

Primary mediastinal yolk sac tumor with pulmonary involvement in a young adult: a case report

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Tumor primario del saco vitelino mediastínico con compromiso pulmonar en un adulto joven

Los tumores del saco vitelino (YST), también conocidos como tumores del seno endodérmico, son neoplasias malignas de células germinales poco frecuentes y muy agresivas que suelen aparecer en las gónadas, pero que también pueden desarrollarse en localizaciones extragonadales de la línea media, como el mediastino anterior. En estas localizaciones atípicas, afectan predominantemente a varones jóvenes y suelen presentar síntomas inespecíficos, como dolor torácico, disnea y fiebre. Los tumores de células germinales mediastínicos representan entre el 10 y el 20% de las neoplasias mediastínicas y se clasifican en subtipos seminomatosos y no seminomatosos, perteneciendo los YST al segundo grupo. Su rápido crecimiento y su naturaleza invasiva suelen impedir la intervención quirúrgica inmediata, lo que requiere un enfoque terapéutico multimodal. Presentamos el caso de un varón de 32 años, previamente sano, que acudió con un cuadro de dos meses de fiebre, dolor precordial irradiado a la extremidad superior izquierda y disnea de esfuerzo. Las pruebas de imagen revelaron una gran masa mediastínica anterior, y la biopsia percutánea con análisis histopatológico e inmunohistoquímico confirmó el diagnóstico de tumor del saco vitelino. El paciente se sometió a cuatro ciclos de quimioterapia neoadyuvante BEP (bleomicina, etopósido, cisplatino), lo que dio lugar a una regresión parcial del tumor y a la identificación de un nódulo pulmonar cavitado. Posteriormente, se sometió a una resección quirúrgica mediante esternotomía media, que incluyó la extirpación de la masa mediastínica, la segmentectomía pulmonar y la timectomía, con márgenes quirúrgicos libres de tumor. El postoperatorio transcurrió sin incidentes y el paciente permanece en remisión bajo seguimiento periódico. Este caso destaca la importancia del diagnóstico precoz, la planificación individualizada del tratamiento y un enfoque multimodal –que combina la quimioterapia y la resección quirúrgica completa– para el tratamiento eficaz de los YST mediastínicos. La vigilancia a largo plazo es esencial para reducir la recurrencia y mejorar el pronóstico general.

Palabras clave: Mediastino; Neoplasias Mediastínicas; Tumores del seno endodérmico; Terapia neoadyuvante; Terapia multimodal.

Abstract

Yolk sac tumors (YSTs), also known as endodermal sinus tumors, are rare and highly aggressive malignant germ cell neoplasms that typically arise in the gonads, but may also develop in extragonadal midline locations, such as the anterior mediastinum. In these atypical sites, they predominantly affect young males and often present with nonspecific symptoms, including chest pain, dyspnea, and fever. Mediastinal germ cell tumors account for 10-20% of mediastinal neoplasms and are classified into seminomatous and non-seminomatous subtypes, with YSTs belonging to the latter group. Their rapid growth and invasive nature frequently preclude immediate surgical intervention, necessitating a multimodal therapeutic approach. We report the case of a 32-year-old previously healthy man presenting with a

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two-month history of fever, precordial pain radiating to the left upper limb, and exertional dyspnea. Imaging revealed a large anterior mediastinal mass, and percutaneous biopsy with histopathological and immunohistochemical analysis confirmed the diagnosis of yolk sac tumor. The patient underwent four cycles of neoadjuvant BEP chemotherapy (bleomycin, etoposide, cisplatin), resulting in partial tumor regression and identification of a cavitated pulmonary nodule. He subsequently underwent surgical resection via median sternotomy, including excision of the mediastinal mass, pulmonary segmentectomy, and thymectomy, with tumor-free surgical margins. The postoperative course was uneventful, and the patient remains in remission under regular follow-up. This case highlights the importance of early diagnosis, individualized treatment planning, and a multimodal approach—combining chemotherapy and complete surgical resection—for effective management of mediastinal YSTs. Long-term surveillance is essential to reduce recurrence and improve overall prognosis.

