CASE REPORT

Mediastinal germ cell tumour causing superior vena cava tumour thrombosis

Suman S Karanth, Ashok K Vaid, Sandeep Batra, Devender Sharma

Department of Medical Oncology, Medanta—The Medicity, Gurgaon, Haryana, India

Correspondence to

Dr Sandeep Batra, sandeepriya2000@yahoo.com

Accepted 13 February 2015

SUMMARY

We report a rare case of a 35-year-old man who presented with a 1-week history of retrosternal chest pain of moderate intensity. A positron emission tomography CT (PET-CT) showed a large fluorodeoxy-glucose (FDG)-avid heterogeneously enhancing necrotic mass in the anterosuperior mediastinum with a focal FDG-avid thrombosis of the superior vena cava (SVC) suggestive of tumour thrombus and vascular invasion. α -Fetoprotein levels were raised (5690 IU/L). Image guided biopsy of the mediastinal mass was suggestive of non-seminomatous germ cell tumour (NSGCT). The patient received four cycles of BEP (bleomycin, etoposide and cisplatin) along with therapeutic anticoagulation with low-molecular-weight heparin. Follow-up whole body PET-CT revealed complete resolution of mediastinal mass and SVC tumour thrombosis. The documentation of FDG-PET-avid tumour thrombus resolving with chemotherapy supports the concept of circulating tumour cells being important not only in common solid tumours such as breast and colon cancer but also in relatively less common tumours such as NSGCT. The detection of circulating tumour cells could help deploy aggressive regimens upfront.

BACKGROUND

Testicular cancers account for 2% of all cancers. Germ cell tumours (GCTs) are the most common malignancies in young males aged 15–34 years with seminoma being the least aggressive.¹ Less than 10% of all GCTs arise from extragonadal sites. Primary mediastinal GCTs account for 10–15% of all mediastinal masses.^{2–3} Thirty per cent of patients remain asymptomatic while others present with non-specific symptoms. Superior vena cava (SVC) syndrome is less common in about 10% of patients.⁴ In addition, the occurrence of SVC obstruction due to tumour thrombosis rather than venous thrombosis is extremely rare in GCTs with very few cases reported in the literature. We describe this rare phenomenon of occurrence of fluorodeoxy-glucose (FDG)-avid tumour thrombosis in the SVC in a case of mediastinal GCT showing complete resolution following completion of chemotherapy. We further explore the relevance of detection of circulating tumour cells in less common tumours such as GCTs, to help predict further disease progression and complications.

CASE PRESENTATION

A 35-year-old man presented to our out-patient department with a 1-week history of non-radiating, retrosternal chest pain of moderate intensity.

He did not suffer from breathlessness, syncope, cough, fever, weight loss or night sweats. Clinical examination did not reveal any cyanosis, exophthalmos, conjunctival injection, swelling of face and neck, engorgement of veins, or enlargement of cervical or supraclavicular lymph nodes. Testicular examination was normal.

INVESTIGATIONS

CT of the thorax showed an anterior mediastinal mass measuring 83×66×99 mm. Tumour markers α -fetoprotein (AFP: 5690 IU/L) and lactose dehydrogenase levels (LDH: 744 U/L) were elevated. β -Human chorionic gonadotropin level (β -HCG: 2.39 mIU/L), complete blood picture, liver function tests and renal function tests were normal. A Positron emission tomography CT (PET-CT) of the whole body showed a large FDG-avid heterogeneously enhancing necrotic mass in the anterosuperior mediastinum measuring 9.9×9.6×8.3 cm more to the right, with no chest wall or rib invasion (figure 1). A focal FDG-avid thrombosis of the SVC and the proximal left brachiocephalic vein was also seen with thrombus extending superiorly to the junction of the SVC and right innominate vein and inferiorly up to the right atrium, suggestive of tumour thrombus and vascular invasion (figure 2). D-dimer levels were normal. Image guided biopsy of the mediastinal mass was suggestive of non-seminomatous GCT (NSGCT). Immunohistochemistry pattern was positive for placental alkaline phosphatase, c-kit (CD117), keratins (8, 18, 19) and CD30. The definitive diagnosis of NSGCT, stage III with tumour thrombus in SVC with no signs of SVC syndrome was made.

