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624.HODGKIN LYMPHOMAS AND T/NK CELL LYMPHOMAS: CLINICAL AND EPIDEMIOLOGICAL

Safety of Total Skin Electron Therapy with Concurrent Systemic Therapy

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Introduction:
Mycosis fungoides has a long, waxing and waning course. Multimodality therapy is needed to control disease. Total skin electron beam therapy (TSE) is an effective means of controlling cutaneous disease, though response duration is limited necessitating incorporation of additional therapeutics. There are limited data informing the safety of systemic agents used concurrently with TSE. We characterize acute toxicities of patients undergoing TSE +/- concurrent or recent systemic therapy.

Methods:
We retrospectively analyzed 114 patients comprising a total of 121 consecutive courses of full body TSE from 2013-2023. Median follow up was 1.75 years from start of TSE. Toxicities occurring up to 3 months following radiation were recorded and graded per CTCAEv5 criteria when applicable; grade was characterized as low (grades 1-2) and high (3-4). Given conflating cutaneous symptoms prior to TSE, toxicities were further characterized as "new or worsened" (N/W) from baseline. Incidence of N/W toxicity was further categorized by class of systemic therapy: interferon, retinoic acid derivative, immunotherapy, systemic steroid, histone deacetylase inhibitor, folic analogue antimetabolite, and other. Recent systemic therapy included receipt of therapy within 1 and 3 months preceding TSE given multi-month half lives of some systemics.

Results:
During 75 courses, patients received systemic therapy concurrently with TSE (CS), and 46 had no concurrent systemic therapy (NCS). The majority of concurrent systemic therapies were interferons (49, 41%) and retinoic acid derivatives (32, 27%); "other" concurrent systemics included lenalidomide, imatinib, and ibrutinib. TSE dose included 36Gy (5%), 24Gy (6%), 12Gy (84%), and other (5%). Most patients had ECOG performance status 0-1 (88% overall). Patient characteristics were well balanced, excepting stage at TSE (stage III/IV CS 45.3% vs NCS 26.1%, $p<0.05$), though T stage and blood involvement were evenly distributed. At baseline among CS and NCS patients, 29% vs 30% had skin ulceration, 27% vs 35% had large cell transformation, and 12% vs 13% had concurrent infection, respectively (all $p>0.05$). Incidence of any N/W toxicity was 98.7% and 100% ($p>0.05$)among CS and NCS patients, respectively (95% vs 94% low grade and 13% vs 26% high grade, both $p>0.05$).
Prior to TSE, baseline rates of common symptoms among CS vs NCS courses were as follows: dermatitis 96% vs 94%, hyperpigmentation 28% vs 28%, edema 15% vs 24%, pruritus 97% vs 87%, and skin pain 32% vs 45%, respectively (all $p>0.05$). From start of TSE through 3 month follow up, the overall incidences of CS vs NCS N/W common toxicities included the following: N/W dermatitis 73% vs 83%, N/W hyperpigmentation 33% vs 37%, and N/W edema 21% vs 24% (all $p>0.05$). Twenty-five percent of CS patients experienced skin pain flare during TSE vs 13% NCS, and 20% of CS patients vs 11% NCS experienced pruritus flare (all $p>0.05$). At end of treatment, 59% of CS patients with baseline pruritus experienced improvement compared to 68% NCS, with 73% vs 70% experiencing improvement at 1-3 months in follow up (all $p>0.05$). One patient received a known concurrent radiosensitizer - methotrexate - and developed N/W grade 3 dermatitis (baseline grade 3), new grade 2 hyperpigmentation, worsened grade 1 anorexia, new grade 2 superficial soft tissue fibrosis, and pain flare.

The median number of all reported N/W toxicities among systemic classes when given concurrently was low and well balanced. This persisted when the number of toxicities per class were assessed among systemics administered within 1 month preceding TSE, and within 3 months preceding TSE.

Conclusions:

Concurrent or recent receipt of systemic therapy can be safe among most commonly used concurrent agents that are not radiosensitizers. There was no notable increase in incidence of low or high grade toxicity, or median number of low or high grade toxicities recorded in CS vs NCS patients. Most patients experienced some acute toxicity, which is not unexpected given radiation to a tissue with high cell turnover, and the interplay of toxicity with expected disease response to TSE. High rates of baseline dermatitis and high rates of N/W dermatitis highlight this observation. Notably most systemic therapies included interferons and retinoic acid derivatives. Additional data is needed to better characterize the toxicity profile of other systemic therapies used concurrently with TSE.