Keywords: Mediastinum; Mediastinal Neoplasms; Endodermal sinus tumors; Neoadjuvant Therapy; Multimodal therapy.

Introduction

A yolk sac tumour (also known as an endodermal sinus tumour) is a rare malignant germ cell neoplasm that primarily affects the reproductive organs, but can also occur in other midline structures, such as the anterior mediastinum. In these locations, it is more prevalent among young men and tends to present with non-specific symptoms such as chest pain, dyspnoea and fever. Among extragonadal tumours, germ cell tumours (GCTs) located in the mediastinum are particularly significant, accounting for 10-20% of all mediastinal neoplasms. These are divided into two main categories: seminomas and non-seminomas. The latter include subtypes such as yolk sac tumours, choriocarcinoma, embryonal carcinoma and mixed germ cell tumours. These neoplasms exhibit aggressive behaviour and a high potential for malignancy, attributed to the accelerated growth of germ cells. Therefore, resection is often not possible at the time of diagnosis. This study presents a case of primary yolk sac tumour in the mediastinum, which is a rare and highly aggressive form of GCT¹.

Case description

The patient was a 32-year-old male who was previously healthy and had no relevant personal or family history of illness, including previous surgeries, smoking, alcoholism, or neoplasms. Approximately two months prior to hospital admission, he began experiencing a fever and precordial pain radiating to his left upper limb. This was associated with exertional dyspnoea and led him to seek care at the emergency department. Initial evaluation included an electrocardiogram (ECG), which showed no significant changes, and

measurement of cardiac enzyme levels, which were within normal limits. A chest X-ray showed an enlarged heart (Figure 1), leading to a referral to the regional cardiology service for diagnostic clarification and a transthoracic echocardiogram. The echocardiogram revealed an ejection fraction (EF) of 56%, normal cardiac cavity dimensions and systolic function, and grade II diastolic dysfunction with normal valves. Moderate pericardial effusion was also observed, with signs of restriction of right ventricular filling, as well as elevated pulmonary venocapillary and pulmonary arterial pressures. Notably, the presence of a large mediastinal mass juxtaposed to the pericardium was also observed.



Figure 1. Chest X-ray (posterior-anterior). Image showing a marked enlargement of the cardiac silhouette.

In this regard, a contrast-enhanced chest computed tomography (CT) scan was performed, revealing a heterogeneous, expansive formation with lobulated contours centred in the upper portion of the anterior mediastinum, measuring $12.5 \times 10.5 \times 7.2$ cm. (Figure 2).

The lesion had solid components that were enhanced by the contrast medium, as well as hypoattenuating areas that were suggestive of necrosis or liquefaction. Compression of the innominate vein was observed, with circumferential contact of more than 180 degrees and contact with the superior vena cava, ascending aorta and pulmonary artery trunk, all involving less than 180 degrees. There were no unequivocal signs of

vascular invasion. The mass also had extensive contact with the anterosuperior pericardium. A small pericardial effusion and a mild pleural effusion were present on the left, neither of which had any detectable solid components. The trachea, carina and main bronchi were patent. No mediastinal or hilar lymphadenopathy was identified, but calcified lymph nodes were present in the lower right paratracheal region, consistent with a fibrotic process. Atelectatic opacities were also observed in the lower left lobe, underlying the pleural effusion. In addition, a solid pulmonary nodule of non-specific appearance measuring 1.1 cm was in the posterior apical segment of the upper left lobe (Figure 3).

