Comprehensive Treatment of a Rare Primary Mediastinal Yolk SAC Tumour with Immature Teratoma

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ABSTRACT

Primary anterior mediastinal yolk SAC tumours are rare but fatal, and primary mediastinal endodermal sinus tumours with immature teratomas are even rarer. This article reports a 31-year man with a yolk SAC tumour with an immature teratoma who was admitted to the hospital for repeated chest pain for more than 3 months. The patient was admitted with a serum alpha-fetoprotein (AFP) level of 3000 ng/mL (reference value: 0-9 ng/mL). Computed tomography (CT) of the chest revealed a solid mass in the left anterior mediastinal area, left lung inflammation, and a small amount of effusion in the left pleural cavity. CT-guided biopsy for diagnosis indicated endodermal sinus tumour. On September 12, 2018, the tumour was resected by a median anterior thoracotomy under general anaesthesia. Left upper lobectomy, partial pericardial resection, pericardial repair, and bilateral closed chest drainage were performed. Postoperative pathological results revealed germ cell-derived malignant tumour, consisting of 70% endodermal sinus tumour, and 30% immature teratoma. Next-generation sequencing of tissue specimens after surgery revealed DDR2, exon 5, c.286T> G, p.F96V, and a mutation abundance of 49.58%; PDL1 testing of tissue specimens showed a low expression level (<1%). The patient was treated with carboplatin plus docetaxel for four cycles. A re-examination on February 26, 2019, of the chest CT revealed a new anterior mediastinal mass, suggesting recurrence of the tumour after surgery and metastasis to the left posterior pleura. The patient died of recurrence and metastasis in August 2019.

Key Words: *Yolk SAC tumour*, *Teratoma*, *Immature*, *Gene mutation*.

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INTRODUCTION

Primary mediastinal germ cell tumours (GCTs) are classified into seminomatous and non-seminomatous GCTs based on histological analysis. The mediastinum is the most common site of primary GCTs outside the gonads. In 2002, Govender and Pillay reported a case of an endodermal sinus tumour with an immature teratoma. Mediastinal immature teratomas with yolk SAC tumours and granulocytic leukaemia are related to Klinefelter syndrome.[1] The most common teratomas are in the gonads (testis and ovary), and only 10-15% occur in the extragonadal region.[2] Due to the abnormal migration of germ cells along the urogenital ridge during embryogenesis, endoderm sinus tumours can be found in the midline, pineal gland, anterior mediastinum, and posterior abdominal wall. Primary mediastinal endodermal sinus tumours are rare and highly malignant because of their rapid growth and early metastasis to the lungs, brain, liver, and bone.

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The patient's long-term survival rate and the prognosis are poor.[3] The disease almost always occurs in young men between the ages of 14 and 35 years.[4] The onset is insidious and asymptomatic at the early stage. Tumour invasion and compression of related organs can cause symptoms such as chest pain, cough, dyspnoea, and haemoptysis. Primary mediastinal endodermal sinus tumours with immature teratomas are even rarer.[5] The following report describes the diagnosis and treatment of one patient with a primary mediastinal endodermal sinus tumour associated with immature teratoma.

CASE REPORT

A 31-year male patient was admitted to the hospital on August 27, 2018, because of repeated chest pain for more than 3 months. The patient was married with one child. The patient had no cough, sputum, chills, fever, or drooping eyelids.

The admission examination results were as follows: Temperature, 36.6°C; pulse, 89 beats/minute; respiration, 20 breaths/minute; and blood pressure, 122/75 mmHg. A skull examination revealed no abnormalities; the neck was soft; and the trachea was centred. Physical examination of the thyroid, thorax, heart, lungs, and abdomen revealed no abnormalities. No local swelling or depression was detected. The results of routine blood examination were as follows: White blood cells, 15.32×10^9/L; and the neutrophils percentage was 83.6%. Blood biochemistry revealed a potassium level of 3.2 mmol/L. Liver

function indicators were as follows: Glutamic-pyruvic transaminase, 81.4 U/L; total bilirubin, 17.3 μmol/L; glutamic oxaloacetic transaminase, 83.6 U/L; and normal renal function. Serum alpha-fetoprotein (AFP) was 3000 ng/mL (Reference value: 0-9 ng/mL), while Carcinoembryonic antigen (CEA) and carbohydrate antigen 199 (CA199) levels were normal. The electrocardiogram (ECG) was normal. No abnormalities were found in other examinations. The patient had no other medical history.

