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A case report of NUT cancer in nasal sinus

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Abstract: Uclear protein in testis (NUT) carcinoma is a rare, aggressive, poorly differentiated squamous cell carcinoma caused by NUT gene rearrangement on chromosome 15. Because it occurs in the middle line structure of the head and neck and the chest, it is also known as midline cancer. These tumors favor midline and quasi-midline structures in the upper digestive tract and mediastinum and can affect patients of a wide age range, including children.

1. Introduction

NUT Carcinoma is a rare and highly aggressive malignant tumor of unknown origin, characterized by chromosome rearrangement associated with NUTM1 gene. NUT cancer usually occurs in midline organs such as the mediastinum of the head and neck, and mostly in the nasal sinuses. Currently, the treatment method is not clear, and the treatment process is usually characterized by short-term remission, rapid recurrence and rapid death[1].No epidemiological studies on the pathogenesis of NUT cancer have been conducted, its incidence and susceptibility factors are unknown, and no association with any specific risk factors (such as smoking, family background, genetic diseases, environmental factors, or infectious pathogens) has been found.

NUT cancer is characterized by chromosomal rearrangements involving the NUTM1 gene, but lacks specific clinical and histomorphologic features. NUT cancer can occur at any age, but it mainly occurs in children and young adults. In addition, men and women are equally affected. Most clinicians lack a clear understanding of the disease, and NUT cancer diagnostic reagents are still not widely used; Therefore, misdiagnosis often occurs clinically. Because the disease is highly aggressive and insensitive to non-specific chemotherapy or radiation, many patients die before NUT cancer is diagnosed. In fact, the true incidence of NUT cancer is much higher than current statistics suggest.However, a growing number of studies have found that NUT cancer appears not only in midline structures, but also in the lungs [2], kidneys[3], pancreas [4], bladder[5], salivary glands [6], bones[7], ovaries[8], and other organs or soft tissues.

At present, conventional treatment for NUT cancer is not effective, and most patients have a poor prognosis. At present, the lack of understanding of this gene variant is a major obstacle to the progress of diagnosis and treatment of NUT cancer. The lack of standardized guidelines for the

clinical characteristics, diagnosis and treatment of NUT cancer in clinical practice limits clinicians' full understanding of the disease.

The purpose of this paper is to review and discuss the diagnosis and treatment process of a case of NUT cancer in our department, so as to provide valuable clinical data for the diagnosis, treatment and prognosis evaluation of NUT cancer in the nasal cavity and sinuses.

2. Clinical data of cases

This paper reports a case of NUT cancer in the nasal cavity and sinuses of a 56-year-old woman in our hospital, aiming to raise awareness of the disease.

The patient complained of pterygium excision in August 2023, and found a frontal mass with a size of about 4cm without tenderness, rebound pain, dizziness, headache, nausea, vomiting, and chills and fever after surgery. No treatment was given. In February 2024, the mass was larger than before, about 10cm in size, hard, without tenderness, rebound pain, and blurred vision in the right eye. The local hospital gave anti-inflammatory treatment (specific is not known), and there was no significant change in the tumor. 2024-2-22 External hospital CT: Right nasal cavity, right orbital and frontal subcutaneous mass, involved right ethmoidal sinus, maxillary sinus and bilateral frontal sinus, right nasolacrimal duct, right internal rectus muscle, right optic nerve, superior rectus muscle compression and displacement, right eyeball compression and protrusion, left superior oblique muscle is suspicious and may be laborious. 2024-2-28 External pathology:(right nasal mass) microscopic examination showed malignant tumor, immunohistochemistry consistent with NUT cancer.

