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CASE REPORT

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Tracheal resection and reconstruction under non-intubated anesthesia for nuclear protein in testis carcinoma: a case report

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Abstract

Background Nuclear protein in testis (NUT) carcinoma is a rare and highly aggressive solid tumor with a poor overall survival outcome. There's no recognized treatment or consensus on the management for NUT carcinoma. To date, few cases of tracheal NUT carcinomas have been reported, and the prognosis of these cases was dismal. We report a rare case of tracheal resection and reconstruction performed under non-intubated anesthesia for tracheal NUT carcinoma with good outcomes, aiming to contribute our experience in the surgical treatment of tracheal NUT carcinoma.

Case presentation A 42-year-old male with a 20-packyear smoking history presented to the hospital with dyspnea and cough and was diagnosed with a tracheal malignant carcinoma. Fluorodeoxyglucose positron emission tomography showed FDG accumulation in the upper tracheal wall. The patient underwent tracheal resection and reconstruction under non-intubated anesthesia, with the final diagnosis of NUT carcinoma confirmed via immunohistochemical staining. The patient then received adjuvant platinum-based chemotherapy postoperatively. Neither complication nor cancerous recurrence was observed during the 12-month follow-up.

Conclusions Surgery remains the preferred choice for early tracheal malignant tumors, including rare tumors like NUT carcinoma. This case report provides valuable insights into the imaging characteristics, pathological diagnosis, and treatment approach for tracheal NUT carcinoma. Future studies should aim to expand the case series to enhance our understanding and management of this aggressive neoplasm.

Keywords NUT carcinoma, Tracheal tumor, Tracheal resection and reconstruction, Non-intubated anesthesia

Background

Nuclear protein in testis (NUT) carcinoma is an extremely uncommon malignant and rapidly progressive solid neoplasm that is characterized by the rearrangement of the NUTM1 gene. This lethal tumor exhibits a higher prevalence in the adolescent and young adult demographic. Head, neck, and mediastinum are the commonly affected regions, with tracheal NUT carcinoma being a rare finding [1]. So far, recognized therapeutic guidelines for NUT carcinoma are yet to be established, and the reported median survival time was 6.7 months, with a 19% overall survival(OS) rate at 2 years [2]. To

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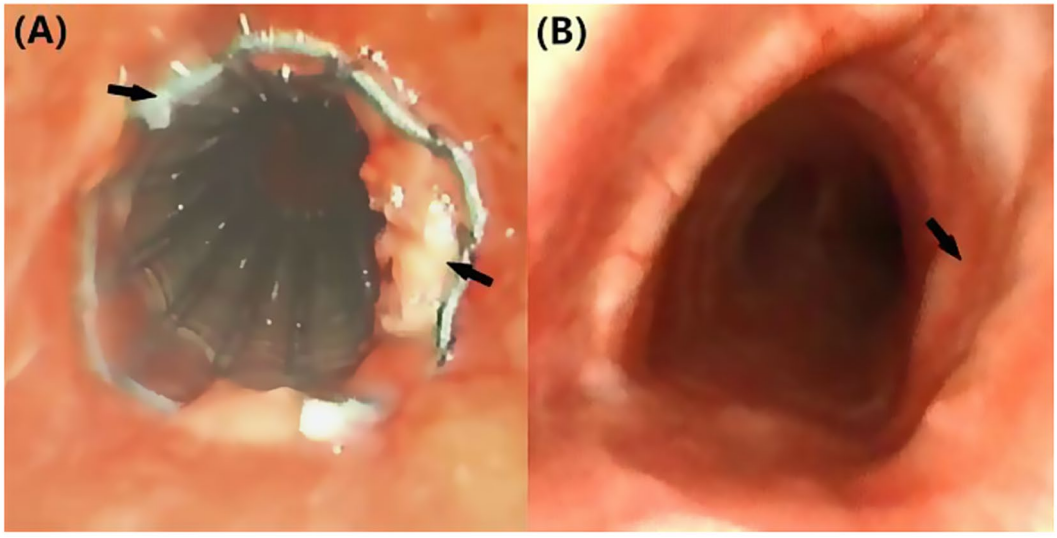