TREATMENT

The patient received four cycles of BEP (bleomycin, etoposide and cisplatin) in standard doses and therapeutic anticoagulation with low-molecular-weight heparin. On completion of four cycles of chemotherapy, end of treatment response evaluation was evaluated with whole body PET-CT scan.

OUTCOME AND FOLLOW-UP

Repeat whole body PET-CT revealed complete metabolic regression of the mediastinal mass with significant size reduction (13×12×13 mm) and complete resolution of the SVC tumour thrombosis. The AFP showed normalisation to 6.28 IU/L (baseline 5690 IU/L). The patient also underwent video-assisted thoracic surgical resection of the mediastinal mass, which revealed only necrotic

CrossMark

To cite: Karanth SS, Vaid AK, Batra S, et al. *BMJ Case Rep* Published online: [please include Day Month Year] doi:10.1136/bcr-2014-208356

Figure 1 Positron emission tomography CT scan showing a large FDG-avid heterogeneously enhancing necrotic mass in the anterosuperior mediastinum measuring 9.9×9.6×8.3 cm.

tissue. At 1-year follow-up, the levels of tumour markers (AFP, β -HCG and LDH), and CT of the chest (figure 3) and abdomen study were normal.

DISCUSSION

NSGCT, though most commonly arising in the gonads, can uncommonly be found in the mediastinum, sacrococcyx, retroperitoneum, thymus, and head and neck. Of these extragonadal sites, the mediastinum is the most common site for primary extragonadal involvement. It has been proposed that the multipotent primitive germ cells that get misplaced along the midline during early embryogenesis, during their migration from the yolk endoderm to the gonad, are responsible for the development of mediastinal involvement. The exact cause of extragonadal involvement still remains unclear.⁵ Presence of FDG-avid tumour thrombosis in vessels, not in direct continuity with the tumour, suggests the presence of circulating tumour cells.

Tumour thrombosis occurs as a rare complication of mainly solid tumours such as those of the pancreas, colon, and hepatocellular carcinoma and renal cell carcinoma. It is mainly composed of viable cancer cells as opposed to venous thromboembolism, which is composed of activated macrophages, platelets and fibrin mesh.⁶ The introduction of PET-CT has revolutionised imaging through its ability to fuse anatomical and functional data, serving as an important tool for staging, monitoring response and prognostication of tumours. The literature on PET-CT localising and detecting tumour thrombosis due to its increased metabolic activity remains limited. Tumour thrombi are FDG avid on PET-CT scans due to increased uptake through glucose transporter receptors in the malignant cells. Inflammatory cells interspersed in a venous thrombosis can cause increased glucose uptake and appear to be FDG avid, thus

causing some diagnostic dilemma.^{7 8} In this case, we demonstrated a serial response and ultimately complete resolution of the tumour thrombus as evidenced by PET-CT scan following chemotherapy administration.

The existing tumour markers at our disposal for diagnosis of GCTs are—AFP, LDH and β -HCG, each having a significant role in diagnosis and follow-up.⁹ However, in cases of pure teratoma, the markers are not elevated. In addition, at the time of diagnosis, elevated levels of AFP, β -HCG and LDH are found in 10–60%, 10–40% and 40–60% of patients of non-seminomatous tumour, respectively.¹⁰ Occult metastases, present in 10–20% of stage 1 seminomatous GCTs and 30% of NSGCTs at the time of diagnosis, can lead to future relapses.^{11 12} Therefore, research is starting to identify the role of circulating tumour cells (CTCs), which are detected in approximately 18% of GCTs. Non-seminomatous tumours associated with CTCs have more aggressive, clinically advanced cancer with increased metastatic potential and disease progression, and are treatment refractory.¹³ While numerous clinical studies exist on the role and detection of CTCs in metastatic breast, colon and prostate cancer,^{14–16} little is known in the context of GCTs. This will prove to be useful, particularly in cases of teratomas, which are notorious for relapses and not known to produce tumour markers. CTCs are more commonly detected with non-seminomatous than seminomatous tumours, especially teratomas and yolk sac tumours.¹⁷ In a recent study carried out by Nastaly *et al*, CTCs were detected using a label-free enrichment method to detect epithelial markers such as keratin (8,18,19), and EpCAM and germ cell markers, namely SALL4 (Sal-like protein 4: a stem cell marker) and OCT3/4 (transcriptional factor).^{18 19} In addition, they found a greater yield of CTCs in the testicular vein as opposed to the peripheral