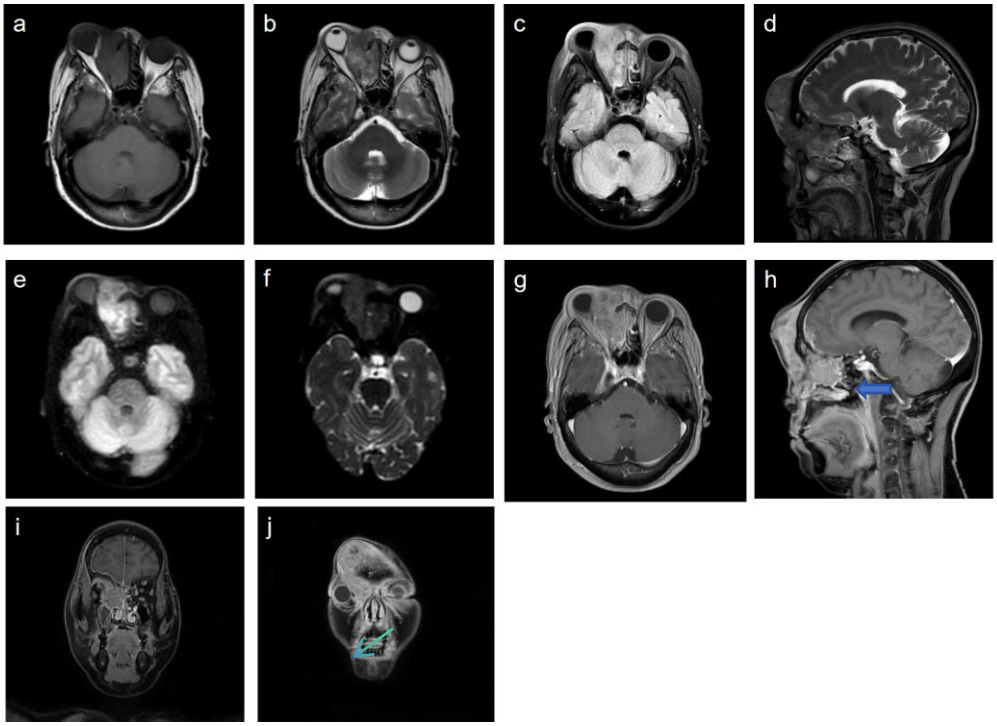

Fig. 1a) The mass on the sinus MRI TWI showed equal and low signal; b,d) T2W in axial and sagittal positions is a mixed slightly higher signal; c)T2W_FLAIR is obviously high signal; e)DWI is a high signal, f) ADC is a low signal; g~j) enhancement showed uneven and obvious enhancement. The mass invaded the right prefrontal cortex across the frontal bone, and the right frontal bone was destroyed and thinned (⬅) ; The skin of the right eyelid was thickened, and thickened and strengthened(⬅).

2024-3-14 MR Examination in our hospital (FIG. 1a-i): The tumor showed isolow signal shadow on T1WI, isohigh signal shadow on T2WI, low and high signal shadow on lipomatous sequence, obvious and uneven enhancement on enhanced scan, scattered in weak enhancement focus, obvious limited mass diffusion, the tumor invaded the right prefrontal cortex across the frontal bone, and the right frontal bone was destroyed and thinted. The skin of the right eyelid was thickened, and thickened and strengthened. There were several enlarged lymph nodes in the carotid sheaths on both sides, and the enhancement was observed. The short diameter of the larger one was about 9mm, and the dispersion was limited. Brain MRI showed no brain metastases. 12 tests of female tumor :CEA(quantitative)17.97 ng/nt, carbohydrate antigen 24268.44 u/t, Squamous cell carcinoma associated antigen 4.91 pg/nl; 2024-03-14 Difficult pathological consultation (FIG. 2) : (right nasal mass) a poorly differentiated carcinoma with necrosis and a small amount of keratinized epithelium.

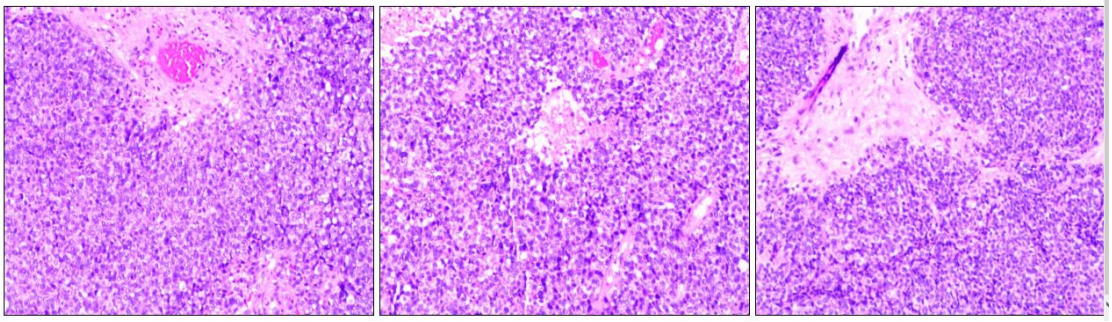

Fig. 2 Microscopically, the tumor cells were segmented, nested, and infiltrated. The nuclei were large and deeply stained, and the mitotic images were easily seen. Some of the tumor cells were eosinophilic in cytoplasm, accompanied by necrosis and a few keratinized epithelium.