Fig. 1 (**A**) Preoperative bronchoscopy shows a circumferential, irregular mass (arrow) in the upper trachea, covered by a stent. (**B**) Postoperative bronchoscopy at 12 months follow-up reveals a patent tracheal lumen with no evidence of recurrence at the anastomotic site (arrow)

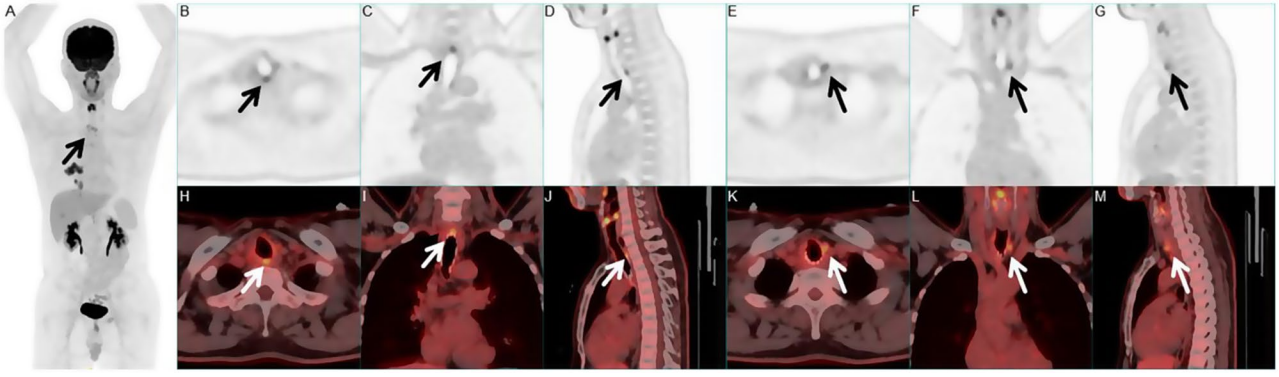

Fig. 2 18 F-FDG PET/CT images: (**A**) Anterior maximum intensity projection (MIP) PET image highlights hypermetabolic foci in the upper trachea (SUVmax 4.7, arrow) and mediastinal lymph node (SUVmax 4.1, arrowhead). (**B**-**D**) Transverse, coronal, and sagittal PET/CT fusion images localize the tracheal tumor (arrows) to the posterior wall, with intense FDG uptake (SUVmax 4.7). (**E**-**G**) Additional hypermetabolic foci in the mediastinal lymph node (arrows, SUVmax 4.1) and dorsal right lower lung (SUVmax 8.0, not shown) suggest regional metastasis and inflammatory changes, respectively

date, there have been no retrospective studies on tracheal NUT carcinoma, and reports of NUT originating in the trachea are limited to isolated case reports. Herein, we present a rare case of a primary tracheal NUT carcinoma that was completely resected, resulting in a favorable prognosis.

Case presentation

A 42-year-old male with a 20 pack-year smoking history presented with progressive dyspnea accompanied by productive cough. No noticeable abnormality was found on physical examination and routine laboratory tests. Computed Tomography (CT) scan revealed a mass in the upper trachea. He then received the bronchoscopic biopsy and the pathological diagnosis was squamous cell carcinoma. Given the limited surgical capacity at the primary care facility, the patient underwent palliative interventions including tracheal stent implantation combined with cryoablation-hyperthermia therapy at an external institution to alleviate airway obstruction(Fig. 1A). Despite these measures, the patient still suffered the recurrence and aggravation of the symptoms. Subsequent referral to our center prompted comprehensive restaging with 18 F-FDG Positron Emission Computed Tomography-Computed Tomography (PET-CT) (Fig. 2), which revealed focal tracheal wall thickening (SUVmax 4.7) with a posterior mural nodule and metabolically active mediastinal lymphadenopathy (SUVmax 4.1), confirming locally advanced tracheal malignancy with nodal metastasis. Multidisciplinary evaluation deemed the lesion surgically resectable. The patient underwent segmental tracheal resection (4.2 cm length, 4.1 cm distal to vocal cords, 4.5 cm proximal to carina) with reconstruction under