Figure 2 Positron emission tomography CT scan showing a focal FDG-avid thrombosis of the superior vena cava.

Figure 3 CT scan showing complete resolution of the superior vena cava tumour thrombosis.

circulation, as was observed in the mesenteric vein and central venous blood in cases of breast and colon cancers.^{20 21} These CTCs act as seeds for future distant metastasis. The clinical utility of CTCs in GCTs, however, is still not defined. The current management of mediastinal GCTs includes initial systemic platinum-based chemotherapy. This is followed by complete resection of the residual tumours.^{2 22} The postoperative outcomes depend on the pathological findings of the residual tumours. Complete necrosis predicts good survival.^{22 23} As opposed to the excellent response seen in mediastinal seminoma, only 40–45% mediastinal NSGCTs experience good disease-free survival after therapy.^{2 22–24}

In conclusion, we highlight this rare case of mediastinal NSGCT presenting as FDG-avid SVC tumour thrombosis showing complete resolution following standard chemotherapy. We also highlight the possible role of CTCs as potential biomarkers in GCTs in addition to the available tumour markers, to predict a more aggressive and metastatic disease. Research into its clinical utility in GCTs will help pave the way to identify patients with higher chances of getting recurrent metastatic disease requiring intensification of treatment.

Learning points

- ▶ Young males presenting with superior vena cava obstruction should be investigated extensively for proper diagnosis and management.
- ▶ The role of positron emission tomography CT is evolving in the diagnosis and management of germ cell tumours (GCTs).
- ▶ By documenting circulating tumour cells in GCTs, one may predict patients having higher chances of metastatic recurrence and thus employ aggressive treatment pre-emptively.

Acknowledgements The authors thank the Department of Nuclear Medicine and PET-CT, Medanta—The Medicity, Gurgaon, Haryana.

Contributors SSK, SB and DS contributed to writing of the manuscript along with review of the literature. AKV proofread and approved the final manuscript.

Competing interests None.

Patient consent Obtained.

Provenance and peer review Not commissioned; externally peer reviewed.

