Yolk sac tumour in the anterior mediastinum

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SUMMARY. The case is presented of a patient who was hospitalized for the investigation of an anterior mediastinal mass, which proved to be a yolk sac tumour. The patient was a 33 year-old male non smoker who presented at the emergency respiratory department with a one month history of persistent dry cough with no relevant past medical history. Clinical examination revealed non specific chest sounds, restriction on spirometric testing, anaemia, an abnormal blood of albumin/globulin ratio and a high serum level of LDH. Chest X-ray and computed tomography (CT) showed marked widening of the anterior mediastinum with a lobed edge to the right cardiac margin, right sided pleural effusion and nodular opacities in the left upper and lower lung fields. The blood level of beta human chorionic gonadotropin (β-HCG) was zero, while the level of alpha 1 fetoprotein (AFP) was extremely high. The histological examination revealed a germ cell neoplasm with the characteristics of a yolk sac tumour. Pneumon 2013, 26(4):361-365.

CASE REPORT

A 33 year-old male non smoker attended the emergency respiratory department complaining of a persistent dry cough for one month. He had not previously consulted a doctor and had no other symptoms. The chest X-ray showed sizable widening of the anterior mediastinum, coin lesions in the left upper and lower lung fields and right sided pleural effusion (Figure 1). Diagnostic thoracentesis was performed, which produced a polymorphonuclear exudate with 7,000 cells/μl (neutrophils: 45%, lymphocytes: 40%, monocytes: 15%). Further tests of the pleural fluid showed: Hct: 1.4%, glucose: 63 mg/dl, total protein: 5.20 g/dL, LDH: 5,740 IU/L, pH: 7.39, and the fluid sample was sent for cytology. Blood testing revealed: Hb: 10.2 gr/dL, Hct: 32.2%, LDH: 1,271 IU/L, albumin: 3.3 g/dL, globulin: 4.2 g/dL.

Computed tomography (CT) of the chest showed a sizeable mass occupying the anterior mediastinum, nodular lesions in the left lung (two in the left upper lobe and a larger lesion in the left lower lobe) and a pleural effusion on the right side, as already seen on the chest X-ray. The CT showed, in addition, pericardial effusion and evidence of pressure on the superior vena cava with narrowing but no infiltration from the central mass (Figures
therapy scheme was prescribed, consisting of Bleomycin-Etoposide-Cisplatin (BEP). The possibility of future surgical resection would depend on the positive response to chemotherapy after the first four cycles and restaging of the disease.

DISCUSSION

The most common diseases which may present as a mediastinal mass are thymomas, neurogenic tumours and benign cysts, with a cumulative rate of approximately 60%.

Bronchogenic cysts, germ cell tumours and neurogenic tumours represent 80% of the mediastinal masses presenting during childhood, while primary neoplasms
of the thymus, thyroid masses and lymphomas are the most common in adults.\(^1\)

The mediastinum can be described in many anatomical ways. Most clinicians simply divide it into anterior, middle and posterior mediastinum, based on the lateral chest X-ray.\(^2,3\) Mediastinal masses are detected in the anterior mediastinum in 50% of cases.\(^4\)

Regarding the anterior mediastinum, masses with a wide variety of dimensions could be attributed to: thymomas (thymic carcinoma, carcinoid of the thymus, thymolipoma, cysts of thymus, thymus hyperplasia), lymphomas (Hodgkin, non-Hodgkin), germ cell tumours (seminoma, non seminomatous germ cell tumour and teratoma), goitre, parathyroid adenoma, pericardial cysts, and more rarely: lipoma, liposarcoma, angiosarcoma, mediastinal lymphangioma.\(^5\)

Mediastinal masses are usually discovered incidentally. At least half of the patients with a mediastinal mass are asymptomatic and their disease is detected on chest X-ray performed for another reason. Approximately 80% of asymptomatic masses are benign, while more than half of the masses that present with symptoms are malignant.\(^5,7\)

The symptoms are due to the external pressure from the mass or its infiltration into adjacent intrathoracic structures.\(^5,6\)

