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Case report Free Access

Tenosynovial giant cell tumour (diffuse type) with a background of malignant melanoma: a case report from South Africa

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Abstract

Introduction: Tenosynovial giant cell tumour (TGCT) is a rare mesenchymal tumour that affects joints and tendon sheaths, little is known about conditions associated with TGCT.

Case presentation: Mr X, a 89-year-old male, known with a history of malignant melanoma was initially thought to have metastatic lung lesions from the melanoma. Following a lung biopsy, Mr X was diagnosed with a second primary lesion – TGCT: diffuse type – rather than a metastatic lesion. The patient was not considered for referral to a multidisciplinary sarcoma team due to the advanced stage of disease. Mr X deteriorated and demised after commencing Imatinib.

Discussion: Although one would think that a pulmonary lesion in a patient with a history of cancer is metastatic disease, it is not always the case. The patient may have two primary cancers that are unrelated. One other case report has previously been published on a patient with a TGCT and Melanoma.

Conclusion: TGCT is a rare condition that may or may not be associated with melanoma. We recommend that suspected metastatic melanoma lesions be biopsied to establish or refute this association.

Keywords: Tenosynovial giant cell tumour, Malignant melanoma, Metastatic, Oncology, Histology, Rare diseases

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Introduction

Tenosynovial giant cell tumour (TGCT) is a rare mesenchymal¬ tumour that affects joints and tendon sheaths. The diffuse-type TGCT has a high risk of relapse following surgical resection of the tumour (1).

The classification of it can be categorised into 'nodular' and 'diffuse' TGCT depending on the imaging findings of the pathology. TGCT can be either benign or malignant – the likely incidence of malignant TGCT is lower than that of benign TGCT at less than 1 per million per year, with a mortality rate of around 30% and a metastatic rate of around 50% (1). Estimates suggest that there are approximately 10 per million persons/year for the localised type, while the diffuse type is about 4 per million persons/year (2). Burton et al. highlights that little is known on the burden of disease and that the common presentation of TGCT is benign (3). This illustrates the rarity of the above condition.

A Japanese-authored article published by Takeuchi et al., illustrated case reports of two cases of TGCT, with one having an ocular cancer (Choroidal Melanoma), while the other was associated with multiple type 1 neurofibromatosis (4). This is important as choroidal melanoma is the second most common site of ten malignant melanoma sites in the body (5). An article published in 2021 by Italian authors highlighted that pure muscle tenosynovial giant cell tumour mimics a metastasis in a patient with melanoma. In this study, a 50-year-old female with a diagnosis of malignant melanoma presented for a routine scan and an intense FDG focal uptake corresponding to peri-trochanteric medial part of right iliopsoas muscle was discovered (6). Once biopsied, the final diagnosis was derived. This is of importance as the TGCT lesions may reproduce a malignant appearance on FDG-PET. Hence, TGCT may be under-diagnosed as patient's may be diagnosed as 'metastatic melanoma' rather than biopsying the lesion which may show that the histology is actually a second primary lesion. Furthermore, a recent article published in 2025 by Patel et al. has documented that second primary cancers does occur in the setting of melanoma. His focus looked at a more common cancer (colo-rectal cancer) and associations between the two. In this study, it was confirmed that it can be influenced by various factors e.g. biological, lifestyle, genetic factors (7).

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Case presentation

Mr X, an 87-year-old South African male with a background history of malignant melanoma (excised in 1982), in remission; presented with shortness of breath and a cough. He was a non-smoker and of sober habits and had a history of a pacemaker inserted for a tachyarrhythmia. He had no other comorbidities. An initial baseline chest X-Ray (CXR) performed on 26 May 2024 revealed a right pleural effusion (Figure 1). This caused the shortness of breath in the patient and was considered treatable as the fluid could be drained, which would lead to symptomatic relief.

