

CASE REPORT

Radiation therapy in primary mediastinal large B-cell lymphoma treated with DA-R-EPOCH

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Abstract

DA-R-EPOCH is used in PMBCL due to its good outcomes without radiation. We present three cases that required consolidation with radiation despite using this regimen. More studies are needed before considering DA-R-EPOCH standard of care.

KEYWORDS

chemotherapy, lymphoma, primary mediastinal B-cell lymphoma, radiation therapy

There are several proposed chemotherapy regimens for primary mediastinal large B-cell lymphoma (PMBCL) but no standard treatment. A prospective phase II study by Dunleavy et al postulated that DA-R-EPOCH could obviate the need for consolidation radiotherapy (RT). Their results showed a 5-year event-free survival (EFS) and 5-year overall survival (OS) rates of 93% and 97% without RT.¹ However, there is still debate whether all patients should avoid RT. We treated six PMBCL patients with DA-R-EPOCH from 2016 to 2018; we are reporting three cases that required consolidation RT given poor response/recurrence after end of treatment (EOT) PET scan (Table 1). The Houston Methodist Review Board approved the report for publication.

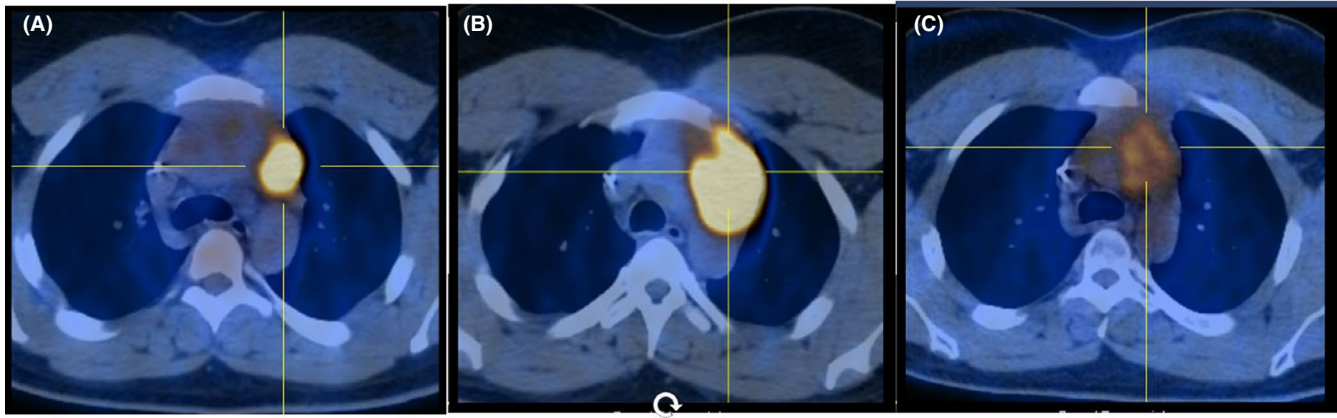
Patient A. A 23-year-old male with no past medical history presented with right shoulder pain, shortness of breath, and persistent cough. PET showed a large mass involving most of the mediastinum (SUV = 28.2). Other areas of uptake included bilateral supraclavicular lymph nodes and small pleural/diaphragmatic metastasis. Biopsy was consistent with PMBCL; treatment with DA-R-EPOCH was given. PET scan after three cycles showed response (SUV = 15.8). EOT PET

scan had evidence of local recurrence with progression of anterior mediastinal mass (7.4 cm × 4.4 cm, SUV = 35). He was treated with involved site RT (50 Gy in 25 fractions) followed by salvage chemotherapy (B-ICE) for three cycles. Post-treatment PET scan showed marked improvement (SUV = 3.8) (Figure 1). He underwent consolidation with autologous hematopoietic cell transplant (auto-HCT) and remains in remission a year after auto-HCT.

Patient B. A 27-year-old female with no past medical history presented with cough and facial swelling. CT of the neck and chest showed a large invasive anterior mediastinal mass extending into the right upper lobe and several left upper lobe pulmonary metastatic lesions. PET scan showed marked uptake in the mediastinal mass (SUV = 25). Excisional biopsy showed PMBCL. Chemotherapy was started with DA-R-EPOCH. After two cycles, PET scan showed remission by PET criteria, no significant residual tissue (1 cm × 6 mm, Deauville score 1). EOT PET continued to show remission. Four months after chemotherapy, PET scan showed a focal uptake in the anterior mediastinum (SUV = 3.3, Deauville score 4), correlating with a 2.1 cm × 1.3 cm mass. The patient