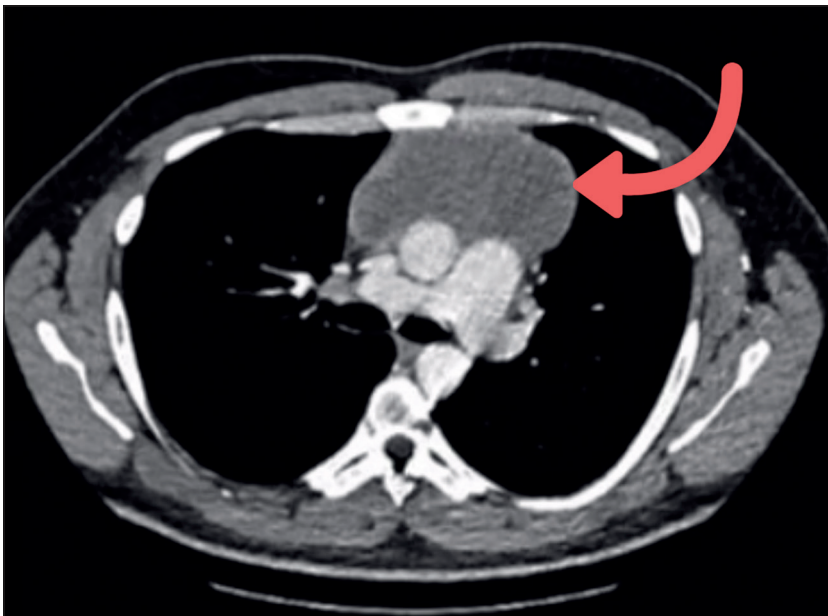


Figure 2. Contrast-enhanced computed tomography (CT) scan of the chest (axial view). The image displays an expansive, heterogeneous formation (illustrated by the arrow) located in the upper anterior mediastinum. The mass exhibited lobulated contours, with its dimensions measuring $12.5 \times 10.5 \times 7.2$ cm prior to treatment.



Figure 3. Pulmonary nodule in the posterior apical segment of the left upper lobe. Computed tomography (CT) image of the chest, axial section, showing a solid nodule of nonspecific appearance measuring 1.1 cm (arrow) in the posterior apical segment of the left upper lobe.

In consideration of these findings, a percutaneous biopsy of the mediastinal lesion was performed, and the tissue sample was sent for histopathological analysis. Initial analysis revealed a proliferation of neoplastic cells with large, pleomorphic and hyperchromatic nuclei, which is consistent with a diagnosis of malignant germ cell neoplasia. The main diagnostic hypotheses raised were embryonal carcinoma and endodermal sinus tumour. The case was discussed with the oncology team, who recommended measuring tumour markers, including beta-hCG (negative) and alpha-fetoprotein (0.0 ng/ml). Due to the non-specific morphology, the tissue sample was submitted for immunohistochemical analysis.

After one week, immunohistochemistry showed positivity for AE1/AE3, SALL4, glypican-3 and alpha-fetoprotein, suggesting germ cell differentiation, albeit non-specific (Figure 4). The markers CD30, OCT4, PLAP and CD117 were negative. The cell proliferation index, as determined by Ki-67, was estimated to be 30%. Correlating the immunohistochemical findings

with the clinical context enabled us to diagnose an endodermal sinus tumour (yolk sac tumour).

A contrast-enhanced magnetic resonance imaging (MRI) scan of the chest was subsequently performed to confirm the presence of a large mediastinal lesion and a nodule at the apex of the left lung, which suggested a possible secondary implant.

The case was discussed at a multidisciplinary meeting involving the pulmonology, oncology, radiotherapy and thoracic surgery teams to determine the course of action, and it was decided that the patient would undergo neoadjuvant treatment. The patient underwent four cycles of neoadjuvant chemotherapy with the BEP regimen (bleomycin, etoposide and cisplatin), followed by a PET/CT scan to reassess the situation.

A new contrast-enhanced chest CT scan was requested after three cycles of chemotherapy to reassess the response to treatment. This revealed a reduction in the mediastinal mass to $10.0 \times 9.5 \times 6.0$ cm. Additionally, a cavitated pulmonary nodule measuring 1.2×1.0 cm was identified in

