NUT carcinoma: a rare and devastating neoplasm

Shinban Liu, George Ferzli

General Surgery, NYU Langone Medical Center, Brooklyn, New York, USA

Correspondence to
Dr Shinban Liu,
shinban.liu@nyumc.org

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DESCRIPTION

A 45-year-old woman with no significant medical history had 1 month of productive cough empirically treated with azithromycin and dyspnoea on exertion. She was never a smoker and denied any constitutional symptoms, including unexpected weight loss. A CT of the chest was performed after she developed haemoptysis, which demonstrated a 6.3×4.6 cm right hilar mass with hilar, subcarinal and cardiophrenic adenopathy (figure 1A). She underwent bronchoscopy which revealed complete occlusion of the right middle lobe by a tumour extending into the bronchus intermedius. Debridement of this mass was performed, with re-establishment of airway patency to the right lower lobe. Pathology from the debried tumour as well as the subcarinal lymph node was consistent with poorly differentiated non-small cell lung carcinoma with Thyroid Transcription Factor 1 (TTF-1) and Programmed Death-Ligand 1 (PD-L1) negativity. Due to high clinical suspicion, the tissue samples were transferred to another facility for additional assessment. MRI of the head was performed and found to be negative for metastatic disease. This was followed by a positron emission tomography-CT performed 3 weeks after the original CT, which demonstrated intense Fludeoxyglucose (FDG) activity and significantly enlarged mass now measuring 11×10 cm with bilateral pleural effusions, pericardial effusion, and mass effect on the superior vena cava, right atrium, left atrium and right pulmonary veins (figure 1B). Shortly after imaging, the patient's clinical status rapidly deteriorated and she expired after transition to hospice care. Her pathology would ultimately return indicative of NUT (nuclear protein in testis) carcinoma with a nuclear speckled pattern of staining, expression of BRG1 (SMARCA4) and BAF-47 INI1 (SMARCB1) retained in tumour cells.

Figure 1 (A) CT of the chest with 6.3×4.6 cm right hilar mass. (B) Positron emission tomography-CT 3 weeks later with significantly increased 11×10 cm right hilar mass, bilateral pleural effusions, pericardial effusion, and mass effect on the superior vena cava, right atrium, left atrium and right pulmonary veins.

Figure 2 Characteristic histopathology of NUT (nuclear protein in testis) carcinoma with sudden, abrupt islands of well-differentiated squamous epithelium without gradual transition.

NUT carcinoma (formerly recognised as NUT midline carcinoma or NMC) is a very aggressive neoplasm characterised by a balanced translocation of the NUT gene on chromosome 15q14.¹ The most frequent translocation is t(15;19) and the role of this gene is largely unknown. However, this mutation is believed to alter squamous differentiation causing characteristic abrupt islands of well-differentiated squamous epithelium on histology (figure 2). NUT tumours can affect any organ system but typically appear in the midline upper respiratory tract and chest. This leads to generalised symptoms such as pain, weight loss and fatigue, with local obstructive mass effect depending on the organ system affected. The presence of sudden squamous differentiation without gradual differentiation on histology, in addition to midline location, should prompt further work-up with cytokeratin testing or NUT-specific antibody testing. It is exceptionally rare, with only 20–30 diagnoses reported in the USA each year.² However, this may be a gross underestimate as few facilities have the reagents and expertise to make the diagnosis, and NUT tumour histology often overlaps with other carcinomas. Most patients have advanced metastatic disease at the time of diagnosis, and treatment is often limited to chemotherapy

Learning points

- ▶ NUT (nuclear protein in testis) carcinoma is a rare neoplasm that should be clinically suspected with aggressive midline masses.
- ▶ Specialised pathology may be required to obtain accurate diagnosis.
- ▶ Chemotherapy and radiation are the mainstay of treatment as surgical resection is limited.

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and/or radiation therapy as surgical resection is not achievable. Treatment for these locally aggressive tumours generally follows the guidelines for tumours of similar histology and anatomical location.

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