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Diagnostic Pitfalls in Fine-Needle Aspiration Biopsy of Cervical Lymph Nodes: A Case Report of Simultaneous Dual Primary Malignancies in the Head and Neck Regions Missed on Initial Cytological Examination

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Case Report

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Abstract

Background

Synchronous multiple primary malignant tumors of the head and neck are clinically rare, this report describes a case of synchronous dual primary malignancies—papillary thyroid carcinoma and tonsillar squamous cell carcinoma—that were missed due to the inherent limitations of fine-needle aspiration biopsy of cervical lymph nodes.

Case presentation

The patient presented to the Department of Thyroid and Breast Surgery with multiple enlarged cervical lymph nodes as the chief complaint. The patient underwent ultrasound examination and fine-needle aspiration; the aspiration pathology results indicated a mass in the left lobe of the thyroid suspicious for papillary carcinoma, and the right cervical lymph node was considered to contain cells consistent with papillary thyroid carcinoma. Further examinations, including head and neck CT and laryngoscopy, revealed no significant abnormalities; the patient subsequently underwent extended radical thyroidectomy. Postoperative pathology revealed lymph node metastasis in the right Region II consistent with squamous cell carcinoma. A subsequent PET-CT scan ultimately identified a lesion in the tonsils, and a biopsy confirmed squamous tonsillar squamous cell carcinoma.

Conclusions

This article aims to enhance clinicians' ability to diagnose and recognize synchronous multiple primary malignant tumors of the head and neck, avoid misdiagnosis or missed diagnosis resulting from a single-lesion diagnostic mindset, and circumvent diagnostic pitfalls caused by the limitations of imaging techniques.

Background

Multiple primary malignant tumors (MPMT) refer to the occurrence of ≥ 2 histologically independent primary malignant tumors in the same individual, excluding metastases and recurrences; a time interval of ≤ 6 months between the diagnosis of the two primary cancers is defined as synchronous multiple primary malignant tumors(SMPMT), while an interval of > 6 months is defined as metachronous multiple primary malignant tumors. (MMPMT)[1]. Papillary thyroid carcinoma (PTC) is the most common malignant tumor of the thyroid; it is low-grade and slow-growing, with cervical lymph node metastasis being the primary route of spread, and its global incidence is on the rise[2]. The tonsils are the most common site for oropharyngeal squamous cell carcinoma. Tonsillar squamous cell carcinoma (TSCC) is clinically characterized by early lymph node metastasis; approximately 75% of patients present with cervical lymph node metastasis at initial diagnosis. In some cases, cervical lymph node metastasis is the first clinical manifestation, making it extremely prone to being missed[3].

SMPMT of the head and neck is clinically rare; there are fewer than 50 reported cases worldwide of oropharyngeal squamous cell carcinoma (OPSCC) combined with PTC[4], and in most of these cases, OPSCC was diagnosed first, followed by PTC[4–6]. Cases with the reverse diagnostic sequence and a lesion located in the tonsil are extremely rare. This article reports a case of a patient in whom PTC was confirmed by fine-needle aspiration biopsy (FNAB) and who subsequently underwent surgical treatment; postoperative lymph node pathology revealed that the patient also had concurrent TSCC.

Case presentation

Three months ago, a 42-year-old man presented to the Breast and Thyroid Surgery Department of this hospital with a chief complaint of a mass in the right neck that had been present for 12 days. Previously, an ultrasound examination at an external hospital indicated a solid nodule in the left thyroid lobe and an enlarged lymph node in the right neck (Fig. 1). Another hospital FNAB: The mass in the left thyroid lobe was suspicious for papillary carcinoma with a BRAF V600E mutation; the right neck lymph node was considered to contain PTC cells. Past medical history of the patient: Previously in good health; history of alcohol consumption for over 20 years; no history of smoking; no family history of malignant tumors; no other significant findings. Specialized physical examination: The neck is soft; the trachea is midline; both thyroid lobes are of normal size and slightly firm in consistency; no masses were detected in either lobe; an enlarged lymph node measuring approximately 3 × 2 cm is palpable in the right lateral neck region at the angle of the mandible; it is firm in consistency, with indistinct borders, limited mobility, and fixed to the mandible; no clearly enlarged lymph nodes were detected in the left lateral neck.