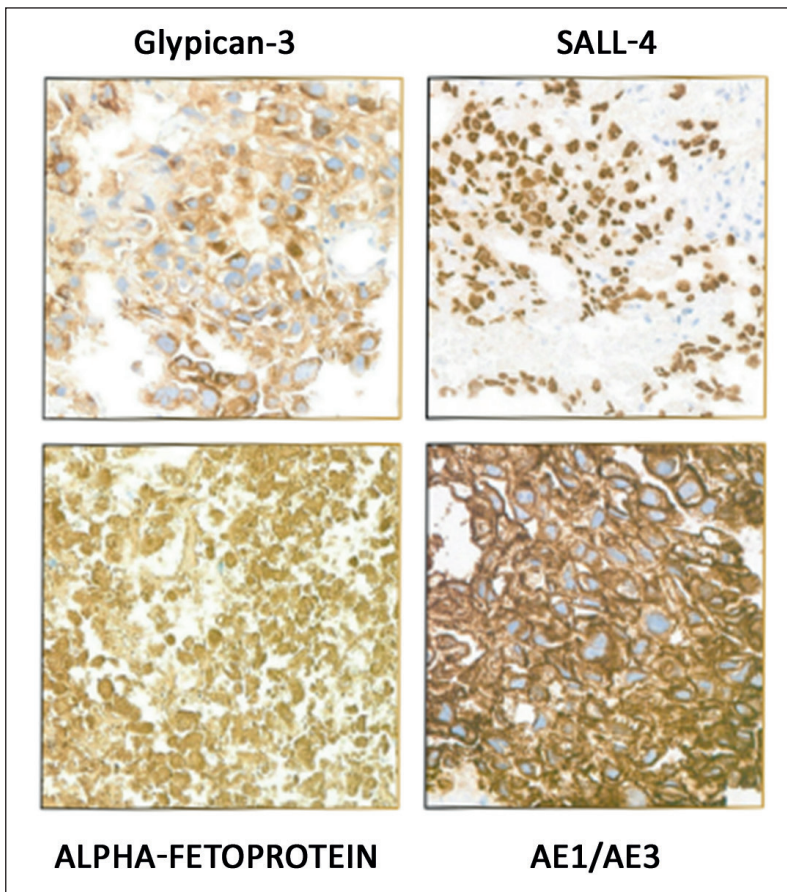


Figure 4. Immunohistochemical profile of mediastinal yolk sac tumour. The panel demonstrates notable immunoreactivity to germ cell lineage markers with embryonic differentiation (staining: DAB, counterstaining: hematoxylin). (A) Glypican-3 (strong cytoplasmic expression); (B) SALL4 (strong nuclear expression); (C) Alpha-Fetoprotein (AFP) (strong cytoplasmic expression); (D) AE1/AE3 (cytokeratin).

