (MTX), treatment used was Rituximab, cyclophosphamide, vincristine, doxorubicin, and dexamethasone (HyperCVAD) part A for four cycles prior to scheduled induction at 30 weeks plus intrathecal chemoprophylaxis using cytarabine
- Following cesarean section delivery of healthy baby girl, restaging via PET/CT demonstrated a complete metabolic response and she continued with HD MTX, rituximab, and high dose cytarabine (part B).
- At treatment end she received a total of 6 cycles of R-HyperCVAD Part A and B, with complete response by PET/CT
- Currently 24+ months post treatment with no evidence of disease by imaging and her daughter is a healthy 2 years old



Left: Before treatment MRI; Right: after 4 cycles R-HyperCVAD + Rituximab

RESULTS

- Standard treatment is multiagent chemoimmunotherapy including MTX, which is highly teratogenic
- Chemotherapy during pregnancy requires multidisciplinary team approach with care coordination and close monitoring
- This patient was co-managed with maternal fetal medicine physician with ultrasound prior to each dose of chemotherapy and monitored up to 2-3 times/week
- Advanced Practioners (AP's) played an important role in our patient's care, including side effect management and coordination of care

CONCLUSIONS/DISCUSSION

- Treating and managing BL in a pregnant patient is rare and extremely challenging.
- Patients require proper education and risk versus benefit discussions prior to treatment and close monitoring by a multidisciplinary team of both mother and fetus during treatment with multi-agent chemoimmunotherapy
- Studies have demonstrated improved outcomes in pregnant patients when they receive upfront aggressive chemotherapy
- Providers must also balance the potential life-threatening effects of this disease while minimizing treatment's toxic effects to the fetus
- AP's play a critical role in this care coordination and managing of patient's potential toxicities while undergoing therapy and in the post-partum period
- Recent data has shown that delaying treatment until after the first trimester is preferred if able to do so without adverse patient outcomes due to malignancy

Pt Age, yrs	GA wk	Stage	Treatment	Patient/Fetal Outcome	Ref
32	12	IV	HD-MTX, ABL, VBL, ETO, Ara-C, CPA	Dead/Dead	Antic et al (2000)
20	18	IV	none	Dead/Dead	Armon (1976)
18	10	IV	CPA mono, MTX	Dead/Dead	Armon (1976)
42	12	IV	CPA mono Ara-C Ara-C, VCR (with XRT of CNS) MTX	Dead /Dead	Armitage et al (1977)
36	40	II	none	Dead/Alive	Bannermann (1966)
20	12	II	R-CODOX-M/IVAC (4 cycles) MTX, Ara-C	Alive/Dead	Barnes et al (1998)
20	11	III	CALGB 9521	Alive/Dead	Barnes et al (1998)
30	30	IV	COP (1 cycle) MTX	Dead/Alive	Berrebi et al (1983)
34	26	IV	CPA mono	Dead/Dead	Bornkamm et al (1908)
40	27	II	French R-LMB protocol (withheld IT MTX and arabinosylcytosine) R-LMB protocol (1 cycle) DEX R-LMB protocol MTX, Ara-C	Alive/Alive	Cordeiro et al (2009)
18	26	II	CPA mono	Dead/NR	Durodala (1979)
32	27	II	none	Dead/Dead	El-Sonbaty et al (2001)
27	28	II	CPA, MTX, VCR, prednisone MTX, Ara-C	Alive/Dead	Fadiora et al (2005)
24	20	II	CPA mono	Dead/Dead	Finkle and Goldmann (1974)
35	15	II	R-CHOP (4 cycles) HD-BEAM (with ASCT	Alive/Alive	Friedrichs et al (2006)
34	32	IV	R-CPA/DEX	Alive/NR	Gnecco et al (2018)
32	28	II	CPA mono (with XRT of orbital)	Dead/Alive	Hardin (1972)
34	19	IV	R-CHOEP, Ara-C (5 cycles); Ara-C, DEX GMALL protocol 2002; 1 MTX, Ara-C	Alive/Alive	Hurley (2013)
24	30	II	CHOP-bleomycin (2 cycles)	Dead/NR	Illes et al (1996)
25	12	II	R-COPAD (4 cycles) MTX, DEX	Dead/Alive	Inácio Júnior et al (2015)
17	15	IV	none	Dead/Dead	Jones et al (1973)
21	26	II	CODOX-M/IVAC (withheld MTX until baby delivered CODOX-M/IVAC (2 cycles) Ara-C CODOX-M/IVAC (2 cycles) MTX, Ara-C	Alive/Alive	Lam et al (2006)
32	22	IV	CHOP-tenoposide (6 cycles) MTX HD-MTX, CPA, Ara-C, TG (with ASCT) MTX, Ara-C SVD	Dead/Alive	Lowenthal et al (1982)
19	12	II	Cyclophosphamide, vincristine, doxorubicin, dexamethasone, rituximab, I.T. cytosine arabinoside; R-CHOP (6 cycles) Ara-C	Dead/Alive	Magloire et al (2006)
27	35	II	CHOP (12 cycles)	Alive/Alive	Miyoshi et al (2006)
28	16	II	CODOX-M/IVAC (without I.T./I.V. MTX) with rituximab Modified CODOX-M/ IVAC (2 cycles) Ara-C HDAC (1 cycle)	Alive/Dead	Peterson et al (2010)
28	37	II	R-CODOX-M/IVAC with HD-BEAM (with ASCT) MTX, Ara-C	Alive/Alive	Savvari et al (2010)
35	24	II	CODOX-M/IVAC (delayed for Cesarean section); CPA, VCR, doxorubicin	Dead/Alive	Serikawa (2011)
20	30	II	none	Dead/NR	Shepherd and Wright (1967)
15	28	IV	CPA mono	Dead/Dead	Shepherd and Wright (1967)
35	24	II	none	Dead/Dead	Shepherd and Wright (1967)
34	19	IV	R-CHOEP, Ara-C (5 cycles); Ara-C, DEX GMALL protocol 2002; MTX, Ara-C	Alive/NR	Stang et al (2013)
25	27	IV	none	Dead/Dead	Steiner-Salz et al (1985)
17	13	I	GMALL protocol 2002 MTX, Ara-C	Alive/Dead	Steininger et al (2012)
26	9	IV	cyclophosphamide, vincristine, prednisone	Dead/Dead	Tazi et al (2011)
26	37	IV	CPA, VCR, prednisone	Dead/NR	Tazi et al (2011)
30	16	IV	Modified CODOX-M/IVAC R-CODOX-M/IVAC MTX	Alive/Dead	Testa et al (2013)
32	32	II	CHOP	Alive/Alive	Yoruk et al (2009)
25	24	III	R-CHOP (progressive disease) LMB protocol	Alive/Alive	Zagalo et al (2013)

*Methotrexate (MTX), Cyclophosphamide (CPA mono), VCR (vincristine), Cytarabine (ARA-C), Ifosfamide, etoposide, cytarabine (IVAC), Autologous Stem Cell Transplant (ASCT), Cyclophosphamide, Doxorubicin, Vincristine, Methotrexate (CODOX-M), Rituximab, Cyclophosphamide, Vincristine, Doxorubicin, Prednisone (R-CHOP), methotrexate, high-dose cytosine arabinoside, cyclophosphamide, etoposide, ifosfamide, dexamethasone (GMALL Protocol)