Two cases of electron microscopy-proven SMARCA4 deficient undifferentiated large cell neuroendocrine carcinoma presenting as subcutaneous masses

K.J. Knowles[1], K.J. Jiang[1], J. Hassan[1], D.E. Escobar[2], J. Harrison-Howard[2], G.A. Herrera[1]

[1] Departments of Pathology, University of South Alabama/ Whiddon College of Medicine; [2] University of South Alabama/ Whiddon College of Medicine.

Abstract

SMARCA4 is a subunit of the SWI/SNF (mammalian switch/sucrose nonfermenting) complex and functions as a tumor suppressor gene. Large cell neuroendocrine carcinoma (LCNEC) of the lung is aggressive, and SMARCA4 deficiency LCNEC is linked to poorer outcomes. We report two cases of metastatic SMARCA4-deficient undifferentiated LCNEC presenting as subcutaneous masses: a 3 cm asymptomatic right flank mass in a 59-year-old male and a 5 × 10 cm painful, ulcerated left perineal mass in a 56-year-old female. Both patients had primary lung cancers along with long smoking histories. Tumors were positive for synaptophysin and napsin (seen in up to 15% of LCNEC) and negative for CD56 and TTF-1. Electron microscopy showed abundant neuroendocrine granules and desmosomes, confirming the diagnosis of LCNEC. Both patients were treated with atezolizumab, carboplatin, and etoposide. The male patient achieved an initial response lasting nine months, followed by disease progression, and died 20 months after the initial diagnosis. The female patient showed no response to this regimen and was subsequently treated with tarlatamab-dlle, also without response, with ongoing disease progression. To our knowledge, this is the first report of SMARCA4-deficient LCNEC confirmed by electron microscopy. Few cutaneous cases have been reported, and these have all relied on immunohistochemistry, which can demonstrate neuroendocrine marker expression but cannot definitively confirm neuroendocrine differentiation. Electron microscopy provides ultrastructural evidence which provides greater diagnostic certainty. A high index of suspicion and the use of appropriate techniques, including electron microscopy, may be necessary to establish a definitive diagnosis in challenging cases.

References

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