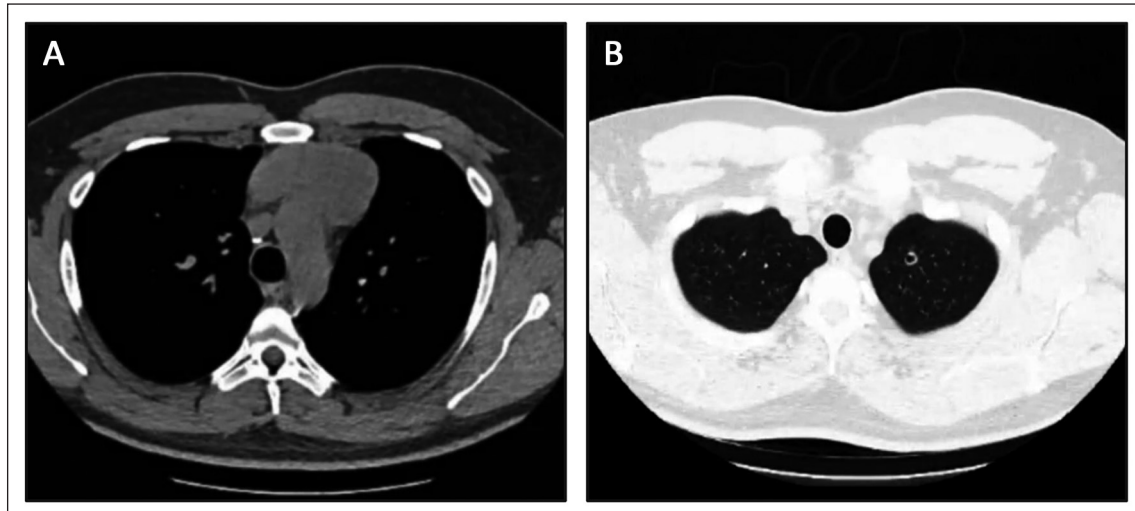


Figure 5. The following image depicts post-chemotherapy chest computed tomography (CT). (A) Axial slice showing volumetric reduction of the anterior mediastinal mass, measuring 8.3 x 4.9 cm. (B) Slice illustrating the presence of a cavitated pulmonary nodule in the upper left lobe, with dimensions measuring 0.9 x 0.9 cm.

the apicoposterior segment of the left upper lobe. A subsequent CT scan, performed before the surgical procedure and after completion of the four cycles of chemotherapy, showed a further reduction in the size of the mediastinal mass to 8.3 × 4.9 cm, as well as a decrease in size of the pulmonary nodule to 0.9 × 0.9 cm (Figure 5).

Due to the regression of the neoplastic lesion, a surgical approach was taken via median sternotomy. This involved the resection of the mediastinal mass, pulmonary segmentectomy and thymectomy, with clear surgical margins achieved. During the procedure, a tumour was observed in the mediastinum with firm adhesions to the chest wall, pericardium, thymus and pericardial fat, as well as close contact with the left phrenic nerve and left mammary vessels. Tumour thrombosis of the left innominate vein was identified and resected, then sutured. Pulmonary segmentectomy involved the resection of a hollow nodule at the apex of the left upper lobe, with findings consistent with predominantly necrotic metastatic neoplasia. Partial pericardiectomy was performed while preserving the cardiac structures and with careful dissection of the phrenic nerve. Ligation of the left thoracic duct was necessary due to the presence of chyle discharge. Titanium clips were applied to control haemostasis in the resected regions. The postoperative period was uneventful, and the patient has undergone continuous outpatient follow-up. There has been no recurrence of the disease to date (Figure 6).

The resected nodule from the pulmonary seg-

mentectomy was sent for intraoperative frozen section, which demonstrated a fibrotic nodule with old hemorrhage. The final anatomopathological analysis on paraffin sections confirmed extensive morphological changes in the pulmonary segment, including areas of diffuse necrosis



Figure 6. Surgical specimen obtained during resection of a mediastinal tumor on January 31, 2025, including the left upper lobe segment with stapled margin, distal vascular margin, and proximal vascular margin. (The size of the scalpel placed as a length reference is 15 cm).

