# Synchronous primary mediastinal seminoma in a patient with colorectal adenocarcinoma

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## Abstract

Primary mediastinal germ cell tumours are a rare primary tumour of the mediastinum. They share the same immunomorphological features to their gonadal counterparts but carry a worse prognosis. Primary mediastinal seminomas are exclusively found in male patients. Their diagnosis requires exclusion of primary gonadal germ cell tumours.

**Keywords** mediastinal seminoma; primary mediastinal germ cell tumour; synchronous tumours

## Case report

This is a case of a 43-year-old man who was found to have two mediastinal lesions, radiologically suspected to be lymph node involvement by colorectal cancer on thoracic computed tomography (CT). On endoscopic screening for colorectal cancer, due to a strong family history, he was found to have a tubular adenoma with high-grade dysplasia. After incomplete mucosal resection, he underwent anterior resection of his sigmoid colon. The resection showed focal submucosal invasion, thus changing the diagnosis to an early-stage adenocarcinoma that was mismatch repair proficient (TNM8: pT1 N1b Mx). As part of his work-up, a postoperative completion thoracic CT was done which found two anterior mediastinal lesions, thought to be involved lymph nodes.

Macroscopic examination of the mediastinal resection specimen revealed two distinct well-defined solid nodules with a yellow cut surface, measuring 20 mm and 10 mm in maximum dimension.

Histological examination showed encapsulated well-circumscribed tumour nodules, composed of rather monomorphic, round to polygonal cells growing in a sheet-like pattern, traversed by delicate fibrous septa. The tumour cells had a clear to lightly eosinophilic cytoplasm with distinct cell membrane and round to oval central nuclei containing prominent nucleoli. The fibrous septa were infiltrated by CD5-positive mature lymphocytes. The tumour was associated with a granulomatous reaction and focal lymphoid aggregates with germinal centres. The lymphoid follicles were seen within and adjacent to one of the tumour nodules (Figure 1).

On immunohistochemistry the tumour cells had distinct perinuclear MNF116 positivity and widespread PLAP, OCT3/4 and C-KIT (CD117) positivity. There was no staining with CD30 or TTF1 (Figure 1).

The immunomorphological findings were entirely consistent with pure seminoma (two tumour nodules). After discussion at the multidisciplinary team meeting and following exclusion of a testicular seminoma on radiology and in absence of raised serological markers post-operatively, the diagnosis was confirmed to be primary mediastinal seminoma. The presence of lymphoid aggregates with prominent germinal centres also raised the possibility of lymph node involvement.

He did not require further treatment for his colorectal adenocarcinoma but received three cycles of chemotherapy for the mediastinal seminoma. He is currently under close follow-up for up to 5 years, mainly due to the implications of a germ cell tumour diagnosis, and not the colorectal carcinoma, on his employment.

## Discussion

Primary mediastinal germ cell tumours (MGCTs) account for 1−15% of the mediastinal neoplasms in adults and 11−20% in children. They are thought to arise from migrating primordial germ cells during embryogenesis.[1−3]

Individuals can present with symptoms associated with the local pressure effect and/or invasion of surrounding structures. Children with MGCT present with severe symptoms such as airway obstruction. Half of adults with MGCTs are asymptomatic with incidental anterior mediastinal lesion, discovered on imaging. There is a strong predilection to develop primary MGCTs in patients with Klinefelter syndrome, however the exact pathogenesis and risk factors associated with these tumours are not well understood.[2−5]