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	Total cohort n=121 (%)	No concurrent systemic therapy n=46 (%)	Concurrent systemic therapy n=75 (%)	p value
Development of new or worsened toxicities				
All	120 (99)	46 (100)	74 (99)	1.00
Low grade*	114 (94)	43 (93)	71 (95)	1.00
High grade*	22 (18)	12 (26)	10 (13)	0.08
Number of documented new or worsened toxicities per case				
All (med, range)	3 (0-7)	2.5 (1-6)	3 (0-7)	
Low grade (med, range)	2 (0-5)	2 (0-5)	2 (0-5)	
High grade (med, range)	0 (0-3)	0 (0-3)	0 (0-1)	
COMMON TOXICITIES				
Dematiitis				
Prior to RT	115 (95)	43 (94)	72 (96)	0.67
During-1month post RT	121 (100)	46 (100)	75 (100)	
New/worsened dermatitis	93 (77)	38 (83)	55 (73)	0.24
Hyperpigmentation				
Prior to RT	34 (28)	13 (28)	21 (28)	0.98
During-1month post RT	53 (44)	21 (46)	32 (43)	0.75
New/worsened hyperpigmentation	42 (35)	17 (37)	25 (33)	0.68
Edema				
Prior to RT	22 (18)	11 (24)	11 (15)	0.20
During-1month post RT	39 (32)	16 (35)	23 (31)	0.64
New/worsened edema	27 (22)	11 (24)	16 (21)	0.74
Fatigue				
Prior to RT	62 (51)	25 (54)	37 (49)	0.59
During-1month post RT	102 (84)	42 (91)	60 (80)	0.10
New/worsened fatigue	71 (59)	30 (65)	41 (55)	0.25
Anorexia				
Prior to RT	21 (17)	7 (15)	14 (19)	0.63
During-1month post RT	34 (28)	15 (33)	19 (25)	0.39
New/worsened anorexia	18 (15)	9 (20)	9 (12)	0.26
Skin pain				
Focal Prior to RT	27 (22)	13 (28)	14 (19)	0.22
Diffuse Prior to RT	18 (15)	8 (17)	10 (13)	0.54
Pain flare during RT	25 (21)	6 (13)	19 (25)	0.11
Pain improved by EOT	29/44† (66)	13/20† (65)	16/24 (67)	0.91
Pruritus				
Prior to RT	113 (93)	40 (87)	73 (97)	0.05
Pruritus flare during RT	20 (17)	5 (11)	15 (20)	0.19
Pruritus improved by EOT	70/113 (62)	27/40 (68)	43/73 (59)	0.37
Pruritus improved at 1-3month follow up	81/113 (72)	28/40 (70)	53/73 (73)	0.77

Abbreviations: RT=radiation therapy; EOT=end of treatment

*Skin pain flare and itch flare are not included in the low grade or high grade characterization as they were unable to be reliably graded

†One patient had both focal and diffuse skin pain

Table 2. Median number and range of new or worsened acute toxicities per total skin electron beam therapy case by timing of systemic therapy

Therapy type	No systemic therapy	Interferon	Retinoic acid derivative	Immunotherapy*	Systemic steroid	HDAC inhibitors†	Folate analogue antimetabolite††	Other systemic§
n (case)	n=46	n=49	n=32	n=9	n=8	n=2	n=1	n=3
Concurrent with RT course	2.5 (1-6)	3 (0-7)	3 (1-5)	2 (1-5)	3.5 (2-7)	3 (1-5)	5 (5-5)	2 (1-4)
n (case)	n=29	n=50	n=36	n=14	n=11	n=5	n=4	n=7
Within 1 month prior to RT course	3 (1-6)	3 (0-7)	3 (1-6)	2 (1-5)	4 (2-7)	2 (1-5)	4.5 (2-5)	2 (1-6)
n (case)	n=22	n=51	n=39	n=23	n=13	n=9	n=9	n=11
Within 3 months prior to RT course	3 (1-6)	3 (0-7)	3 (1-6)	3 (1-6)	4 (2-7)	3 (1-5)	4 (1-5)	2 (1-6)

Abbreviations: RT=radiation therapy; HDAC=histone deacetylase

*Immunotherapy included mogamulizumab, pembrolizumab, nivolumab, dupilumab, ustekinumab, interleukin 12, secukinumab, and alemtuzumab

†HDAC inhibitors included romidepsin and vorinostat

††Folate analogue antimetabolites included methotrexate and pralatrexate

§Other systemics included lenalidomide, cyclophosphamide, cyclophosphamide/doxorubicin/vincristine/prednisone, cyclophosphamide/doxorubicin/prednisone, cerdulatinib, doxorubicin, gemcitabine, duvelisib, etoposide/prednisone/vincristine/cyclophosphamide/doxorubicin, TTI-621 (CD47 inhibit0r)