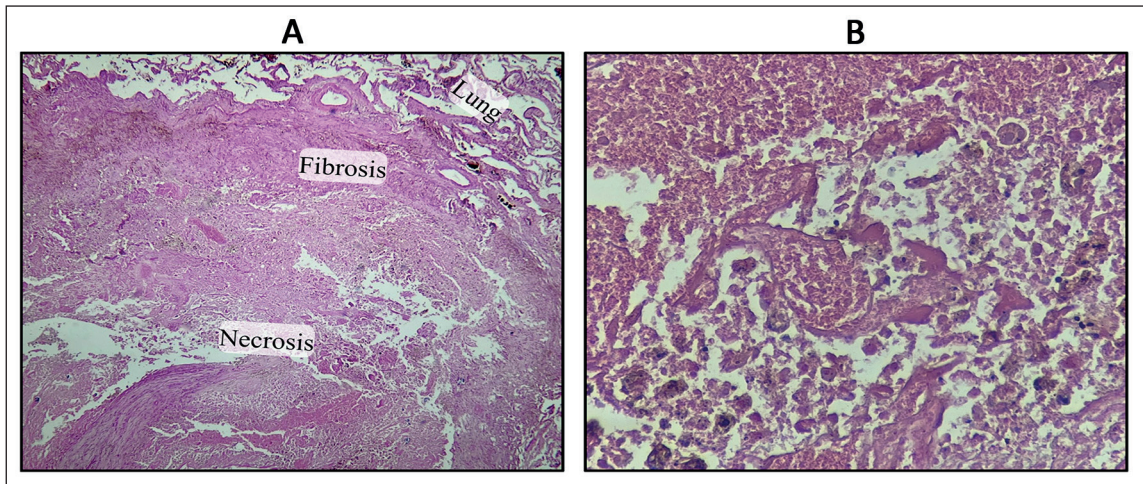


Figure 7. Histopathological findings from left lung segmentectomy. The micrograph (HE) displays a pattern of complete tumour regression, characterized by (A) extensive fibrosis, diffuse necrosis, and (B) subpleural fibrosis in the lung segment. The examination confirms the absence of viable tumour cells, documenting a Complete Pathological Response (pCR) after neoadjuvant therapy.

and fibrosis, subpleural fibrosis, and a fibrotic nodule with old hemorrhage (Figure 7). Crucially, the analysis showed the absence of viable tumor cells (HE stain) in the specimen, thus supporting a complete pathological response to the neoadjuvant therapy.

During follow-up, additional tests were performed for staging and monitoring clinical evolution. Initially, a total abdominal CT scan showed no significant changes. A transthoracic echocardiogram revealed normal cardiac chambers, but with moderate pericardial effusion associated with slight collapse of the atria and the free wall of the right ventricle, as well as signs of pulmonary arterial hypertension. Additionally, scrotal ultrasound revealed bilateral hydrocele with no evidence of testicular masses. During treatment, tumour markers were monitored and a significant initial elevation of alpha-fetoprotein (AFP) was observed, with a progressive reduction after the chemotherapy sessions. Beta-hCG remained mostly undetectable or at low levels, with transient variations that were not clinically significant.

Discussion

Yolk sac tumours (YSTs) in the mediastinum are rare, aggressive and highly malignant. While they are more prevalent in the gonads, they can also develop in extraembryonic locations such as the mediastinum, sacrococcygeal region, retroperitoneum, brain, and pelvis, with a tendency to affect the midline of the body².

Of extraembryonic origins, 10-15% are found in the mediastinum, retroperitoneum and sacrococcygeal regions of the midline. YST is one of the histological subtypes of germ cell tumours in the mediastinum. It occurs mainly in young men and has an incidence of 12% in children (aged 0-14 years) and 73.5% in adolescents and young adults (aged 15-39 years). These tumours are classified into two main categories: seminomatous and non-seminomatous. Non-seminomatous tumours are subdivided into yolk sac tumours, choriocarcinoma, embryonal carcinoma, and mixed germ cell tumours³.

This tumour is named after the yolk sac, a membrane responsible for nourishing the embryo in the early stages of development, due to its histological similarity to it. Composed of primordial germ cells, the precursors of oocytes and spermatozoa, their pathogenesis is not yet fully understood, although a link to abnormalities in the development of these cells has been suggested⁴. Germ cell tumours are believed to originate from primitive cells. When they occur in normally positioned gonads, they arise from germ cells that have migrated from the yolk sac to their final location in the pelvis or scrotum. Extragenital manifestations, for example in the pineal region or anterior mediastinum, may result from the abnormal migration of these cells⁵.

Depending on their location and extent, these tumours present with varied symptoms, ranging from abnormal bleeding to compressive symptoms such as back pain or difficulty breathing⁶. Associated risk factors include a history of

cryptorchidism and genetic syndromes such as Klinefelter's and Turner's syndromes⁷.

A diagnosis of yolk sac tumours requires a clinical evaluation, imaging tests, laboratory tests and a histopathological examination. The investigation begins with taking a medical history and conducting a full physical examination to check for palpable lumps, swollen lymph nodes or other symptoms that could suggest a tumour.

The most used imaging tests are ultrasound, computed tomography (CT) and magnetic resonance imaging (MRI), with the latter being particularly useful for accurately assessing the location and extent of involvement of adjacent structures. On CT and MRI scans, yolk sac tumours typically present as large, solid, and cystic masses with contrast enhancement and intratumoral haemorrhage⁴.