REFERENCES

- 1 Albers P, Albrecht W, Algaba F, *et al.* EAU guidelines on testicular cancer. 2011 update. *Eur Urol* 2011;60:304–19.
- 2 Takeda S, Miyoshi S, Ohta M, *et al.* Primary germ cell tumors in the mediastinum: a 50-year experience at a single Japanese institution. *Cancer* 2003;97:367–76.
- 3 Ravenel JG, Gordon LL, Block MI, *et al.* Primary posterior mediastinal seminoma. *AJR Am J Roentgenol* 2004;183:1835–7.
- 4 Polansky SM, Barwick KW, Ravin CE. Primary mediastinal seminoma. *AJR Am J Roentgenol* 1979;132:17–21.
- 5 Rosado-de-Christenson ML, Templeton PA, Moran CA. From the archives of the AFIP. Mediastinal germ cell tumors: radiologic and pathologic correlation. *Radiographics* 1992;12:1013–30.
- 6 Lai P, Bomanji JB, Mahmood S, *et al.* Detection of tumor thrombus by 18F-FDG-PET-CT imaging. *Eur J Cancer Prev* 2007;16:90–4.
- 7 Mochizuki T, Kuge Y, Zhao S, *et al.* FDG uptake and glucose transporter subtype expression in experimental tumor and inflammation models. *J Nucl Med* 2001;42:1551–5.
- 8 McGowan KM, Long SD, Pekala PH. Glucose transporter gene expression; regulation of transcription and mRNA stability. *Pharmacol Ther* 1995;66:465–505.
- 9 Trigo JM, Tabernero JM, Paz-Ares L, *et al.* Tumor markers at the time of recurrence in patients with germ cell tumors. *Cancer* 2000;88:162–8.
- 10 Gilligan TD, Seidenfeld J, Basch EM, *et al.* American Society of Clinical Oncology Clinical Practice Guideline on uses of serum tumor markers in adult males with germ cell tumors. *J Clin Oncol* 2010;28:3388–404.
- 11 Peckman MJ, Hamilton CR, Horwich A, *et al.* Surveillance after orchiectomy for stage 1 seminoma of the testis. *Br J Urol* 1987;59:343–51.
- 12 Vergouwe Y, Steyerberg EW, Eijkemans MJ, *et al.* Predictors of occult metastasis in clinical stage I nonseminoma: a systematic review. *J Clin Oncol* 2003;21:4092–9.
- 13 Nastaly P, Ruf C, Becker P, *et al.* Circulating tumor cells in patients with testicular germ cell. *Clin Cancer Res* 2014;20:3830–41.
- 14 Cristofanilli M, Budd GT, Ellis MJ, *et al.* Circulating tumor cells, disease progression, and survival in metastatic breast cancer. *N Engl J Med* 2004;351:781–91.
- 15 Cohen SJ, Punt CJ, Iannotti N, *et al.* Relationship of circulating tumor cells to tumor response, progression-free survival, and overall survival in patients with metastatic colorectal cancer. *J Clin Oncol* 2008;26:3213–21.
- 16 de Bono JS, Scher HI, Montgomery RB, *et al.* Circulating tumor cells predict survival benefit from treatment in metastatic castration-resistant prostate cancer. *Clin Cancer Res* 2008;14:6302–9.
- 17 Michael H, Lucia J, Foster RS, *et al.* The pathology of late recurrence of testicular germ cell tumors. *Am J Surg Pathol* 2000;24:257–73.
- 18 Ulbright TM. Germ cell tumors of the gonads: a selective review emphasizing problems in differential diagnosis, newly appreciated, and controversial issues. *Mod Pathol* 2005;18:61–79.
- 19 Cao D, Li J, Guo CC, *et al.* SALL4 is a novel diagnostic marker for testicular germ cell tumors. *Am J Surg Pathol* 2009;33:1065–77.
- 20 Denève E, Riethdorf S, Ramos J, *et al.* Capture of viable circulating tumor cells in the liver of colorectal cancer patients. *Clin Chem* 2013;59:1384–92.
- 21 Peeters DJ, Van den Eynden GG, van Dam PJ, *et al.* Circulating tumour cells in the central and the peripheral venous compartment in patients with metastatic breast cancer. *Br J Cancer* 2011;104:1472–7.
- 22 Ganjoo KN, Rieger KM, Kesler KA, *et al.* Results of modern therapy for patients with mediastinal nonseminomatous germ cell tumors. *Cancer* 2000;88:1051–6.
- 23 Kesler KA, Rieger KM, Ganjoo KN, *et al.* Primary mediastinal nonseminomatous germ cell tumors: the influence of postchemotherapy pathology on long-term survival after surgery. *J Thorac Cardiovasc Surg* 1999;118:692–701.
- 24 Kiffer JD, Sandeman TF. Primary malignant mediastinal germ cell tumours: a literature review and a study of 18 cases. *Australas Radiol* 1999;43:58–68.

Copyright 2015 BMJ Publishing Group. All rights reserved. For permission to reuse any of this content visit <http://group.bmj.com/group/rights-licensing/permissions>.
BMJ Case Report Fellows may re-use this article for personal use and teaching without any further permission.

Become a Fellow of BMJ Case Reports today and you can:

- ▶ Submit as many cases as you like
- ▶ Enjoy fast sympathetic peer review and rapid publication of accepted articles
- ▶ Access all the published articles
- ▶ Re-use any of the published material for personal use and teaching without further permission

For information on Institutional Fellowships contact consortiasales@bmjgroup.com

Visit casereports.bmj.com for more articles like this and to become a Fellow