3. Discussion

NUT cancer is a rare, poorly differentiated squamous cell carcinoma that was first identified in the early 1990s. Initially thought to be a childhood tumour, cases have now been found across a wide age range, with men and women equally affected [9, 10].The most common sites include the mediastinum or thymus as well as the head and neck. Involvement in the head and neck, sinuses or nasopharynx is most common. It is a highly aggressive malignancy with a median survival of 6.7 months and a 2-year overall survival rate of 19%[11].

NUT cancer occurs due to chromosomal rearrangement of the NUT (also known as NUTM1) gene, most commonly a translocation between the NUT and BRD4 genes to form the BRD4-NUT oncoprotein[12]. NUT cancer is mainly diagnosed by immunohistochemistry. Specific monoclonal antibodies that recognize NUTM1 protein are used for immunohistochemical staining. When more than 50% of the nuclei of paraffin-embedded sections fixed with formaldehyde are stained, NUT cancer is diagnosed, and its specificity and sensitivity for NUT cancer diagnosis are 100% and 87%[13].Its prognosis is closely related to factors such as different NUTM1 fusion partners[14].

The clinical symptoms and laboratory results of NUT cancer are not specific[15].It often presents as a rapidly increasing mass, some accompanied by pain, low fever, and 60% to 77% of cases have distant metastasis at first diagnosis[16], and the most common distant metastasis was to bone, followed by lung, pleura, liver, brain, adrenal gland, kidney and skin, etc. 68% of cases showed local lymph node involvement[17].About 41% of NUT cancer cases involved the head and neck, especially the sinus area. The primary focus of most NUT cancer patients originated in the nasal cavity, of which about 30.2% involved the paranasal sinus and 14.3% involved the parotid gland.The clinical manifestations of NUT cancer patients in head and neck are pain at the lesion, hard and swollen skin, difficulty in opening mouth, nasal congestion and other symptoms. About

56.7% of NUT cancer patients in head and neck have tumor invaded surrounding tissues at the first diagnosis, and 26.7% of NUT cancer patients have local lymph nodes involved[18].Patients with NUT cancer in the head and neck may also show pain, swelling, vision loss, double vision, facial numbness, cough when drinking water, and epistaxis due to tumor invasion of neighboring tissues. Nasal and sinus NUT cancer patients first visit mainly due to nasal pain, nasal congestion and other symptoms. Because of the high degree of malignancy of NUT cancer, it is easy to develop early distant metastasis, so it is recommended to check all parts of the body when patients first visit to confirm whether distant metastasis has occurred.

The imaging findings of NUT cancer are generally nonspecific, and are usually similar to those of other common solid tumors at the anatomical site, except for low-density masses with uneven enhancement and aggressive features[19]. Most of the primary NUT carcinomas in the lung were central type with invasive invasive growth and irregular shape. 36.8% were combined with pleural effusion, and 57.9% were combined with obstructive atelectasis or obstructive pneumonia[20].In MRI examination, thoracic NUT cancer showed low signal on T1-weighted images and medium-high signal on T2-weighted images, accompanied by uneven enhancement[21].NUT cancer in the head and neck mainly presents as a large and borderless space-occupying mass with necrosis and bleeding inside the mass, accompanied by invasion of adjacent tissues such as sinus wall, muscle and nerve, and involvement of cervical lymph nodes[18].On CT, NUT cancer of the nasal cavity and paranasal sinus mostly presents low-density mass, necrosis and bleeding within the mass, while on MRI, it mostly presents mass with uneven signal, irregular shape, invasive and invasive growth, low signal on T1WI and slightly high signal on T2WI in general, and uneven enhancement, with osteolytic bone metastasis being the most common.