Further examinations were conducted after the patient’s admission. CT scan of the neck (plain, contrast-enhanced, and 3D reconstruction): A small nodular, slightly hypodense lesion measuring approximately 0.4 cm in diameter was observed in the left lobe of the thyroid; the structural walls of the pharynx and larynx were symmetrical, with no obvious abnormal density shadows; no significant narrowing was observed in the pharyngeal cavity, glottis, or trachea. No significant abnormalities in the morphology or density of the bilateral submandibular and parotid glands were observed. Multiple lymph node shadows were visible on both sides of the neck, with a larger cluster on the right side, measuring approximately 2.0 cm in short axis diameter (Fig. 2). These showed marked enhancement on the contrast-enhanced scan; some lymph nodes exhibited heterogeneous density, with cystic non-enhancing areas visible within them. Laryngoscopy: Both vocal cords appeared smooth with normal mobility. No other significant abnormalities were noted in the preoperative laboratory tests and examinations; therefore, on April 20, 2026, the patient underwent extended radical surgery for left-lobe thyroid cancer (total thyroidectomy + Region VI lymph node dissection + right cervical lymph node dissection) combined with autologous transplantation of the left inferior parathyroid gland.

Postoperative pathology results are as follows (Fig. 3): □ PTC of the left lobe with calcifications, classic type. The tumor maximum diameter was 0.4 cm; it did not invade the thyroid capsule, and no clear nerve invasion was observed. Peripheral nodular lesions of thyroid follicles were present. □ No cancer was detected in the right lobe of the thyroid.□ Metastatic cancer was found in the left recurrent laryngeal

nerve-adjacent lymph node (1 of 1), right Region III lymph node (1 of 3), and right Region VI lymph node (1 of 3); the origin is considered to be the thyroid; No metastatic cancer was found in the left zone VI lymph nodes (1 node), right zone IIA lymph nodes (3 nodes), right zone IV lymph nodes (12 nodes), or right zone V lymph nodes (2 nodes). □ Metastatic carcinoma was found in right zone II lymph nodes (1/1) and right zone IIB lymph nodes (4/4); the tumors were poorly differentiated. Based on HE morphology and immunohistochemical results, the findings are consistent with squamous cell carcinoma, and further clinical investigation is recommended. □ Immunohistochemical results (right Region II lymph node): CK (+), Vimentin (–), TTF1 (–), Tg (–), CK5/6 (+), P40 (+), CD56 (–), Syn (–), CgA (–), Ki-67 (80%). The patient recovered well following thyroid surgery. Discharge diagnosis: □ Stage I PTC of the left lobe, pT1aN1bM0; □ Metastatic carcinoma in the right Region II lymph nodes (squamous cell carcinoma).

After one month, the patient underwent a PET-CT scan at another hospital. The results indicated: absence of the thyroid gland; increased glucose metabolism in the right thyroid region, considered a postoperative change; and enlarged right supraclavicular and presternal lymph nodes, with metastasis ruled out. Elevated glucose metabolism in the right pharyngeal tonsil; biopsy is recommended. The left submandibular lymph nodes showed elevated glucose metabolism, consistent with hyperplasia.

Later, the patient presented to the Department of Otolaryngology at our hospital, and a biopsy of the right tonsillar mass was performed. The pathology results are as follows (Fig. 4): □ Right TSCC (moderate to low differentiation);□ Immunohistochemistry results: CK5/6 (+), P40 (+), P16 (diffuse +), TTF1 (-), Pax-8 (-), Ki-67 (90%+). the following discharge diagnoses: □Stage □ TSCC of the right lobe, cT4aN2M0; □Stage I PTC of the left lobe, pT1aN1bM0.

Finally, the patient presented to the Department of Medical Oncology at our hospital. Based on the patient's current condition, it was recommended to undergo 2–3 cycles of induction chemotherapy, followed by concurrent chemoradiotherapy at a later date after evaluating treatment efficacy. Treatment regimen: albumin-bound paclitaxel 400 mg, cisplatin 40 mg, and tirrelizumab 200 mg.

The patient is currently undergoing treatment.