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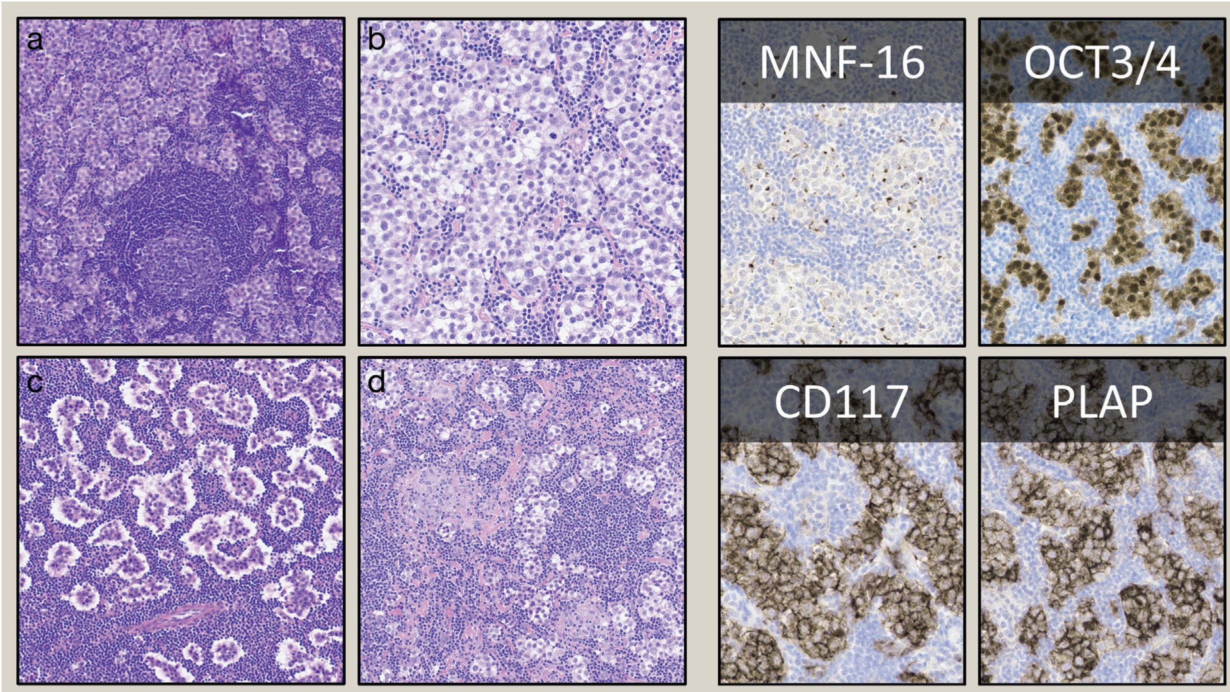


**Figure 1** Primary mediastinal seminomas can be associated with florid lymphoid hyperplasia with prominent germinal centres (**a,c**), varying degree of lymphocytic infiltration (**b-c**) and granulomatous reaction (**d**). The immunopanel shows typical profile of seminomas.

Histologically MGCTs are classified as seminomas, non-seminomatous germ cell tumours and teratomas. Teratomas are the most common, followed by mixed germ cell tumours and seminomas. Regardless of their subtype, they tend to have a worse prognosis compared to their gonadal counterpart, even though they share many histological and molecular characteristics[1–4]

Primary mediastinal seminomas were first histologically described by Woolner et al. in 1955.[6] They are composed of uniform polygonal cells growing in sheets, cords, lobules, or multinodular clusters that are separated by fibrous septa which may be infiltrated by lymphocytes. Tumour cells have a characteristically distinct membrane, lightly eosinophilic to clear cytoplasm, and large central nuclei with vesicular chromatin containing prominent single or multiple nucleoli.[1,2] Other features of uncertain significance have also been described, such as granulomatous reaction and florid lymphoid hyperplasia[6] (Figure 2). The exact implications of such findings are unclear; however, a florid inflammatory reaction may hide smaller tumour nests, making it an important pitfall to consider when dealing with a biopsy specimen.[6] Similarly, lymphoid hyperplasia with germinal centres, albeit seen rarely in pure seminomas, can be misinterpreted as involved lymph node rather than tumour evoked inflammatory reaction as part of the disease process.

Mediastinal and testicular seminomas have a similar immunohistochemistry profile (Table 1). They are positive for OCT3/4, SALL4, C-KIT (CD117) and PLAP. Unlike testicular seminomas, mediastinal seminomas are frequently positive for low and high molecular weight cytokeratins as well as D2-40. Like their gonadal counterpart, they also have the characteristic structural aberration of the short arm of chromosome 12 (isochromosome of 12p) and may have activating KIT mutations or rarely with KRAS mutations. Cases with KIT mutation may show negative CD117 staining on immunohistochemistry.[1–6]