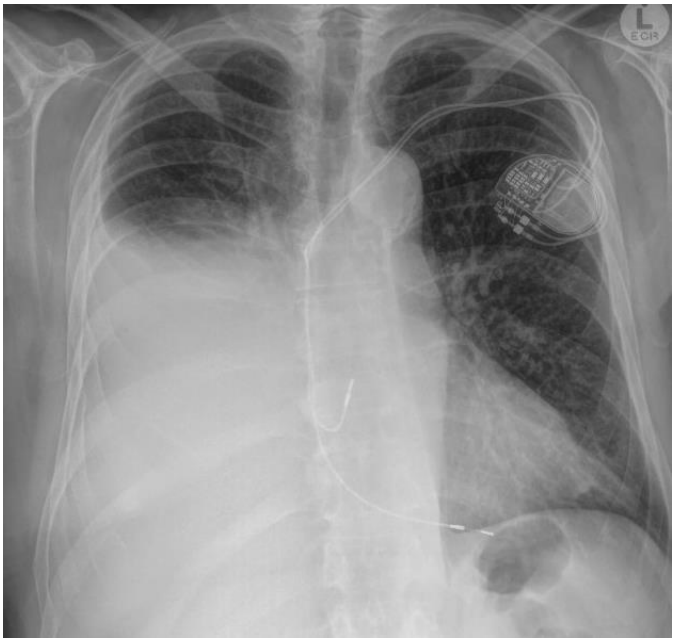

Figure 1. CXR performed on 26 May 2024.

A CT scan was thereafter performed which demonstrated multiple pleural-based nodules and masses, the largest of which was adjacent to right 6th and 7th ribs and measured 3.3cm x 4.7cm (figure 2) The second mass was noted adjacent to the right side aspect of T8 and T9 vertebral bodies and measured 2.0 x 2.6cm (figure 3).

There was also associated pleural thickening in the right costophrenic angle with an associated pleural based lesion measuring 2.0 x1.9cm as well as a right hilar node which was 1.4cm (figure 4).

There was also a right large pleural effusion.

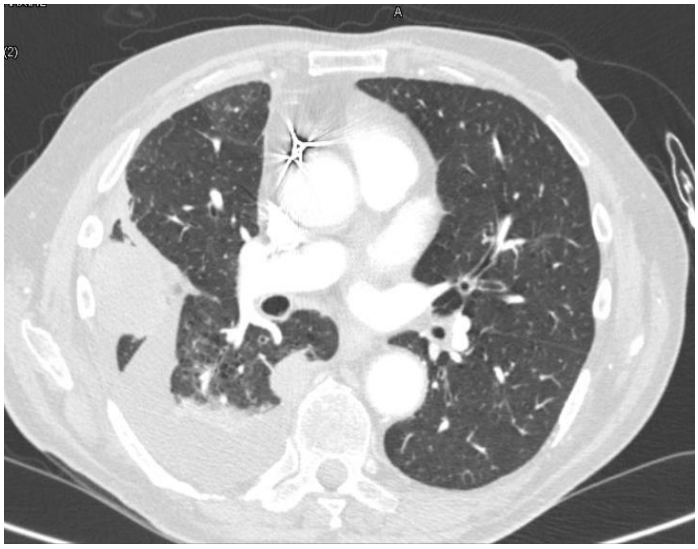

Figure 2. CT scan: multiple pleural-based nodules and masses, the largest of which was adjacent to the right 6th and 7th ribs.

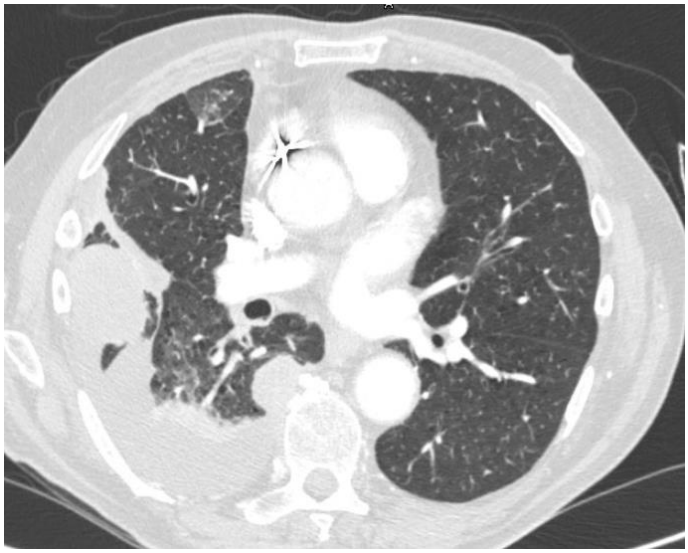

Figure 3. The second mass was noted adjacent to the right side aspect of T8 and T9 vertebral bodies.