non-intubated anesthesia. Histopathological analysis confirmed R0 resection margins. The patient successfully regained oral nutrition and ambulation 4 h postoperatively. Definitive histopathological evaluation (Fig. 3) demonstrated nests of poorly differentiated tumor cells with abrupt keratinization and necrosis. Immunohistochemistry (IHC) revealed strong nuclear NUT expression, P40(+), and CK5/6(+), excluding squamous cell carcinoma and confirming the diagnosis of NUT carcinoma per WHO criteria [1, 3]. The PET-CT findings, including elevated SUVmax values in the tracheal lesion and mediastinal node, aligned with the aggressive behavior typical of NUT carcinoma [2, 4]. The patient received 4 cycles of adjuvant chemotherapy, with the strategy of Abraxane 100 mg/m2 + Carboplatin (AUC = 6). During the one-year follow-up, the patient received surveillance bronchoscopies and repeated CT, revealing no evidence of recurrence and metastasis(Fig. 1B).

Discussion and conclusions

NUT carcinoma is an extremely rare and highly aggressive carcinoma, first described in the thymus in 1991 [5]. It is defined by the rearrangements or mutations in the NUTM1 gene, most commonly through chromosomal translocations such as t(15;19), which fuses NUTM1 with BRD4 or other partners [1]. The internationally reported median survival time was 6.7 months, with an OS rate of 19% at 2 years [2]. Chau et al.'s study of 124 cases indicates thoracic NUT carcinomas have a worse prognosis, with an OS of only 4.4 months and a 2-year survival rate of 5% [6, 7]. Unfortunately, NUT carcinoma is unresponsive to conventional treatments, including chemotherapy and radiotherapy, and most cases are not surgical candidates due to distant metastasis at the time of diagnosis [8, 9]. Until now, there have been few reported cases of primary tracheal NUT carcinoma in the literature [4, 10]. We present a rare case of primary tracheal NUT carcinoma that underwent tracheal resection and reconstruction under non-intubated anesthesia, with progression-free survival exceeding one year. To contextualize our findings, we have compiled a comparative summary of reported primary tracheal NUT carcinoma cases (Table 1), which highlights critical differences in treatment approaches and outcomes.

Early diagnosis of NUT carcinoma plays a crucial role in its treatment due to its highly aggressive nature [11]. However, diagnosing NUT carcinoma is a formidable challenge. The manifestation and imaging findings of tracheal NUT carcinoma lack specific features [8]. Histopathologically, the origin of NUT carcinoma tissue is still unknown, and it sometimes resembles a poorly differentiated squamous cell carcinoma [12]. These challenges often lead to the misdiagnosis as squamous cell carcinoma, making the timely preoperative diagnosis of NUT carcinoma particularly difficult. The presented case was initially misdiagnosed as tracheal squamous cell carcinoma and was finally confirmed as NUT carcinoma postoperatively by IHC. The NUT antibody for IHC provides a robust diagnostic approach for NUT carcinoma, with a specificity of 100% and a sensitivity of 87%, effectively differentiating it from other poorly differentiated carcinomas [3, 13]. IHC is deemed a pivotal technique for diagnosing NUT carcinoma and should be used to exclude NUT carcinoma when suspicious histopathological signs, such as focal squamous differentiation with acute keratinization and exhibit a monomorphic pattern, are observed [14]. The molecular hallmark of NUT carcinoma—NUTM1 rearrangement—underscores the importance of genetic sequencing in both diagnosis and therapeutic targeting. Next-generation sequencing (NGS) and fluorescence in situ hybridization (FISH) are pivotal for identifying these alterations, enabling precise subclassification and guiding targeted therapy development [4, 12].

