Successful Treatment of a Gray Zone Lymphoma With Immunotherapy: A Case Report

Nour A.Haidar MD[1] Karine Salignon MD[2], Youssef Jounblat MD[2], Cecile Borel MD[3] , Willy Vaillant MD[2]

[1]Saint Louis Hospital, Paris, France. [2]Hospital AUCH, AUCH, France. [3]The Cancer University Institute of Toulouse - Oncopole, Toulouse, France

The Gray Zone lymphoma, a rare subtype that combines the characteristics of both Hodgkin and non-Hodgkin disease forms. The new era of immunotherapy presents a hopeful treatment for solid tumors and hematologic malignancies. Specifically, immune checkpoint inhibitors like nivolumab and pembrolizumab are being used to treat relapsed/refractory lymphomas where the chemotherapy is effective in 50% of the cases . (1)

Case Presentation

- Here, we report on a 66-year-old woman who presented to the ER in October 2019 with a 4-month history of weight loss, nausea, vomiting, and abdominal pain. CT scan showed lytic spinal metastases and hepatosplenomegaly. PET/CT scan (Figure.1) showed hypermetabolic metastatic lymph nodes with bone lesions, a suspicion of epiduritis, and hepatosplenomegaly suspicious for lymphoma. Lymph node biopsy showed a gray zone lymphoma.
- Multidisciplinary discussion suggested treatment with 6 cycles of R-CHOP and 2 cycles of R-methotrexate, under went a subsequent re-evaluation with the PET , which revealed progressive disease.

- A second line of treatment was performed with three cycles of R-DHAOX , with no response. After that, she received 2 cycles of Brentuximab Vedotin–ICE as preparation for an autologous stem cell transplantation (was a rescue protocol) achieving partial remission). She continued with 2 more cycles of BV. A new PET scan showed refractory disease again.

Treatment with Pembrolizumab, an anti PD-1 monoclonal antibody, was introduced , which resulted in a complete response without any relapse of the lymphoma and stable remission to date (Figure 2)

Discussion

- Few clinical studies have shown effective responses to chemotherapy regimens like CHOP ± R, R-ICE) (2)

The case reported here demonstrates that chemotherapy treatments and antibody-drug conjugated did not lead to disease remission.

- This is consistent with the literature, which highlights the difficulty in establishing a standardized therapeutic regimen for gray zone lymphoma.
- The ideal early-stage chemotherapy regimen often includes CHOP which has shown positive (2.3) responses.
- Regarding autologous HSCT therapy, the procedure is indicated for this young patient diagnosed with lymphoma who did not respond to chemotherapy, as demonstrated by the PET scan evaluation (figure 1)

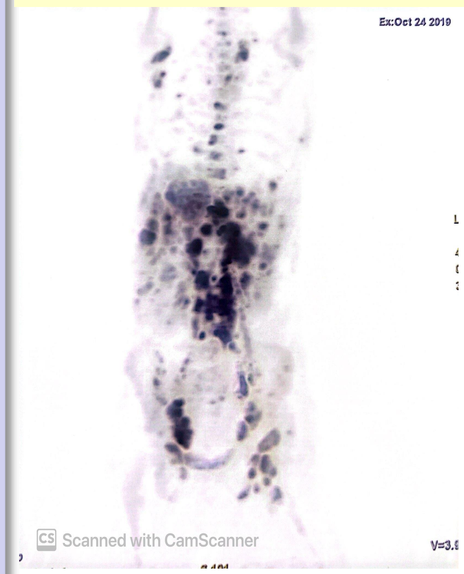


FIGURE 1



FIGURE 2

Fig. 1. PET images of the patient on October 2019 Initial staging and evaluation of the extent of gray zone lymphoma before initiating the chemotherapy
Fig .2 .PET images significant with no evidence of residual disease, consistent with complete remission post KEYTRUDA

- The treatment plan involved initiating therapy with pembrolizumab after the refractory disease post BV , a newly approved anti-PD-1 monoclonal antibody for Hodgkin's and non-Hodgkin's lymphomas.
- The patient was re-evaluated 2 years after starting pembrolizumab, with a PET scan showing a positive response to the treatment (figure 2) ,where the patient had a complete remission response post 1 year of the treatment

Conclusion

- The case report emphasizes the effectiveness of pembrolizumab therapy in treating gray zone lymphomas (4)
  . Pembrolizumab shows a high response rate in recurrent or refractory classic Hodgkin's lymphoma, but not in primary mediastinal B-cell lymphoma.
  . Recent findings suggest that gray zone mediastinal lymphoma may share closer similarities with classic Hodgkin lymphoma , where Gray zone mediastinal lymphoma exhibits increased PD-1 and PD-L1 protein expression in mediastinal masses (5)
- The case showed that pembrolizumab therapy is an effective treatment option for patients with rare gray zone lymphoma when it is refractory to different treatment lines. Therefore, both the diagnosis and treatment of gray zone lymphoma remain a challenge for medical and multiprofessional teams, and collaboration between them ensured an effective treatment for the patient described in this clinical case.

References

1.University of Colorado Anschutz Medical Campus. New promise of cancer immunotherapy to treat rare lymphoma. ScienceDaily 2017;37,10 July 2017. http://www.sciencedaily.com/releases/2017/07/170710113722.htm.
2. Kritharis A, Pilichowska M, Evens AM. How I manage patients with grey zone lymphoma. Br J Haematol 2016;174:345e50.
3.Pilichowska M, Pittaluga S, Ferry JA. Clinicopathologic consensus study of gray zone lymphoma with features in termediate between DLBCL and classical HL. BloodAdv 2017;1:2600e9. bloodadvances.2017009472. https://doi.org/10.1182/
3. Mallipudi RM, Alquran L, Shenoy VA, Leslie LA, Conti JA. Arare case of grey zone lymphoma successfully treated with brentuximab vedotin and R-CHP chemotherapy. Case Rep Oncol Med 2019;2019. https://doi.org/10.1155/2019/4121234. Article ID 4121234.
4. Coronado-Edgar A, Puron-Gonzalez E, Ramírez-Morales R. Gray zone lymphoma with intermediate characteristics be tween a diffuse large B-cell lymphoma and a classical Hodgkin lymphoma. Case report and literature review. Colomb J Cancerol 2018;22:146e50. https://doi.org/10.1016/j. rccan.2018.04.001.
5. Melany C, Major A, Schowinsky J, Roschewski M. PD-1 blockade in mediastinal gray-zone lymphoma. N Engl J Med 2017;377:89e91. https://doi.org/10.1056/NEJMc1704767.