In addition to imaging tests, laboratory tests are also important. Yolk sac tumours often produce specific tumour markers that can be detected in the bloodstream; the most relevant of these is alpha-fetoprotein (AFP). Although the patient in question does not present this finding, elevated AFP levels indicate the presence of this type of tumour. Therefore, blood tests that assess AFP concentration are widely used for diagnosis, monitoring treatment response, and detecting early recurrence⁴.

A biopsy is performed for diagnostic confirmation. Histological analysis reveals structures like the yolk sac or other specific cellular components, with cuboidal, polygonal or columnar epithelium organized in groups or rows. Combinations of epithelium and stroma are also present, and these are key characteristics for recognition of the cancer².

Regarding prognosis, analysis of the SEER (Surveillance, Epidemiology, and End Results) database showed that the cancer-specific survival rate (CSS) for patients with mediastinal YST was 70% after 3 years and 56.5% after 5 years⁸.

If left untreated, yolk sac tumours can be fatal or cause serious damage. Depending on the tumour's characteristics and stage, treatment generally involves a combination of surgery, chemotherapy and radiation therapy. In cases where the tumour is localized and has not spread, surgery alone may be curative. However, additional therapies may be necessary if the tumour has spread or if there is a risk of residual disease⁴.

The current standard treatment for non-seminomatous germ cell tumours is based on a combination of chemotherapy and surgical excision of residual mass after systemic treatment, a strategy that has proven essential for achieving prolonged

survival⁹. In this context, Walsh et al. analyzed a series of 20 cases of non-seminomatous germ cell tumours between 1993 and 1998, nine of which corresponded to primary mediastinal yolk sac tumours. All patients received chemotherapy, followed by radical resection of the residual mass, achieving an overall survival rate of 58% in two years¹⁰.

The extant publications indicates that long-term survival is influenced by three main variables: the level of alpha-fetoprotein after preoperative chemotherapy; the pathological status of the residual mass; and the presence of lung metastases¹¹. Nevertheless, complete resection after chemotherapy represents a significant technical challenge, necessitating a high level of surgical expertise. This is because these tumours frequently exhibit dense fibrotic adhesions to vital structures, such as the pericardium and large vessels, thereby significantly hindering safe dissection⁹.

The surgical approach involved a median sternotomy, a lateral thoracotomy and a semi-muscle incision. The specific procedure depended on the tumour's location, size and extent, as well as the patient's underlying condition. Extended excision may be more beneficial for patients whose tumours have invaded surrounding tissues and/or organs, such as the lung and pericardium. The long-term survival rate is significantly better for patients who undergo surgery than for those who undergo chemotherapy and radiotherapy, especially for those who undergo radical resection².

Chemotherapy and radiotherapy are recommended as adjuvant treatments following surgery and for unresectable tumours. Chemotherapy is an essential component of yolk sac tumour treatment and is usually administered before and after surgery. Current chemotherapy regimens for YST involve BEP, VIP (etoposide, ifosfamide and cisplatin) and EP (etoposide and cisplatin), which can be used alone or in combination. Radiotherapy may also be indicated, particularly if the patient has residual disease after surgery or if the tumour has spread to areas that are difficult to treat⁴.

In addition to these considerations, close monitoring of patients with primary yolk sac tumours is imperative, with particular attention given to pertinent clinical associations. Mediastinal non-seminomatous germ cell tumours have been observed to be associated with Klinefelter syndrome¹² and with the frequent development of haematological neoplasms, especially myelodysplastic syndromes and acute leukemias¹³. This particularity has not been observed in gonadal tumours, thereby reinforcing the importance of

rigorous surveillance for the early identification of such complications.

Conclusion

Yolk sac tumours are rare, but early diagnosis and treatment are essential as they can progress aggressively if not treated properly. The case in question highlights the importance of early diagnosis and multimodal treatment, combining resection surgery, chemotherapy and, in some cases, radiotherapy, to optimize clinical outcomes. The literature shows that platinum-based chemotherapy combined with agents such as etoposide and bleomycin is fundamental to treating the disease, particularly mediastinal tumours. Therefore, the rapid identification of the most appropriate therapeutic strategy can significantly impact patient survival and quality of life. This highlights the importance of rigorous clinical follow-up to minimize the risk of recurrence and improve prognosis.