NUT carcinoma is insensitive to radiotherapy and chemotherapy, with a chemotherapeutic response rate

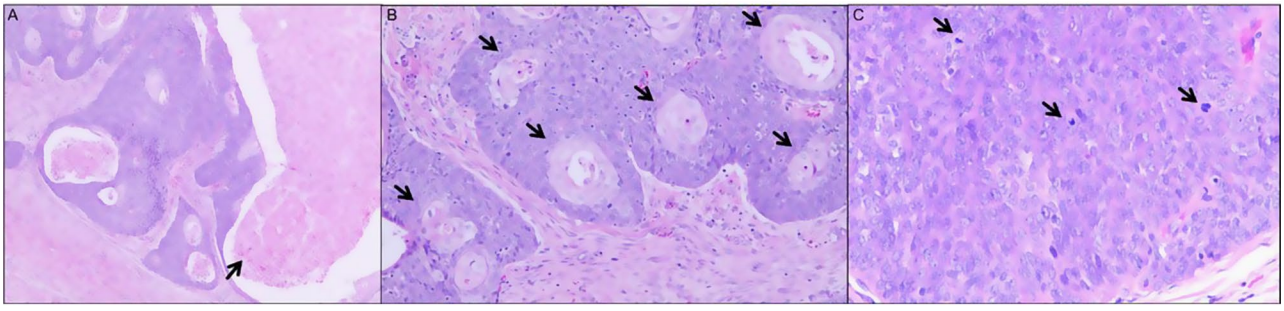

Fig. 3 Postoperative pathological results of tracheal NUT carcinoma with hematoxylin-eosin staining (A:40x, B:100x, C:200x) (**A**) Low-power view (40×) reveals nests of tumor cells (arrow) with central necrosis (asterisk), a hallmark of aggressive neoplasms. (**B**) Intermediate magnification (100×) demonstrates abrupt keratinization (arrow), a feature overlapping with squamous cell carcinoma but later confirmed as NUT carcinoma via immunohistochemistry. (**C**) High-power view (200×) shows monomorphic tumor cells with high nuclear-to-cytoplasmic ratios, vesicular chromatin, prominent nucleoli (arrowheads), and frequent mitotic figures (arrows), supporting a poorly differentiated carcinoma

Table 1 Summary of reported primary tracheal NUT carcinoma cases

Case Reference	Age/Sex	Tumor Location	Tumor Size (cm)	Diagnostic Modality	Treatment Approach	Oncologic Outcomes	Overall Survival (OS)
Current Case	42/Male	Upper trachea	4.2 (resected)	PET-CT, biopsy, IHC (NUT+, P40+, CK5/6+)	Tracheal resection (R0) under non-intubated anesthesia + adjuvant chemotherapy (Carboplatin/Abraxane)	No recurrence/metastasis at 1-year follow-up	12 + months (alive)
Zhang et al. 2022 [10]	34/Male	Lower trachea	3.9 × 3.5	CT, biopsy, IHC (NUT+)	Surgical resection	Recurrence within 1 month; no metastasis at diagnosis	3 months (deceased)
Chen et al. 2023 [12]	49/Male	Right trachea	11.2 × 9 × 13	CT, IHC (NUT+, p63+, p40+, CK7+, Synaptophysin+)	Chemoradiotherapy	Bilateral lung metastasis; death due to disease progression	1.5 months (deceased)
Chen et al. 2023 [12]	45/Male	Left lower lobe/Trachea	2.5 × 2.5	CT, IHC (NUT+, CK5/6+, p63+)	Surgery + chemotherapy (durvalumab)	Metastasis to bilateral lung, liver, and bone; died of disease	4 months (deceased)