Discussion

The main reasons for the missed diagnosis of TSCC in the initial diagnosis stage of this patient are its occult manifestations and the strong misleading nature of FNAB. Globally, the incidence of PTC is significantly higher than that of oropharyngeal squamous cell carcinoma[7, 8], and since this patient is a resident of a coastal region, the incidence is even higher there[6]. Consequently, the patient sought care at a breast and thyroid surgery clinic; however, due to diagnostic pitfalls associated with cervical lymph node aspiration, TSCC was missed during the initial diagnosis. In contrast, numerous previous reports have described patients who were initially diagnosed with OPSCC. This discrepancy is attributed to the fact that, apart from multiple enlarged cervical lymph nodes, the patient in this case exhibited no other positive symptoms or signs. Depending on its location, OPSCC can present with different symptoms and

signs. When located in the oral cavity, mucosal lesions may appear in the early stages; when located in the larynx, hoarseness may be present early on. However, for early-stage squamous cell carcinomas located in the tonsils, pharynx, base of the tongue, or supraglottic region, lymph node metastasis may be the sole initial clinical manifestation, making this a type of cancer with a high rate of clinical misdiagnosis. Early-stage PTC often presents with no positive symptoms or signs; positive signs may only appear when the tumor is large or when lymph node enlargement and metastasis are present. Early detection of PTC relies primarily on screening. In this particular case, because the OPSCC was at an early stage and in a concealed location, and the PTC was also at an early stage with a small mass, neither presented with characteristic symptoms or signs. Consequently, TSCC was missed at the initial diagnosis. This case is unique and clinically rare, serving as a cautionary example.

Diagnostic pitfalls typically refer to clinical situations in which misdiagnosis or missed diagnosis may occur despite adherence to standard diagnostic and treatment protocols, due to the inherent limitations of disease characteristics or diagnostic methods. This differs from misdiagnosis or missed diagnosis resulting from physician negligence. After the patient presented with enlarged cervical lymph nodes, the initial consulting physician performed a cytological aspiration; however, the preoperative FNAB only sampled a lymph node metastasized by PTC. Although the presence of a small unilateral thyroid mass causing contralateral multiple lymph node metastases raised the clinician's suspicion, subsequent laryngoscopy and contrast-enhanced CT of the neck failed to detect the patient's occult TSCC until postoperative pathology. The primary reason for this was that the limitations of cytological aspiration led to significant misdirection, which greatly reduced the clinician's vigilance. These limitations are as follows: Cytological aspiration is subject to significant sampling error; when a patient presents with multiple swollen lymph nodes, the procedure often targets one or a few lymph nodes identified by auxiliary tests as having a high likelihood of malignancy for aspiration biopsy; and the cytological pathology results only indicate the pathological nature of the site(s) where the needle was inserted into that one or several lymph nodes. This can lead to the missed diagnosis of metastatic lymph nodes that were not biopsied, thereby causing significant misdirection in clinical diagnosis. This was precisely the case with the patient in question, serving as a warning to clinicians not to blindly rely on FNAB results and extrapolate from a limited sample to the whole. FNAB provides only cellular morphology; it is difficult to preserve complete histological structures, making it impossible to accurately trace the location of the primary tumor. If metastatic lymph nodes are very small, deeply seated, or adjacent to vascular and neural structures in the neck, this can restrict maneuverability during the aspiration procedure, making it difficult to precisely target and obtain tissue samples. In cases of inflammatory lymph node lesions or lymph node tuberculosis, the small amount of cellular tissue obtained via FNAB makes it difficult to distinguish these conditions from lymph nodes affected by malignant tumor metastasis; a definitive diagnosis requires a complete tissue biopsy. The limitations of cytological FNAB remind clinicians that specialists should avoid fixed thinking during diagnosis and treatment. When clinical features cannot be fully explained by a known primary tumor, they should not rely solely on the conclusions of a cytological FNAB. They should remain vigilant for the possibility of multiple concurrent

primary malignant tumors and, when necessary, perform PET-CT to screen for widespread lesions, thereby avoiding diagnostic pitfalls caused by the limitations of the examination technique.

This study has certain limitations. As this is an isolated case, it is not possible to conduct a statistical analysis of the probability of clinical misdiagnosis resulting from the limitations of FNAB. This pathology represents a case of SMPMT of the head and neck, which has a low clinical incidence. Currently, there are no standardized treatment guidelines for such patients. As the patient is still undergoing treatment, long-term follow-up data on prognosis are lacking. Further accumulation of similar cases is needed to explore diagnostic and treatment strategies for this condition.

Conclusion

In summary, this case represents a missed diagnosis of SMPMT of the head and neck at the initial stage due to the inherent limitations of FNAB. Clinicians must fully recognize the limitations of FNAB, be aware of diagnostic pitfalls, move beyond a single-lesion diagnostic mindset, conduct comprehensive evaluations of patients with metastatic cervical lymph nodes, and, when necessary, perform comprehensive systemic imaging screening to avoid misdiagnosis resulting from a single-specialty perspective.