References

- SILVA LLCD, VERGILIO FS, YAMAGUTI DCC, CRUZ IAND, QUEEN JAG. Yolk sac primary tumor of mediastino: a rare case in a young adult. *Einstein (Sao Paulo)*. 2017 Oct-Dec;15(4):496-9. doi: 10.1590/S1679-45082017RC4008.
- RAVISHANKAR S, MALPICA A, RAMALINGAM P, EUSCHER ED. Yolk sac tumor in extragonadal pelvic sites: still a diagnostic challenge. *Am J Surg Pathol*. 2017;41(1):1-11. doi: 10.1097/PAS.0000000000000722
- MICHEL M, PRATT JW. Anterior mediastinal nonseminomatous germ cell tumor with malignant transformation: a case report. *Curr Surg*. 2004;61(6):576-9. doi: 10.1016/j.cursur.2004.05.021
- PAUL P, KUNDU P, KUMAR MITRA P, GUPTA S., FRANCIS PS. Advances in diagnosis, treatment, and prognosis of yolk sac tumors: a comprehensive review. *Int J Sci Health Res*. 2023;8(2):456-62. doi: 10.52403/ijshr.20230258
- KATTUOA ML, DUNTON CJ. Yolk sac tumors. In: *StatPearls* [Internet]. Treasure Island (FL): StatPearls Publishing; 2023 [cited 2025 Oct 1]. Available from: <https://www.ncbi.nlm.nih.gov/books/NBK563163/>
- ROTH L, PANGANIBAN W. Gonadal and extragonadal yolk sac carcinomas: a clinicopathologic study of 14 cases. *Cancer*. 1976;37(2):812-21. doi: 10.1002/1097-0142(197602)37:2<812:AID-CNCR2820370229>3.0.CO;2-J
- BOKEMEYER C, NICHOLS CR, DROZ JP, SCHMOLL HJ, HORWICH A, GERL A, et al. Extragonadal germ cell tumors of the mediastinum and retroperitoneum: results from an international analysis. *J Clin Oncol*. 2002;20(7):1864-73. doi: 10.1200/JCO.2002.07.062
- GENG R, ZHENG Z, LIN Y, LI Y, GE G, ZHANG J, et al. Clinical characteristics and prognostic factors of male yolk sac tumor: a Surveillance, Epidemiology, and End Results program study. *World J Urol*. 2021;39(4):1211-7. doi: 10.1007/s00345-020-03311-y
- LIU B, LIN G, LIU J, LIU H, SHANG X, LI J. Primary mediastinal yolk sac tumor treated with platinum-based chemotherapy and extended resection. *Thoracic Cancer*. 2018;9(4):491-4. doi: 10.1111/1759-7714.12591
- WALSH GL, TAYLOR GD, NESBITT JC, AMATO RJ. Intensive chemotherapy and radical resections for primary nonseminomatous mediastinal germ cell tumors. *Ann Thorac Surg*. 2000;69(2):337-43; discussion 343-4. doi: 10.1016/S0003-4975(99)01472-1
- KESLER KA, RIEGER KM, GANJOO KN, SHARMA M, FINEBERG NS, EINHORN LH, et al. Primary mediastinal nonseminomatous germ cell tumors: the influence of postchemotherapy pathology on long-term survival after surgery. *J Thorac Cardiovasc Surg*. 1999;118(4):692-700.
- HASLE H, MELLEMGAAARD A, NIELSEN J, HANSEN J. Cancer incidence in men with Klinefelter syndrome. *Br J Cancer*. 1995;71:416-20. doi: 10.1038/bjc.1995.85
- HARTMANN JT, NICHOLS CR, DROZ JP, HORWICH A, GERL A, FOSSA SD, et al. Hematologic disorders associated with primary mediastinal nonseminomatous germ-cell tumours. *J Natl Cancer Inst*. 2000;92(1):54-61. doi: 10.1093/jnci/92.1.54

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