The key to diagnosing a primary mediastinal seminoma is to exclude metastatic testicular seminoma. Metastatic germ cells tumours tend to involve the posterior, rather than anterior mediastinum. When primary mediastinal GCTs are being considered, it is essential to exclude a coexisting testicular lesion or any evidence of a regressed testicular lesion (such as scaring or fibrosis on imaging). The serological marker, beta-hCG, can be helpful to distinguish between primary mediastinal and metastatic seminomas. Human chorionic gonadotrophin (beta-hCG) may be raised in only one-third of patients with primary mediastinal seminomas whilst they are almost always raised in testicular seminomas.[3,4,7–9] It is also important to exclude presence of a non-seminomatous component histologically and serologically, which will warrant the diagnosis of a mixed germ cell tumour and carries a worse prognosis. Elevated serum alpha-fetoprotein (AFP) should raise suspicion for residual non-seminomatous component in mediastinal seminoma resection specimen. Other differentials include primary mediastinal tumours such as a thymoma, thymic carcinoma and mediastinal diffuse large B-cell lymphoma or metastatic cancers such as melanoma.

Patients with primary mediastinal germ cell tumours are usually treated surgically, or with neoadjuvant chemotherapy or a combination of both. Primary mediastinal seminomas have a better prognosis than other MGCT subtypes.[1,2] Although there is no official staging system for primary mediastinal germ cell tumours, factors that indicate an unfavourable outcome include: distant metastasis and raised serological markers. Unfortunately, almost half of patients (37–41%) have metastatic disease at presentation.[1–3]

 