Abbreviations

MPMT：Multiple primary malignant tumors

SMPMT：Synchronous multiple primary malignant tumors

MMPMT: Metachronous multiple primary malignant tumors.

PTC：Papillary thyroid carcinoma

TSCC：Tonsillar squamous cell carcinoma

OPSCC：Oropharyngeal squamous cell carcinoma

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 and any accompanying images. A copy of the written consent is available for review by the editor-in-chief of this journal.

Availability of data and materials

Not applicable.

Competing interests

The authors declare that they have no competing interests.

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Authors' contributions

Wang Kaixuan conducted the literature search and prepared the manuscript. Chen Hongshen, Li Pisong, Qu Hui, Wu Yifan. contributed to the literature search discussion of results, and manuscript preparation. All authors read and approved the final article.

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Figures

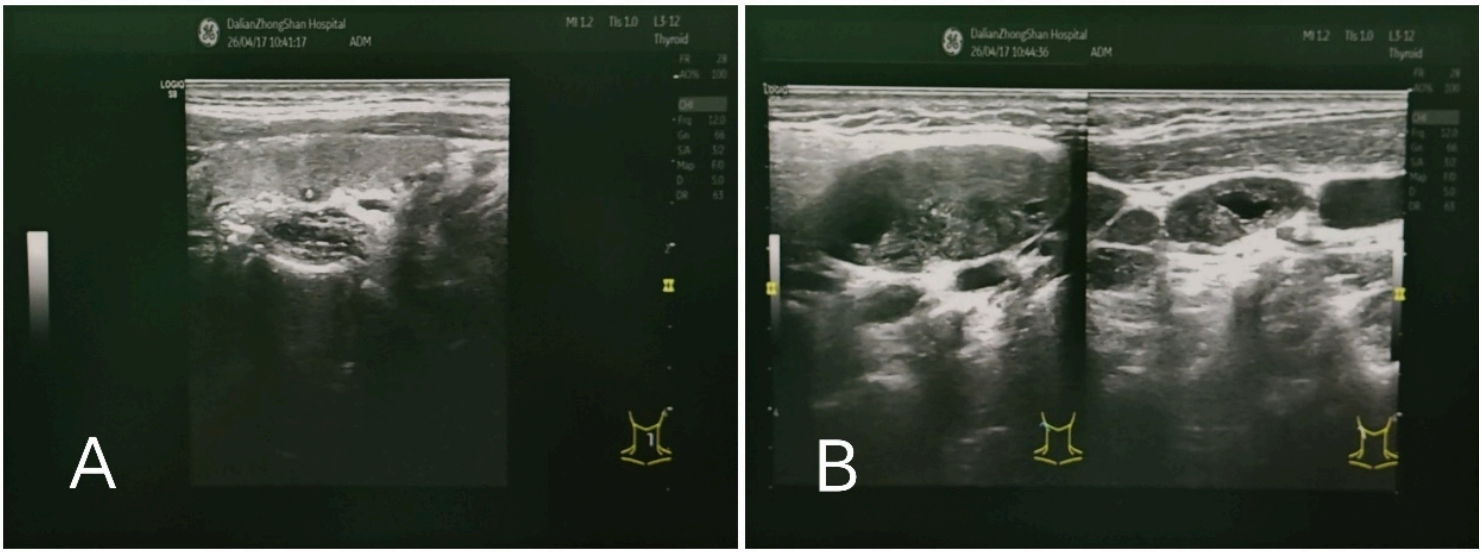


Figure 1

a solid nodule in the left thyroid lobe (A) and an enlarged lymph node in the right neck(B)

