A presentation of SMARC A4/BRG1 deficient lung carcinoma complicated by treatment related immune-mediated pneumonitis

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INTRODUCTION

- A small but increasingly recognized subset of non-small cell lung carcinomas can have mutations in SMARC A4 resulting in abnormal loss and deficiency of BRG1(1).
- SMARCA4 (SWI/SNF–related, matrix-associated, actin-dependent regulator of chromatin, subfamily A, member 4) gene and BRG1 (Brahma-related gene 1) along with many other genes encode a large chromatin remodeling unit which is involved in a wide variety of biological processes(1).

CASE PRESENTATION

- A 69-year-old former tobacco smoking gentleman originally presented with shortness of breath and was found to have a pleural effusion.
- He underwent thoracentesis and resulting cytology showed atypical cells. Subsequent CT scan showed a lower left lung mass. He then had recurrent symptomatic pleural effusions and underwent a video assisted thoracoscopy with pleural biopsy and pleurodesis.
- Pathology showed poorly differentiated SMARCA4/BRG1 deficient malignant neoplasm, most consistent with metastatic carcinoma.
- After consultation with additional specialists ipilimumab and nivolumab along with pemetrexed and carboplatin was recommended(2).
- The patient completed a total of four cycles of treatment and repeat PET scan showed resolution of previously seen lymphadenopathy and improvement in size of the lung mass, along with improvement in bone lesions.
- However, he developed immune mediated pneumonitis and unfortunately passed away despite intubation and treatment with methylprednisolone and infliximab.

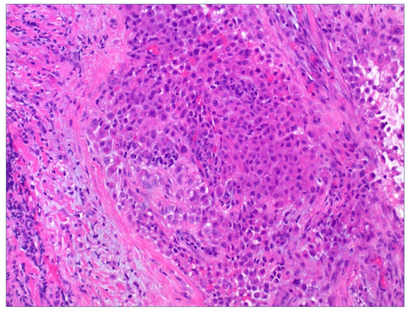

Figure 1) Pleural biopsy showing a poorly differentiated SMARCA4/BRG1 deficient malignant neoplasm, most consistent with metastatic carcinoma.

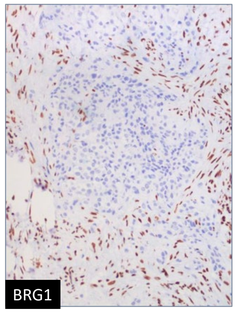

Figure 2) BRG1 staining shows abnormal loss of BRG1/SMARCA4.

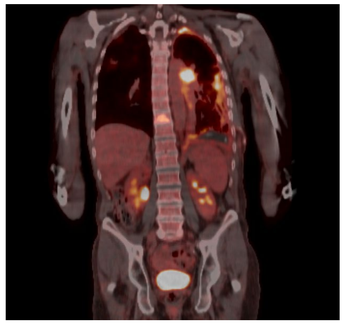

Figure 3) PET scan showing the Left suprahilar mass with moderate FDG uptake. Also showed Hypermetabolic left pleural nodularity and T10 metastasis.

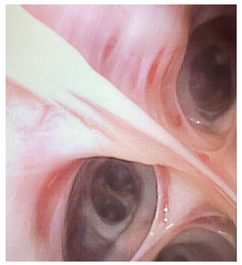

Figure 4) Bronchoscopy showed diffuse inflammation with ulcerated endobronchial mucosal lesions, concerning for checkpoint inhibitor induced pneumonitis.

DISCUSSION

- SMARC A4/BRG1 deficient tumors can arise from multiple different primary sites. Some can are characterized under sarcomas while others are considered poorly differentiated carcinomas(3).
- SMARC A4/BRG1 deficient tumors are associated with a poor prognosis(3, 4, 5, 6).
- Treatment regimens for SMARC A4/BRG1 deficient tumors are currently under investigation, however there have been preliminary observational studies which show responsiveness to treatment with immunotherapies(1,4).
- Some patients with SMARC A4/BRG1 tumors have a hereditary predisposition to develop these malignancies due to a germline SMARCA4 mutation.
- Novel targeted agents for SMARC A4/BRG1 deficient cancers have been proposed, but are not currently available(7).

TAKE HOME POINT

- This case highlights the importance of the need for further randomized controlled trials to establish a standardized treatment and targeted therapies for these aggressive cancers.

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