The images of NUT cancer in the nasal cavity and paranasal sinus are mostly advanced tumor images, and MRI mostly shows lumps with uneven signal, irregular shape, invasive and invasive growth, low signal on T1WI and slightly high signal on T2WI in general, and uneven enhancement, with osteolytic bone metastasis being the most common. PET-CT showed high uptake of fluorodeoxyglucose in mass and metastasis[17].CT, MRI, ultrasound, PET-CT and other radiological examinations are very important for the localization and diagnosis of NUT cancer, clinical staging, evaluation of treatment response and follow-up monitoring. If necessary, endoscopy and other examinations can be selected according to the anatomic site involved.

The diagnosis of NUT cancer is challenging because its clinical manifestations and histopathology are not specific, and it needs to be distinguished from malignant tumors occurring in the sinusoidal region, such as squamous cell carcinoma: The most common, usually in the maxillary sinus, presents as irregular soft tissue mass, invasive growth, obvious bone destruction, and internal heterogeneity when the tumor is large. T2WI mostly shows equal or low signal, and mild or moderate uneven enhancement. Lymphoma: mostly located in the nasal vestibular area, often involving the back of the nose, cheek, eyelid soft tissue; It can cause bone deformation or bone destruction, and the bone destruction is light and limited, and the tumor signal and enhancement are more uniform. Olfactory neuroblastoma: usually occurs in the upper part of the nasal cavity and the top of the ethmoid sinus; There are nasal congestion, reduced sense of smell and other manifestations; When T1 and T2 signal are slightly high and the tumor is large, the density/signal is uneven, accompanied by bone destruction and uneven moderate enhancement. Peripherally cystic lesions may occur when invading brain tissue.Homer-Wright type pseudochrysanthemum cluster or Flexner-Wintersteiner type pseudochrysanthemum cluster was detected by HE staining in the nasal mucosa of the patient, and S100 protein was specifically expressed by immunohistochemical staining.Neuroendocrine carcinoma: MRI shows T1WI and slightly low signal, T2WI and slightly high signal, cystic degeneration and necrosis can be seen in the lesion, peripheral bleeding can be seen, and the enhancement is uneven and enhanced, and calcification can be seen in some masses

on CT, which is prone to bone destruction, and patients often have clinical manifestations of endocrine changes.

There is no clear treatment plan for NUT cancer, which is characterized by short-term remission, rapid recurrence and rapid death. At present, the main treatment methods are surgery, radiotherapy and chemotherapy, and the traditional treatment methods are reported to have poor therapeutic effect.In a study of 124 patients with NUT cancer, the objective response rate to surgery, radiation, and chemotherapy for NUT cancer was 49%[16]. In the absence of surgical resection/radiotherapy and other modes of treatment, it is difficult to rely on chemotherapy alone to achieve a better prognosis[22]. When the NUT cancer focus is limited and no distant metastasis occurs, complete surgical resection should be actively considered, and a better prognosis can be obtained through early surgical intervention and subsequent radiotherapy and chemotherapy[23]. In NUT cancer of the head and neck, some studies suggest that prophylactic neck lymph node dissection should be actively considered even in the absence of lymph node metastasis (N0)[24]. In addition, given the highly aggressive nature of NUT cancer, especially when several anatomic areas are involved, multidisciplinary surgical teams are required to collaborate when necessary; Postoperative radiotherapy for the primary lesion and lymph node area involved should be actively considered, and systemic therapy should be carried out in time[18].

The prognosis of sinus and nasal NUT cancer is generally poor, and the survival of patients is short. This is mainly attributed to the highly aggressive nature of NUT cancer and its resistance to conventional treatments. In the future, with the in-depth research on NUT cancer and the emergence of new treatment methods, we look forward to bringing better treatment results and prognosis for NUT cancer patients.

4. Conclusion

Nuclear protein in testis (NUT) cancer is a rare malignant tumor occurring in the nasal cavity and sinuses, mainly caused by chromosome rearrangement of the NUT gene. NUT cancer is rare and highly invasive, with poor prognosis, and is prone to lymph node and distant metastasis. Its clinical symptoms and imaging findings are non-specific, and the disease is mainly confirmed by pathology.

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