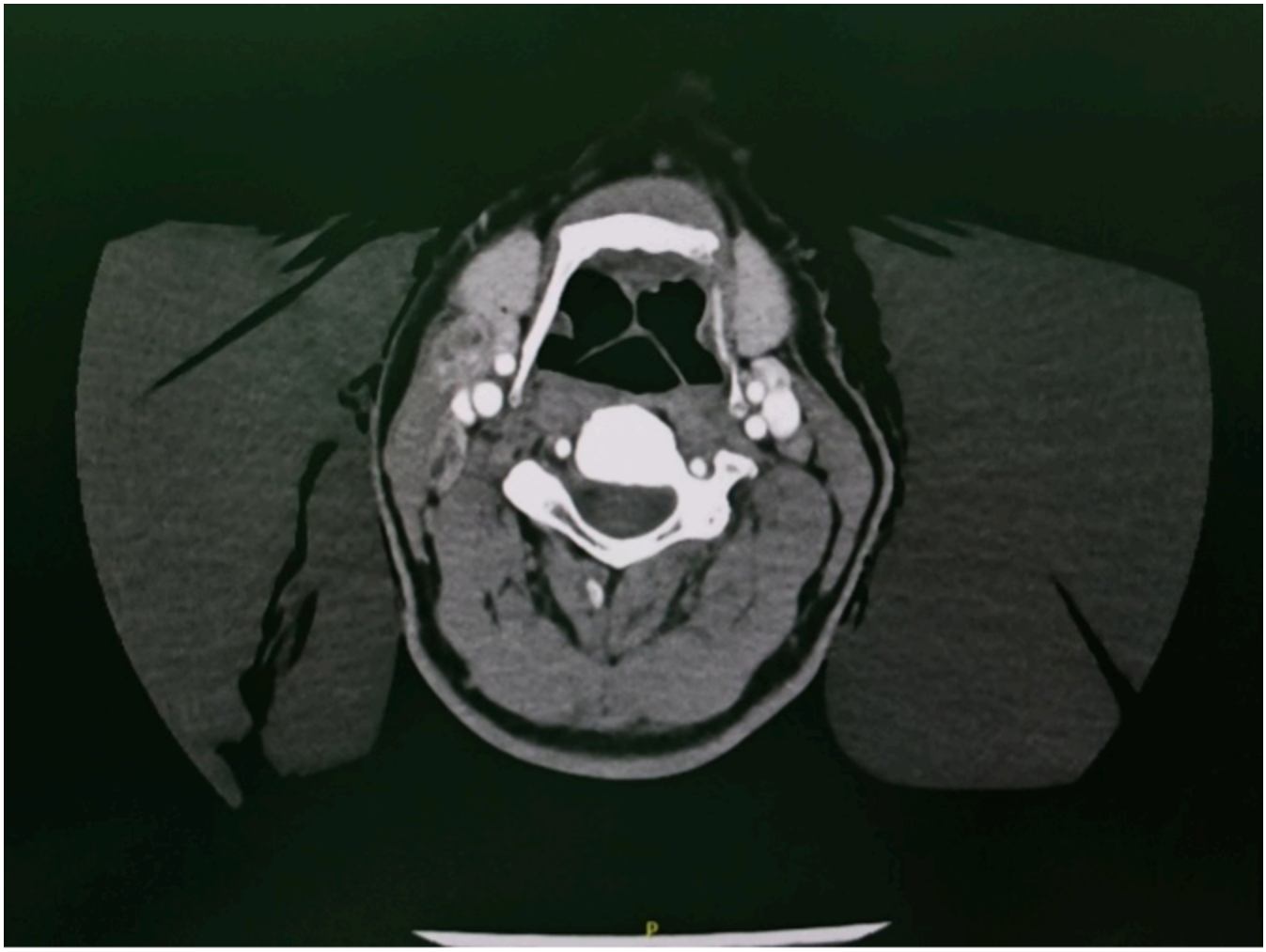


Figure 2

CT scan of the neck

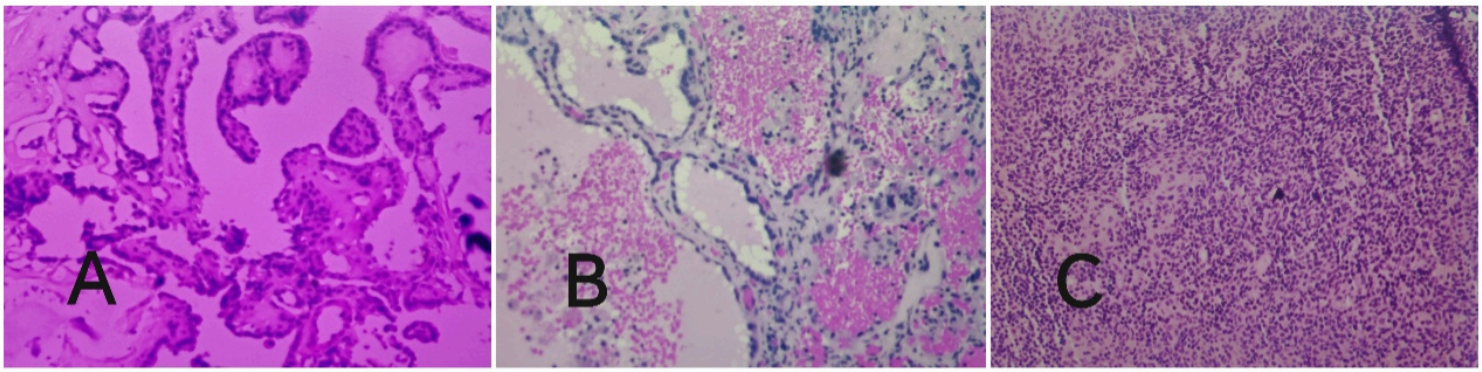


Figure 3

PTC of the left lobe(A), Lymph nodes metastasized by PTC (B) and metastatic carcinoma in right zone II (C)