of only 40% [15]. Since there is still no recognized effective treatment for NUT carcinoma, surgery remains the preferred option for many patients. Achieving an R0 resection is key to the success of surgery. In this patient, preoperative evaluation revealed no distant metastases. Based on our center's experience, we performed upper tracheal resection and reconstruction under non-intubated anesthesia, maintaining a 5 mm negative margin. Traditionally, general anesthesia with endotracheal intubation has been considered essential for most thoracic surgeries [16]. However, for upper tracheal malignancies, repeated endotracheal intubation may increase the risk of tumor cell shedding and seeding, potentially causing recurrence and asphyxia [16, 17]. Additionally, frequent tracheal intubation may lead to postoperative complications, including airway edema and stenosis [16, 17]. The rationale for selecting non-intubated anesthesia in this case was grounded in its documented advantages over conventional intubation. Non-intubated anesthesia, characterized by spontaneous ventilation without endotracheal intubation, has been confirmed to be safe and feasible in most clinical cases [17, 18]. Compared with traditional intubated anesthesia, it accelerates postoperative recovery by preserving diaphragmatic function and reducing residual neuromuscular blockade [19]. Furthermore, for upper tracheal surgery, non-intubated anesthesia provides an improved surgical field, avoids cross-field ventilation, and simplifies the surgical procedure without the interference of endotracheal tubing [16]. In this case, the improved visualization facilitated precise R0 resection and tension-free anastomosis, critical for preventing postoperative dehiscence or stricture. Prior studies on tracheal resection under non-intubated anesthesia reported shorter operative times, reduced hospital stays, and comparable safety profiles to intubated approaches. Potential risks of non-intubated anesthesia include intraoperative hypoxemia or hypercapnia, which may necessitate urgent conversion to intubation. However, meticulous preoperative planning—including strict patient selection, regional nerve blocks, and real-time monitoring—mitigates these risks(16, 18). In this patient, preoperative bronchoscopy confirmed adequate airway patency, and continuous SpO_2 monitoring ensured stable oxygenation throughout the procedure. Conversion to intubation was not required, consistent with prior reports of non-intubated tracheal surgery [20]. Our patient achieved 12 + months of recurrence-free survival following R0 resection under non-intubated anesthesia, a result superior to most reported cases (Table 1). For instance, Zhang et al. (2022) reported a 34-year-old male with lower tracheal NUT carcinoma treated with surgical resection alone, who experienced recurrence within 1 month and succumbed to the disease at 3 months [10]. Similarly, Chen et al. (2023) described a 49-year-old male with a large tracheal tumor (11.2 × 9 × 13 cm) treated with chemoradiotherapy, who survived only 1.5 months due to rapid metastasis [12].

Given the aggressive behavior of NUT carcinoma, the administration of postoperative adjuvant therapy is warranted. Although there is no international consensus on postoperative adjuvant treatment for NUT carcinoma, adjuvant therapy after surgery is necessary [9]. Our in vitro organoid testing demonstrated marked chemosensitivity to platinum-based regimens but minimal response to radiotherapy. In this case, we adopted an adjuvant treatment regimen of Carboplatin plus Abraxane for four courses. The patient's OS has reached 1 year, exceeding the median survival duration.

Current studies investigating emerging therapies targeting the BRD4-NUT oncoprotein, such as bromodomain and extra-terminal (BET) inhibitors, have demonstrated preclinical and early clinical promise [13].

BET inhibitors (e.g., OTX015/MK-8628) disrupt BRD4-histone interactions, suppressing oncogenic transcription driven by the BRD4-NUT fusion. Phase I trials have reported clinical responses in NUT carcinoma patients, particularly those with non-thoracic primaries, though challenges such as dose-limiting toxicity and resistance remain significant barriers [6, 13]. While these agents represent a paradigm shift for advanced or inoperable cases, surgery remains the cornerstone for localized disease.

In summary, we present a rare case of upper tracheal NUT carcinoma who successfully underwent tracheal resection and reconstruction under non-intubated anesthesia, achieving a disease-free interval with no early postoperative complications during a 1-year follow-up period. We aim to share our experience in the surgical treatment of NUT and rare tracheal tumors. We emphasize that the utilization of non-intubated anesthesia and achieving an R0 resection are pivotal for the successful surgical management of tracheal NUT carcinoma. Moreover, more cases need to be included in further research.

Tables.

Abbreviations

NUT	Nuclear protein in testis
CT	Computed Tomography
PET-CT	Positron Emission Computed Tomography-Computed Tomography
MIP	Maximal intensity projection
IHC	Immunohistochemistry
NGS	Next-generation sequencing
OS	Overall survival
BET	Bromodomain and Extra-Terminal

Supplementary Information

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Supplementary Material 1

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None.

Author contributions
Zijian Li. Chudong Wang. Yuxuan Li. and Rui Wang. wrote the main manuscript text, Zijian Li. and Chudong Wang. prepared Figs. 1 and 2, and Zijian Li. and Yuxuan Li prepared Figures 3. All authors reviewed the manuscript.

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Data availability
No datasets were generated or analysed during the current study.

Declarations

Ethics approval and consent to participate
Not applicable.

Consent for publication
Written informed consent was obtained from the patient for publication of this case report.

Competing interests
The authors declare no competing interests.

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