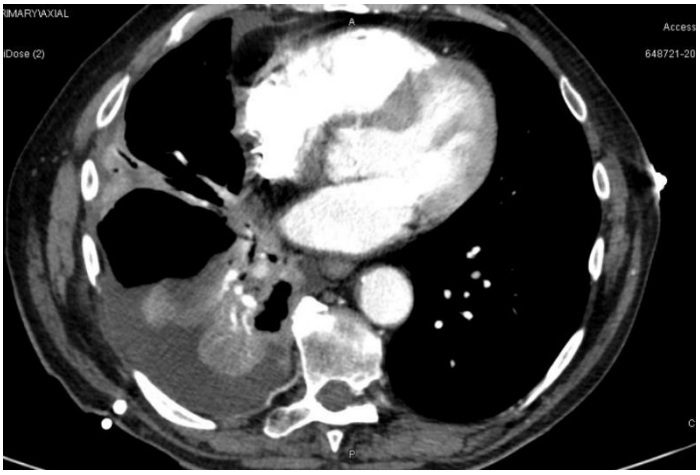

Figure 4. Associated pleural thickening in the right costophrenic angle with an associated pleural-based lesion measuring 2.0 x 1.9 cm as well as a right hilar node which was 1.4cm.

The patient was referred to the cardio-thoracic surgeon and had a pleurocentesis performed. After the drainage, the newer CXR demonstrated improvement in the pleural effusion and unmasked a mass in the right lung which was previously hidden by the fluid. There was right basal atelectasis and a small residual right pleural effusion with a peripheral right mid-zone 51 mm nodule (See Figure 5).

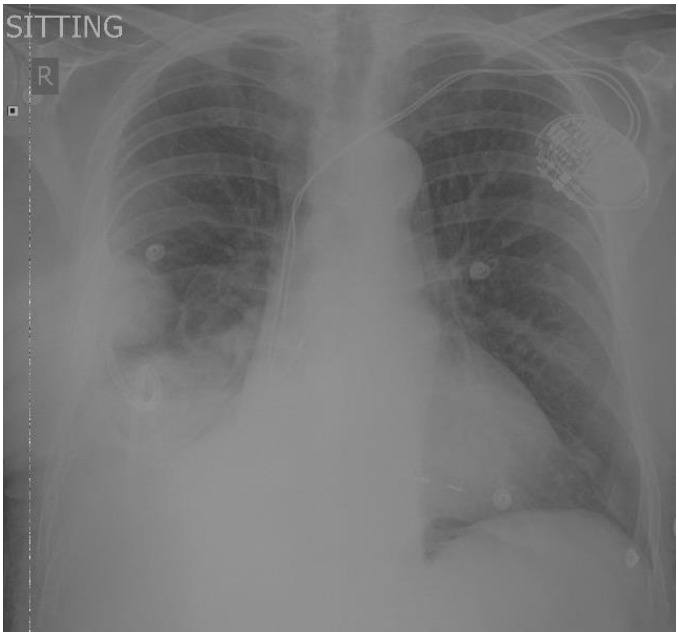

Figure 5. CXR post pleural tap.

Following this, Mr X had a pleural biopsy via a video-assisted thoracoscopic surgery (VATS) procedure and had a right pleural drain inserted. The specimens were reviewed by a local histopathologist at a private

pathology laboratory and the patient was referred to the Oncology unit for further work-up and management whilst awaiting histopathology results.

No PET scan was performed as the nearest PET scanner is over 250km away from the Oncology Practice. With regard to tumour markers (S100), the patient's older records from his melanoma were not available from the 1980s or 1990s. No S100 marker was done as the diagnosis was not a metastatic lesion from the melanoma.

Immuno-histo-chemistry

Histology was done from the biopsy specimens:

Initially, considering the clinical history of previous malignant melanoma, a tentative diagnosis of metastatic malignant melanoma with osteoclast-like giant cells was favoured (Table 1).

Table 1. Immuno-histochemical stains were done and revealed.

Marker	Result	Interpretation
SOX-10	Negative	Rules out melanocytic or neural crest origin (e.g. melanoma, schwannoma).
PRAME	Positive in isolated cells	PRAME is a non-specific marker; can be seen in both benign and malignant settings. Not diagnostic.
Calretinin	Patchy Positive	Suggests presence of mesothelial or reactive mesothelial cells. Not specific to tumour.
OSCAR	Positive in scattered cells	OSCAR (pan-cytokeratin) suggests focal epithelial features, but not a dominant feature.
BAP1	Positive (retained expression)	Nuclear retention of BAP1 argues against malignant mesothelioma.
CD45	Positive in normal lymphocytes	Confirms presence of background lymphoid cells; tumour is not of lymphoid origin.
HMB45	Negative	Rules out melanoma and other PEComas.
Vimentin	Strongly and diffusely positive	Suggests mesenchymal origin, which aligns with many soft tissue tumours, including TGCT.
MUM-1	Negative	MUM-1 negativity excludes significant plasma cell or lymphoid differentiation.
WT-1	Patchy positive	Highlights mesothelial or entrapped mesothelial cells; not specific for the tumour itself.