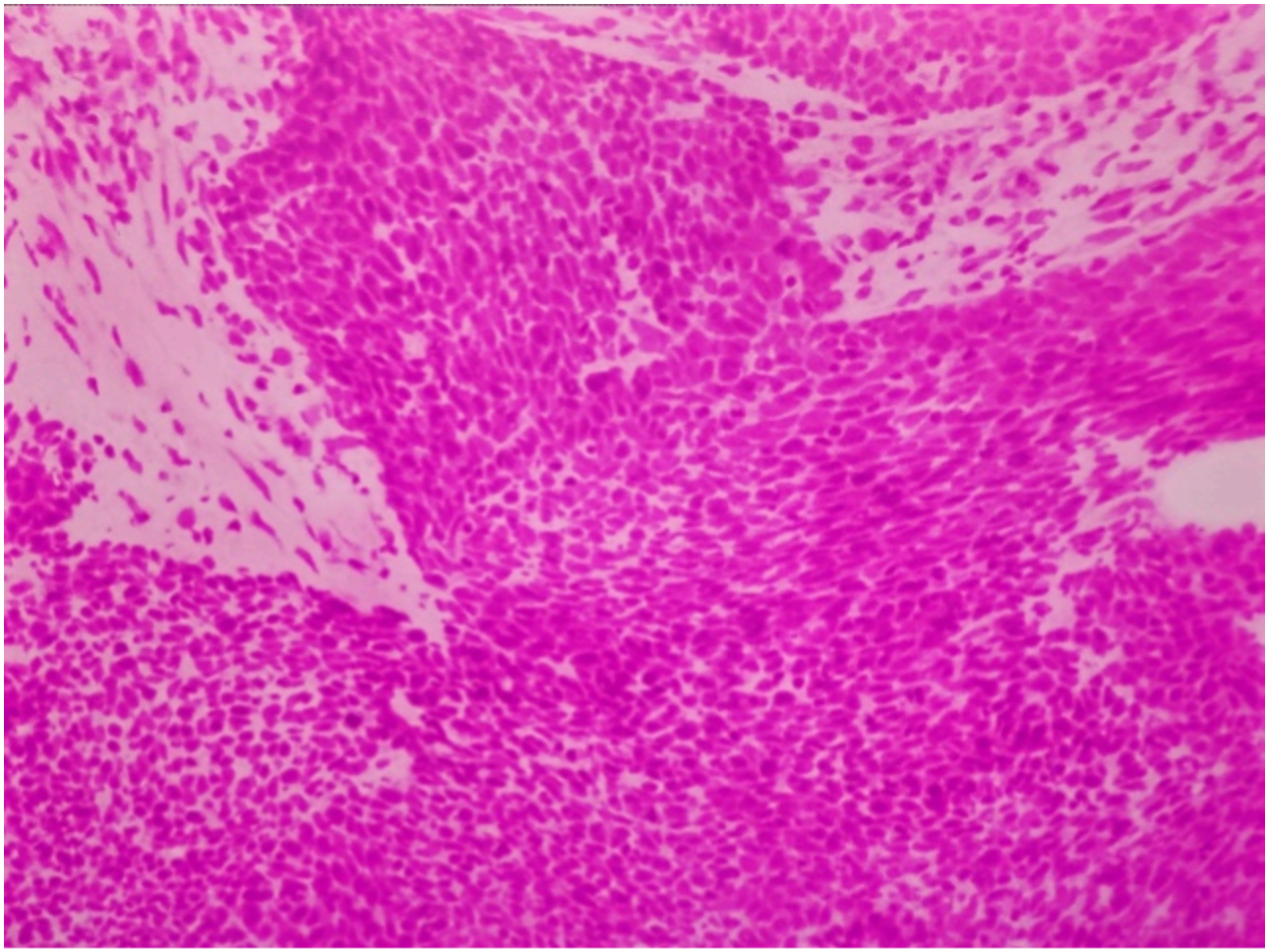


Figure 4

TSCC of the right lobe