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5-2022

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Treatment of Recurrent Wilms Tumor with Irinotecan/Temozolomide

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Background

Despite improvement in relapse free survival (RFS) in recurrent Wilms tumor (WT), the 4-year RFS rate for patients treated with vincristine/ dactinomycin/doxorubicin is approximately 40%. Ifosfamide, carboplatin and etoposide are commonly used in relapsed solid tumors but have significant toxicities and require hospital admission for administration. Our patient focused on quality of life, and this led to exploration of other treatment options.

Results

The patient is an 11-year-old female diagnosed with WT at 6 years of age in Honduras who received approximately 6 months of chemotherapy and a nephrectomy. Staging in Honduras was unknown. Due to financial difficulties, she was unable to continue with treatment and family immigrated to the United States. One year after initial diagnosis, imaging revealed a large chest mass and intracardiac masses. Biopsy confirmed recurrent WT and she received modified NWST/AREN0534 regimen. She responded well to this regimen and underwent surgical resections and whole lung radiation. At 20 months off therapy, she was found to have a lung nodule confirmed to be recurrent WT. As this was her second recurrence, both patient and family chose a chemotherapy regimen allowing for the best quality of life.

Results

She received Irinotecan 90mg/m²/dose PO on days 1-5 and Temozolomide (TMZ) 40mg/m²/dose PO on days 1-5, 8-12, 15-19. She received the 2-drug regimen for 10, 28-day cycles without myelosuppression, need for transfusions or hospitalizations for fever and neutropenia, allowing her to attend school. At the end of cycle 10, she had a third recurrence.

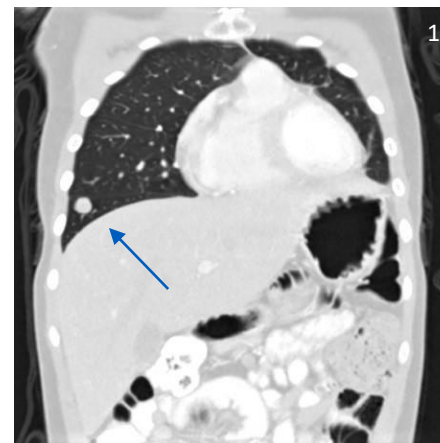
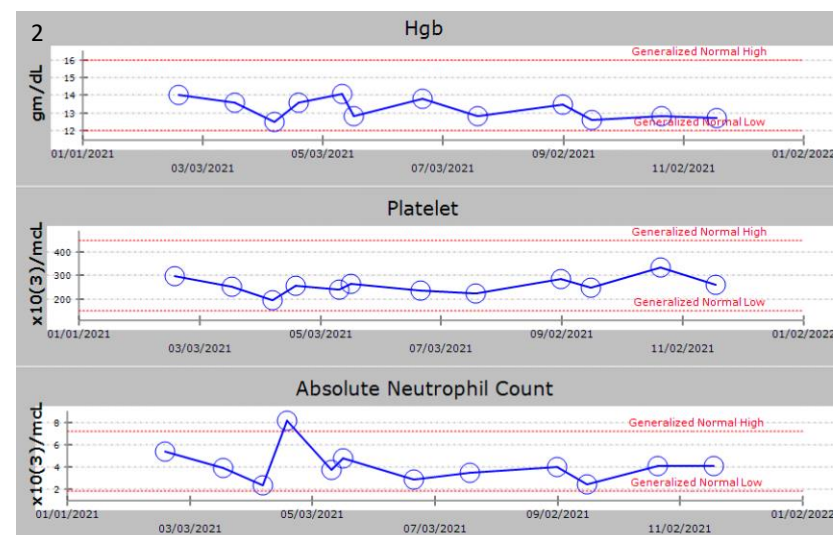


Figure 1 - Right pulmonary nodule measuring 1.2 cm; biopsy confirmed second recurrence.

Figure 2 - Hemoglobin (Hgb), platelet and absolute neutrophil count (ANC) trends while on Irinotecan/Temozolomide.

Ranges:
Hgb - 12.6 - 14.1 gm/dL
Platelet - 196 - 333 x 10³/mcl
ANC - 2.35 - 8.19 x 10³/mcl



Discussion

Irinotecan is a camptothecin prodrug shown to have activity against adult solid tumors. Topotecan of the same drug class also showed activity in children with favorable histology WT with a 48% response rate in heavily pretreated patients. TMZ has activity against adult solid tumors with promising results in xenograft models of pediatric solid tumors. O6-methylguanine-DNA-methyltransferase (MGMT) is a DNA repair enzyme which inhibits the anti-tumor effect of alkylating agents, like TMZ. Negative MGMT protein expression increases the sensitivity to alkylating agents and can predict the response to TMZ. Our patient was MGMT negative.

Conclusion

Irinotecan/Temozolomide should continue to be explored as an option for relapsed/refractory solid tumors as it can achieve remission for a substantial period while allowing for improved quality of life.

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