Key: SOX-10: transcription factor that is part of a gene family with a DNA-binding HMG box domain; PRAME: preferentially expressed antigen in melanoma; BAP1: OSCAR: Osteoclast-associated receptor; BRCA1-associated protein; CD45: Cluster of Differentiation 45; HMB45: Human Melanoma Black 45; MUM-1: multiple myeloma oncogene-1; WT-1: Wilms's Tumour 1; Due to the complexity of the case as described in the Immuno-histochemistry stains seen (see Table 1), it was sent to Cape Town for a second histopathological opinion, where a professor in histopathology/cytopathology reviewed the diagnosis. This caused a delay in commencing treatment of around 3 weeks for the patient.

Microscopy showed the following (verbatim): "multiple cellular fragments of neoplastic tissue. Some of the fragments have overlying surface fibrin. In some of the fragments collagenous areas are present. The tumour comprised both solid and pseudo-alveolar areas. The solid areas comprised diffuse groups of tumour cells. The tumour cells were mononuclear with eosinophilic cytoplasm and slightly conspicuous nucleoli. There were admixed macrophages. In addition, there were unevenly distributed osteoclast-type giant cells. In other areas, the tumour cells were discohesive, forming pseudo-alveolar structures. Within some of these areas, blood lakes were present which were not lined by endothelium. Tumour cells were seen floating in the blood lakes. In these blood lakes, hemosiderin-laden macrophages were present. Some of the tumour cells are surrounded by fibrin. In some of the more collagenous areas, these cells appear more spindled rather than epithelioid. Mitotic activity is present. Melanin pigment was not appreciated".

From Table 2, the final diagnosis stated from the pleural biopsy was 'Extra-Articular Tenosynovial Giant Cell Tumour, Diffuse Type'.

Table 2. Repeat immunohistochemistry revealed the following findings.

Marker / Stain	Result	Interpretation
OSCAR	Positive at periphery, negative in most cells	Suggests epithelial origin in periphery; not significant overall
CD45	Scattered positive cells	Scattered lymphoid cells; not a lymphoid neoplasm
Calretinin	Scattered cytoplasmic positivity in mesothelial cells	Highlights entrapped/reactive mesothelial cells
BAP-1	Diffuse nuclear retention	No loss; argues against mesothelioma
WT-1	Weak nuclear positivity in many cells	Highlights mesothelial cells; not tumour-specific
Vimentin	Diffuse positive staining	Consistent with mesenchymal origin
HMB45	Negative	Rules out melanoma
SOX-10	Negative	Rules out neural crest tumours (e.g., melanoma, schwannoma)
PRAME	Some nuclear positivity	Non-specific; seen in some neoplastic and benign processes
MUM-1	Scattered positivity in plasma cells	Reflects background immune cells
Melan A	Negative	Rules out melanoma
CD68	Diffuse positive; highlights multinucleated giant cells	Typical for histiocytic origin in tenosynovial giant cell tumour
p63	Interpreted as negative	Argues against epithelial or myoepithelial differentiation
AE1/AE3	Positive in some cells, similar to OSCAR	Focal epithelial marker expression; non-specific
ERG	Positive in blood vessels only	Normal vascular staining; not tumour-specific
Desmin	Scattered positive tumour cells	Suggests some myoid differentiation; may be non-specific
Perl's Prussian Blue	Positive in hemosiderophages and some tumour cells	Indicates iron deposition; common in tenosynovial giant cell tumour

Key: SOX-10: transcription factor that is part of a gene family with a DNA-binding HMG box domain; PRAME: preferentially expressed antigen in melanoma; BAP1: OSCAR: Osteoclast-associated receptor; BRCA1-associated protein; CD45: Cluster of Differentiation 45; HMB45: Human Melanoma Black 45; MUM-1: multiple myeloma oncogene-1; WT-1: Wilms's Tumour 1; PRAME: PReferentially expressed Antigen in Melanoma; CD68: Cluster of Differentiation 68; AE1/AE3: Anion Exchanger 1/ Anion Exchanger 3; ERG: ETS-related gene.

Oncology

Mr X presented to Oncology on 5 June 2024, with a history of shortness of breath and cough. A working diagnosis of recurrent metastatic malignant melanoma was favoured at the time, based on histopathological morphological findings and the previous clinical history of melanoma. He had an ECOG performance status of 2 and was planned for systemic therapy for metastatic malignant melanoma.