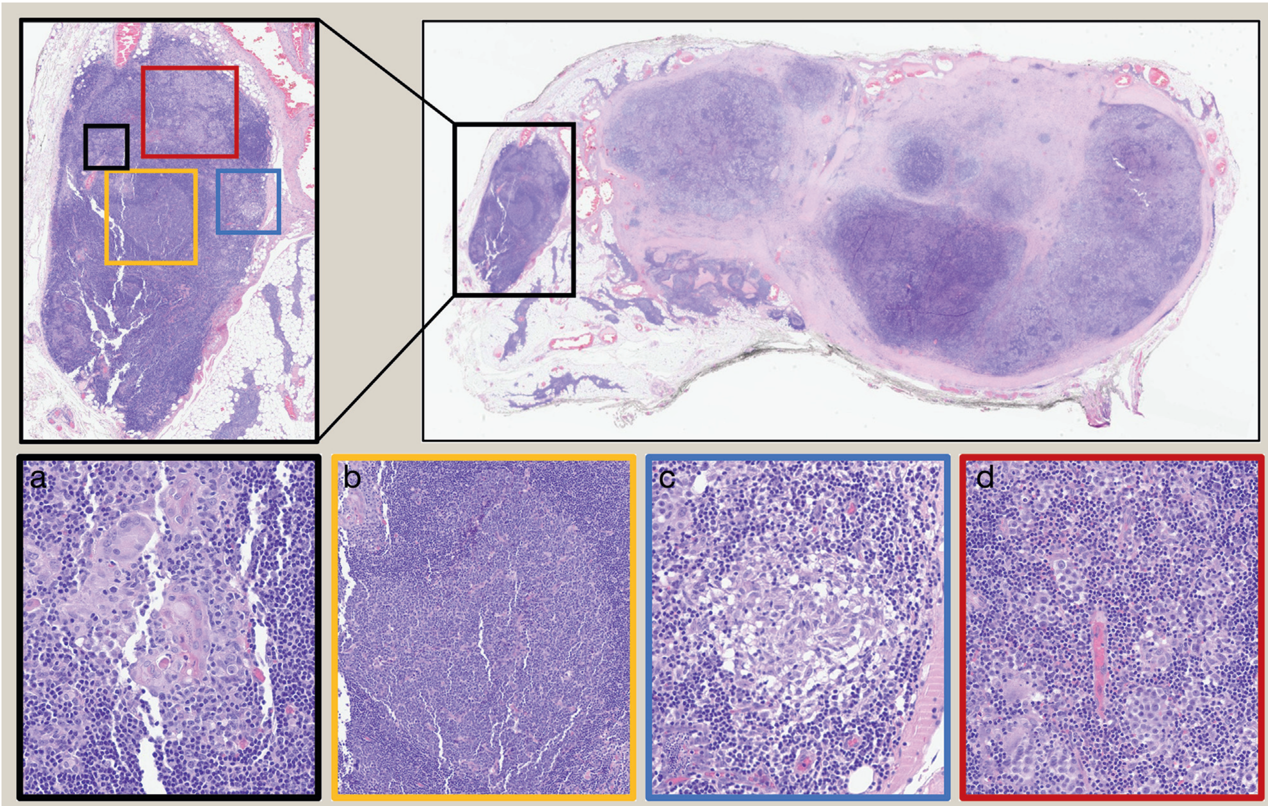


**Figure 2** Identifying Hassall's corpuscles (**a**) in presence of a prominent lymphoid reaction with follicular hyperplasia, forming germinal centres (**b**), with granulomatous inflammation (**c**) is useful when considering if there is lymph node involvement by small tumour nests (**d**) or tumour associated inflammatory reaction in the thymus.

## Conclusion

This was a case of primary mediastinal seminoma in a man in his 40s who was being investigated for possible lymph node/distant metastasis following an unexpected diagnosis of colorectal adenocarcinoma. Primary mediastinal seminoma is the third most common primary germ cell tumour of the mediastinum, seen exclusively in males.[1] The mediastinal and testicular seminomas share similar immunomorphological features.

Primary mediastinal germ cell tumours have a worse prognosis than their gonadal counterpart. Diagnosing primary mediastinal germ cell tumours requires clinicopathological correlation to exclude metastasis from gonads. Serological markers for germ cell tumours (AFP and beta-hCG) are not raised in mature teratomas, and beta-hCG may be normal or mildly elevated in only one-third of primary mediastinal seminomas, unlike testicular seminomas. ◆

### Immunohistochemistry profile of primary mediastinal germ cell tumours

| Marker | Teratoma | Seminoma | Embryonal carcinoma | Yolk sac tumour | Choriocarcinoma |
|---|---|---|---|---|---|
| SALL4 | + | ++ | ++ | ++ | + |
| OCT3/4 | – | ++ | ++ | – | – |
| PLAP | NR | ++ | – | Focal + | – |
| CD117(CKIT) | NR | ++ | – | +/– | NR |
| CD30 | NR | –/+ | ++ | –/+ | – |
| Glypican-3 | NR | – | C– | ++ | – |
| Keratin (AE1/3, Cam5.2, MNF-116) | NR | + | ++ | ++ | ++ |
| AFP | NR | – | – | + | – |
| β-hCG | NR | – | –/+ | – | ++ |

Frequency of expression: >80% (++); 50–80% (+); 10–50% (+/–); 1–10% (–/+); <1% (–); NR, not reported in mediastinal germ cell tumours.

**Table 1**

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## Practice points

Pathological features:

- Clusters and sheets of polygonal epithelioid cells traversed by fibrous septa showing a varying degree of lymphocytic infiltrate
- Tumour cells have a clear to eosinophilic cytoplasm, distinct cell membrane, and central nuclei with prominent nucleoli
- There may be a granulomatous or a florid lymphoid reaction associated with the tumour (uncertain significance)
- Tumour cells express OCT3/4, CD117 and may show PLAP positivity
- Isochromosome 12p (similar to testicular seminoma)

## Multiple choice questions

**1. Which of the following is most in keeping with the immunohistochemistry profile of seminomas?**

a. SALL4+, OCT3/4+, CD117(CKIT)−
b. SALL4+, PLAP+, AFP+
c. SALL4+, OCT3/4−, PLAP−, CKIT+

*Answer: a — CD117 expression may be absent in cases with KIT mutation*

**2. What serological marker is expected to be raised in primary mediastinal mixed germ cell tumour?**

a. AFP and/or beta-hCG and/or LDH
b. AFP and LDH with no rise in beta-hCG
c. None should be raised in primary mediastinal germ cell tumours

*Answer: a — Both AFP and beta-hCG are expected to be elevated in mixed germ cell tumours. Although beta-hCG may be normal in pure seminomas, when raised, it is indicative of poor prognosis and advanced disease.*

**3. What syndrome is associated with primary mediastinal germ cell tumours?**

a. Wiskott-Aldrich Syndrome
b. Turner Syndrome
c. Klinefelter Syndrome

*Answer: c — Klinefelter syndrome is identified in 8–33% of adult males with primary mediastinal germ cell tumour. Children with Klinefelter syndrome have a 67-fold increased risk for developing MGCTs.*