TABLE 1 PMBCL cases that required RT for consolidation

Cases	Age/sex	PET (max SUV) at diagnosis	Follow-up/End of treatment PET (max SUV)	RT dose	PET after RT (max SUV)
A	23/M	28.2	35	50 Gy/25 fr	3.0
B	27/F	25	3.3, Deauville 4	40 Gy/20 fr	No uptake
C	36/F	22	3.6, Deauville 4	36 Gy/18 fr	3.0

**FIGURE 1** Patient A PET scans. A, Scan after three cycles of DA-R-EPOCH with uptake improvement. B, End of treatment scan showing recurrence. C, Post-RT PET scan with minimal uptake

was sent for consolidation RT (40 Gy in 20 fractions). She remains in remission two years after completion of RT.

Patient C. A 36-year-old female with no past medical history presented with shortness of breath and cough. CT chest showed a large mediastinal mass (11.4 × 19.2 × 10 cm) compressing the carina and left main bronchus. Pathology was consistent with PMBCL. PET scan showed marked uptake in the mediastinum (SUV = 22) with no other sites involved. She received treatment with DA-R-EPOCH. PET scan after two cycles demonstrated a significant improvement (8.0 × 5.4 cm, SUV = 4.9). She finished six cycles of chemotherapy. EOT PET showed a decrease in size of the mass (6.5 × 3.5 cm) but still with areas of uptake (SUV = 3.6, Deauville score 4). Consolidation RT (36 Gy in 18 fractions) was given. PET scan done 2 months later showed a decrease in uptake to 3.0. Patient remains in remission two and half years from completion of therapy.

Dunleavy et al reported survival rates over 90% using DA-R-EPOCH in PMBCL, with less than 5% of patients requiring RT. However, given historically better outcomes when RT was added to other chemotherapy regimens, obviating radiation in all patients is an ongoing debate. Further retrospective data demonstrated superior overall survival with consolidative radiotherapy on multivariable analysis even when controlling for possible confounders.^{2,3}

EOT PET scan has been used to determine need for RT. A Deauville score of 1-3 has been categorized as a negative scan while higher scores have indicated need for consolidation treatment. Retrospective studies using regimens such as

R-CHOP and R-MACOP-B have shown rates of positive EOT PETs ranging from 38%-69%.⁴ Despite the low rates of RT reported in the phase II DA-R-EPOCH cohort, a multicenter retrospective study conducted on a larger number of PMBCL patients treated with this regimen (156 adults and children) showed that 15% of them required consolidation RT.⁵

An extension of the phase II DA-R-EPOCH study followed patients with EOT PETs and serial scans.⁶ Out of the 80 patients included for analysis, 25 had positive EOT PETs. Five patients were confirmed to be treatment failures with most of them receiving RT, while 17 patients were noted to have a decrease in SUV on serial scans with no intervention given. The authors argue that by following patients with positive EOT PETs they can spare RT for some of them as they will have eventual uptake resolution (80% in their study). Further analysis per Deauville score showed only one treatment failure out of 17 patients with Deauville 4; however, more than half of these patients had tumor regression of at least 90%. Evidently, the question of sparing radiation safely in patients with persistent uptake higher than Deauville 4 and a less than expected tumor regression remains. Of note, patients with Deauville 5 (10% of their cohort) had worse EFS (71% vs 96%) and OS (84% vs 98%) in comparison to patients with Deauville 1-4, irrespective of who had improved PET on follow-up. Half of those patients (4/8) had confirmed disease progression requiring salvage therapy. An in-depth analysis of outcomes in patients with persistent Deauville 4-5 by EOT PET scan, considering factors such as tumor size regression, is needed before recommending surveillance without RT.

We are reporting outcomes of three consecutive PMBCL patients treated with DA-R-EPOCH that had positive EOT PET scans with a Deauville score of 4 or a significantly high SUV indicating recurrence/progression of disease. They required consolidation RT (median dose 40 Gy), with post-treatment PETs showing significant response with either minimal or no uptake in the mediastinum and continue to be in remission with no significant toxicities. In our experience, half of the patients treated with DA-R-EPOCH required RT (3/6). This is an unexpectedly higher rate than what has been described. We believe data from a prospective multicenter study is needed to adequately validate a regimen that could safely obviate the need for RT in PMBCL patients before this approach should be considered standard of care.

CONFLICT OF INTEREST

The authors do not declare any conflict of interest.

AUTHOR CONTRIBUTION

CG, KA, AP, SD: contributed to acquisition of data, drafted the article and revisions. RP, AF: reviewed it critically for important intellectual content; and finally approved the version to be published.

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