CT chest showed a solid mass in the left anterior mediastinum, suggesting the possibility of a thymoma and small mediastinal lymph nodes, inflammation of the left lung, and a small amount of fluid in the left pleural cavity. Limited emphysema was also observed in the right upper apex. The CT scan of the abdomen revealed no obvious abnormalities (Figure 1).

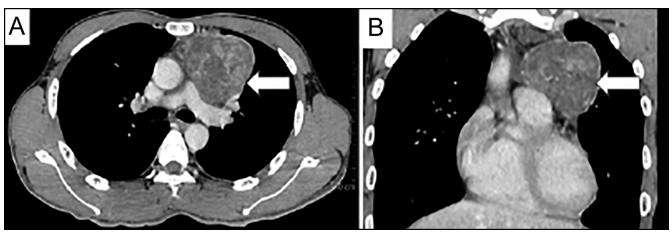

Figure 1: (A, B) Computed tomography scan confirming a solid tumour in the left anterior mediastinum (arrow).

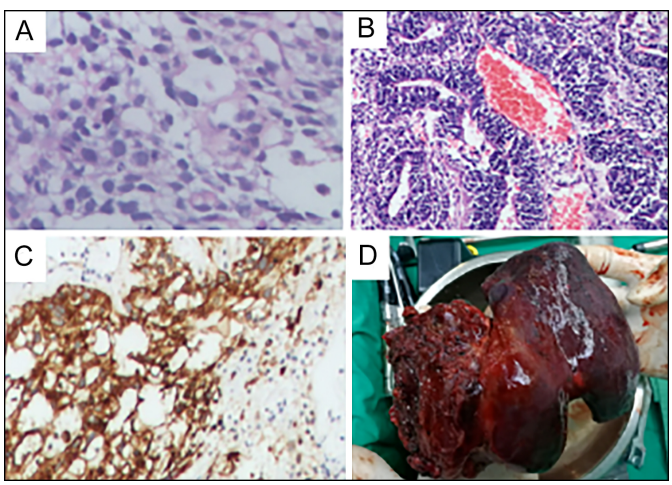

Figure 2: Histological and immunochemical staining of the tumour tissue. (A) Haematoxylin and eosin-stained tumour cells. The tumour cells are diffusely arranged in a loose microcystic structure, and the nucleus of tumour cell was deeply stained (components of the yolk SAC). (B) The tumour contains primitive neuroepithelial tissue (immature teratoma component). (C) Immunohistochemical staining of the tumour tissue showed positive expression of glypican-3 protein. (D) Gross specimen after surgical excision (100 mm × 80 mm).

A CT-guided biopsy was performed to confirm the diagnosis. Anterior mediastinal mass revealed germ cell-derived malignant tumour, comprising endodermal sinus tumour mixed with immature teratoma. The immunohistochemistry results were as follows: Vimentin (+), cytokeratin (+), α-inhibin (-), glypican 3 (+), placental alkaline phosphatase (-), CD117 (+), CD30 (-), Ki67 (50% +), CEA (-), AFP (+), SALL4 (+), and CK19 (+). On September 12, 2018, median anterior thoracotomy was performed to resect the tumour mass + left upper lung lobe under general anaesthesia. In addition, partial pericardial resection, pericardial repair, and bilateral closed thoracic drainage were performed. During surgery, the patient was placed in the supine position, a chest pad was added, and the field was disinfected. A midline incision of the sternum approximately 20 cm long was made, and the tumour was located on the left side of the anterior superior mediastinum. The tumour was approximately 10 × 8 × 7 cm in size. Most of the tumour was solid, but a small part was cystic, and the capsule was incomplete. The mass was tightly adherent to the back of the sternum, the innominate vein, part of the pericardium, the aorta, the left pulmonary artery, the upper-left lobe, and the upper pulmonary arteriovenous structures. The left upper lung surrounded by the tumour could not be separated. The involved pericardium and the tumour were removed together. The amount of bleeding was approximately 100 ml. Postoperative pathological examination revealed a mixed germ cell tumour (70% endodermal sinus tumour and 30% immature teratoma) (Figure 2). The process was smooth, and the postoperative recovery was good. He was discharged on September 26, 2018. From October 14, 2018 to December 27, 2018, docetaxel + carboplatin chemotherapy was carried out for four cycles. The AFP level decreased from >3000 ng/ml to 173 ng /ml. On February 26, 2019, the AFP level rose to 452.36 ng/ml. A chest CT revealed a new mass in the right anterior mediastinum. Recurrence and left posterior pleural metastasis were considered. In August 2019, the patient died of recurrence and metastasis.