After review of the updated histopathology report and the diagnosis of TGCT, Imatinib was considered as part of the therapeutic options as well as radiotherapy to the large thoracic masses for symptomatic control. Other treatment options were not available and Denosumab would have been a good choice, but Mr X had more visceral disease than skeletal involvement. From the initial presentation, his condition declined.

On 18 July 2024, a repeat CT scan was performed. It showed significant disease progression in the necrotic pleural based mass along the right hemithorax with right lower zone empyema. There was also mediastinum and right hilum lymphadenopathy present.

Mr X also had a CT scan of the brain as he was confused to exclude brain metastases which came back negative.

The patient ultimately succumbed to his illness and passed away on 22 July 2024.

Discussion

A South African article published by Tontu et al. in 2024, described Denosumab in managing TGCT in a 21-year-old female (8). Unfortunately, in our patient, this drug was not available. Furthermore, in Mr X, it was initially thought that the lung lesion was a metastatic lesion, rather than second primary lesion. It has been found that a biopsy of a suspicious lesion can confirm if there is a relapse of the tumour or exclude the second primary tumour in metastatic lesions (9). We postulate that biopsies of suspected (likely) metastatic lesions may reveal that some of these lesions may actually be a second primary lesion. This could impact management as a different regimen of drugs may be considered. An article published by Zheng et al. supports this as it was found that around 25% of patients diagnosed with cancer have a second primary malignancy (10). Another interesting finding from Mr X was the association with melanoma. This case may support a rare co-occurrence, although causality is unproven between TGCT and melanoma, as this would be the second case documented (to our knowledge) of such an association in such a rare condition.

Immunohistochemistry assisted greatly with the diagnosis. The initial comment from the histopathologists mentioned that "Vimentin positivity may be seen in melanoma, however, the negative SOX-10, HMB45 and only patchy positive PRAME, demand that other possibilities be considered. Vimentin positivity is seen in a host of other tumours including mesothelioma (excluded with calretinin and BAP1 stains), sarcomas and giant cell tumours, the latter of which may be considered in this case given the morphology of the tumour, except the tumour site is quite unusual" (11). Considering this and the second opinion of an expert immuno-histopathologist, the diagnosis was male.

The "best clinical management of tenosynovial giant cell tumour (TGCT): A consensus paper from the community of experts" published in 2022 was designed to assist with helping clinicians with the management of TGCT (1). Colony-stimulating factor 1 receptor (CSF1R) inhibitors are effective for symptomatic benefit and improves the quality of life of patients with TGCT but is not available in many countries (1). In South Africa, this drug is not available; however, a drug with the tradename "Turalio" is available for treatment of TGCT internationally (12). If a patient is diagnosed with TGCT, it is recommended that they go to expert centres with experienced sarcoma multidisciplinary treatment team (1). Thereafter a joint decision can be made about active surveillance vs active treatment, surgery, radiotherapy, cryotherapy or systemic treatment (1). In South Africa, teams like this exist in Cape Town; however, given the patient's advanced stage of disease, he was not considered for referral for this multidisciplinary team. It is likely that the delay in commencing treatment also led to the progression of disease in this patient, highlighting the need for referring patients like this to such teams.

With regards to clinical decision making, Imatinib was used as it inhibits the tyrosine kinase activity of the CSF1R, which is an important protein which affects the growth and proliferation of these tumours. Using this drug would result in the pathway being blocked, which would lead to shrinkage of the tumour which would improve symptoms (13). The other drug considered was Denosumab which is a systemic monoclonal antibody against the Receptor Activator of Nuclear factor Kappa-B (RANK) ligand, which has been used in patients with giant cell tumours of the bone (14). Our rationale of using Imatinib over Denosumab was that Denosumab is used for bone metastasis in most cases. In the case of Mr X, there was no clear evidence of bone involvement so Imatinib was favoured as his tumour showed mostly soft tissue (lung parenchyma) involvement. Of note, there isn't a clear guideline or consensus on this as the case is uncommon.

Conclusion

TGCT is a rare condition which may or may not be associated with melanoma. We recommend that suspected metastatic melanoma lesions be biopsied to establish or refute this association.

Acknowledgement

Pathcare (private laboratory) assisted with the Histopathology on this case. We would like to thank the histopathologists who were involved in producing the pathology reports: Dr Jaravaza, Dr Sengoatsi and Prof Govender.

Author contribution

RRC and **SK** were both involved in writing/editing the manuscript.

Conflict of interest

The author declares no conflict of interest associated with this paper.

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Ethical considerations

All information was anonymised to ensure patient confidentiality. Permission for using anonymised patient data was granted by Cancercare.

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