The precise incidence of primary mediastinal masses is difficult to calculate accurately, but it has been estimated at approximately 1/100,000 population / year. Mediastinal tumours in almost 10-15% of adults and 25% of children originate from germ cells,\(^6,8,9\) of which 3% develop in the posterior mediastinum.\(^10\) Tumours arising from the germ cells are categorized into teratomas, teratocarcinomas, seminomas and non-seminomatous carcinomas, including choriocarcinoma, embryonal carcinoma, yolk sac carcinoma and mixed type carcinoma. It has been argued that these masses originate from residual germ cells which did not migrate during embryogenesis, remaining in the mediastinum.\(^11,12\)

Yolk sac tumours appear in both men and women and are usually associated with the testes and ovaries. When the testes and ovaries are not the primary site, the tumours are called extragonadal yolk sac tumours and these are usually located in the mediastinum.\(^13\) Other reported sites of yolk sac tumours are the pineal gland, head, neck, lung, stomach, liver, omentum, retroperitoneal space, prostate, intrarenal even the vagina or the pudenda.\(^13-17\)

The yolk sac tumour constitutes about 40-50% of non-seminomatous tumours from germ cells in the testes of adults.\(^18,19\) The pathogenesis is generally unknown, but it has been speculated that hypermethylation of the promoter of the RUNX3 gene and overexpression of GATA-4, a transcription factor that regulates the differentiation and function of the endoderm of the yolk sac, may play an important role.\(^20,21\)

Yolk sac tumours give positive staining on immunohistochemical testing for AFP,\(^22\) and secrete substances such as AFP, \(\beta\)-HCG and cytokeratin (CEA) which can be detected in the serum and may even contribute to clinical symptomatology, (e.g., gynaecomastia) in 50% of cases.\(^5,22\)

AFP is considerably increased in yolk sac tumour, while the \(\beta\)-HCG is raised in choriocarcinoma and absent in yolk sac tumour. AFP is not a specific serum test for yolk sac tumour, however, as it is also detected in other conditions, including hepatocellular carcinoma and hepatoblastoma.\(^23\)

Other diagnostic markers are glypican-3 and SALL4.\(^14,24\) The yolk sac tumour, as all the non-seminomatous germ cell tumours, is associated with Klinefelter’s syndrome (up to 20% of patients suffer from the syndrome)\(^25\), a genetic disorder in which there is at least one extra X chromosome on the standard human male karyotype (i.e., XXY instead of XY) and also with haematological malignancies such as acute leukaemia and myelodysplastic syndrome.\(^26\)

The treatment of yolk sac tumours is similar to that of other non-seminomatous germ cell tumours. Significant results have been documented from chemotherapeutic schemes based on cisplatin, with 50% of patients achieving long-term survival.\(^11,26-28\) A widely accepted chemotherapy scheme is Bleomycin-Etoposide-Cisplatin (BEP), which requires at least 4 cycles.\(^27,29\) The survival rate is higher for patients who show a decrease in the serum level of AFP after chemotherapy, and in cases with resectable tumours.\(^20,21\) Surgical resection is recommended particularly when factors such as AFP remain high after 4 cycles of chemotherapy.\(^30\) Even extremely large tumours in this category may respond to aggressive chemotherapy.\(^31\) Rescue treatment includes bone marrow transplantation when necessary.\(^34,35\)

Concerning prognosis, five year survival is achieved in about 65% of cases following appropriate treatment.\(^36\) The average age at diagnosis is 18 years for yolk sac tumour, while it rarely appears after the age of 30 years.\(^37\) Regarding EGCT, Afro-Americans have the worst prognosis\(^38\) and Chinese have poorer prognosis than the inhabitants of Western countries.\(^39\) One study showed that only 7% of Indians with EGCT achieved long-term survival after chemotherapy\(^39\), and it is clear that the role of race and ethnicity justifies further investigation. It has also been documented that EGCT in the mediastinum has a worse
prognosis compared to other sites.\textsuperscript{38-40} Regarding novel therapeutic approaches, new techniques have been proposed which include the use of humanized antibodies against the receptor surface molecules of cancer cells, inhibitors of serine-threonine, tyrosine kinase inhibitors and others.\textsuperscript{41}

**REFERENCES**

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