DISCUSSION

The mediastinum is the most common anatomic site for extragonadal GCTs, accounting for 3 to 4% of all GCTs in children and adults.[5] At present, the histogenesis of extragonadal yolk SAC tumours is unclear. Three hypotheses have been proposed: Derived from abnormal somatic cell differentiation; derived from migratory germ cells during embryogenesis (weeks 4-6), in which primitive genitalia mistakenly shift from the pelvic cavity to the gonad, germ cells located outside the gonad, and malignant transformation occurs; and metastasis originating from the occult testis.

Ninety-seven percent of patients with endodermal sinus tumour have increased serum concentration of AFP, a serum tumour marker. In this case, this patient was admitted to the hospital with chest pain. The AFP level of the patient was >3000 ng/mL. After the tumour was removed by surgery and chemotherapy, the serum AFP value decreased rapidly. When the tumour recurred, the AFP value increased. The tumours are generally larger with diameters exceeding 10 cm.[4] The definite diagnosis depends on pathological examination. The presence of Schiller--Duval (S-D) bodies and PAS-positive hyaline globules, helps confirm the diagnosis.

Walsh *et al*. reported 20 cases of non-seminomatous GCTs (NSGCTs) from 1993-1998, 9 of which were primary mediastinal yolk SAC tumours (YSTs).[6] All patients underwent radical surgery for residual masses after chemotherapy, with a 2-year survival rate of 58%.[6] Kesler *et al*. reported 40 cases of YSTs from 1981-1998, with a total survival rate of 61%.[7] AFP levels after preoperative chemotherapy, pathological status of residual masses, and lung metastases are associated with the long-term survival rate of the patients.

Platinum-based chemotherapy is considered as the initial treatment for YSTs.[8] It has been suggested that four cycles of VIP (cisplatin, etoposide, and ifosfamide) and PEB (cisplatin, etoposide, and bleomycin) are the alternatives. Chemotherapy and the recurrence of patients with mediastinal YSTs after surgery have had little effect.[9,10] In this case, the sensitivity of patient to chemotherapeutics improved after surgery, suggesting that carboplatin and cisplatin have moderate effects. Chemotherapy (docetaxel + carboplatin) was given for 4 cycles, and AFP decreased significantly after the treatment. A relapse occurred rapidly 2 months after the medicine was stopped, the disease progressed rapidly, and the patient died six months later. The authors detected PD1 and PDL1 in this patient's postoperative specimens and detected low expression (<1%). Considering the poor effect of immunotherapy, genetic testing of the patient's tissue specimens revealed DDR2, exon 5, c.286T> G, p.F96V, and the gene mutation abundance was 49.58%. The medicines to be used for DDR2 mutations are regorafenib (FDA-approved for colorectal cancer) and dasatinib (FDA-approved for chronic myeloid leukaemia). Whether these two medicines are effective for treating mediastinal GCTs, remains to be further studied.

It is very important to adopt a comprehensive treatment plan for primary mediastinal endodermal sinus tumours with immature teratomas. Surgery is currently one of the main treatments. Considering the poor sensitivity of the disease to chemoradiotherapy, in cases where complete resection is expected, surgical treatment may be the first choice and adjuvant chemotherapy may be given after surgery. At present, more clinical data are needed for immunotherapy and targeted therapy. The AFP level can be used as an important index for evaluating the effect of treatment before and after the surgery.

PATIENT'S CONSENT:
Informed consent was obtained from the patient's family for her anonymised information to be published.

COMPETING INTEREST:
The authors declared no conflict of interest.

AUTHORS' CONTRIBUTION:
MD: Conceptualisation and writing of the original draft.
HH: Writing, reviewing, and editing.
Both authors approved the final version of the manuscript to be published.

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