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Case report

Malignant triton tumor of the anterior mediastinum: a rare tumor in a rare location ☆,☆☆

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ABSTRACT

Malignant triton tumors are an extremely aggressive form of malignant peripheral nerve sheath tumor that display rhabdomyosarcomatous features. While these tumors are extremely rare, they have a much higher incidence in patients with neurofibromatosis-1. We present a case of a 64-year-old male with neurofibromatosis-1 who presented to the hospital with sudden worsening of shortness of breath and dysphagia to solids. Radiological examination revealed a large mass in the anterior mediastinum causing significant narrowing and displacement of the upper trachea and esophagus. Biopsy of the mass, done by interventional radiology, demonstrated features of an MTT. The mass was subsequently resected but without confirmation of tumor-free margins and the patient underwent adjuvant radiation therapy. Repeat radiological examination approximately four months later revealed growing malignancy and new metastases, which eventually contributed to the patient's death seven months after his presentation to the hospital.

Introduction

Malignant triton tumors (MTTs) are a rare subtype of malignant peripheral nerve sheath tumors with rhabdomyoblastic differentiation (MPNSTs), which upon gross examination are firm, large, grayish tan masses often with areas of hemorrhage and necrosis [1]. MPSNTs are quite rare themselves, as they comprise 5%-10% of all soft tissue sarcomas, and MTTs account for about 5% of all MPSNTs [2]. They are extremely aggressive, even more so than MPSNTs, and associated with a poor prognosis and high rate of recurrence, even with resection and adjuvant radiation therapy [3]. They are commonly associated with neurofibromatosis-1 (NF-1), with more than half of MTT cases being associated with NF and the rest arising sporadically [2]. Most MTTs have been noted to arise in the head, neck, and trunk regions with occurrence in the mediastinum being fairly rare [4]. We present a case of a 64-year-

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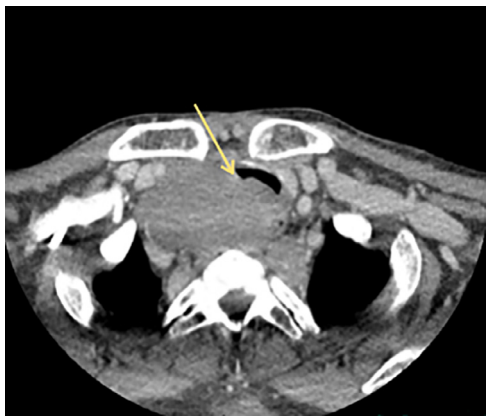

Fig. 1 – Axial and sagittal CT images of the chest with contrast showing large mediastinal mass (yellow arrows) compressing the trachea and esophagus (color version of figure is available online.)

old male with NF-1 who was diagnosed with malignant triton tumor of the mediastinum, underwent subtotal resection and adjuvant radiation therapy, and subsequently had a recurrence that eventually led to his death.

Case report

A 64-year-old African-American male with a past medical history significant for NF-1 presented to the emergency department complaining of worsening shortness of breath, coughing episodes, and occasional episodes of difficulty swallowing solid foods. For the past two weeks, he had a sore throat, rhinorrhea, and occasional chills. He denied any weight loss, voice changes, or sick contacts. At presentation to the emergency department, he had a blood pressure of 112/73 mm Hg, pulse of 108 beats/min, temperature of 36.2°C, respiratory rate of 15 breaths/min, and oxygen saturation of 100% on room air. Initial physical examination revealed palpable anterior neck masses, chest masses, and respiratory distress with stridor but no wheezing or rales.

Initial chest X-ray demonstrated non-specific elevation of the right hemidiaphragm obscuring the right lung base. Computed tomography (CT) scan of the thorax with contrast (Figs. 1-4) demonstrated a large mass measuring 7.7 by 5.2 by 7.3 cm in the upper mediastinum causing significant narrowing and anterior displacement of the upper thoracic trachea and esophagus.

A left chest wall mass and splenic masses consistent with metastasis were also found (Figs. 3 and 4). CT soft tissue of the neck with contrast revealed a large homogenous non-enhancing soft tissue mass at the level of the thoracic inlet, extending inferiorly within the superior mediastinum, measuring 4.8 by 7.1 by 6.1 cm and displacing the trachea, esophagus, and surrounding vascular structures without evidence of invasion or encasement (Figs. 5 and 6). Multiple other smaller subcutaneous soft tissue masses throughout the head and neck consistent with neurofibromatosis noted on CT were also

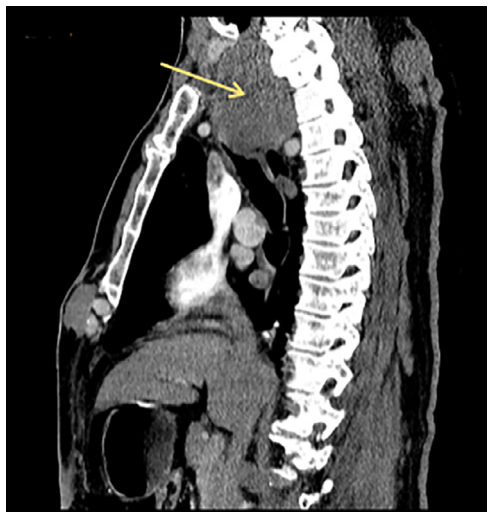

Fig. 2 – Axial and sagittal CT images of the chest with contrast showing large mediastinal mass (yellow arrows) compressing the trachea and esophagus (color version of figure is available online.)

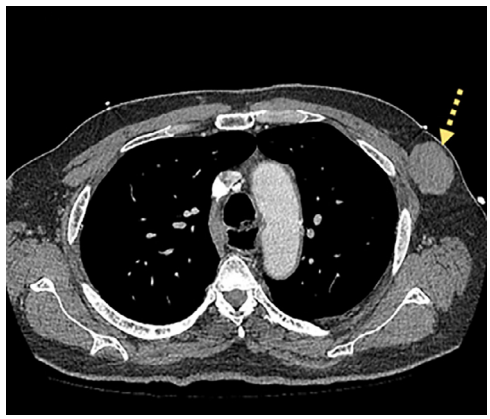

Fig. 3 – Axial and coronal CT images of the chest with contrast showing left chest wall mass (yellow dotted arrow), anterior mediastinal mass (yellow solid arrow), and splenic mass (yellow arrowhead) (color version of figure is available online.)

seen on magnetic resonance imaging (MRI) done more than a decade prior (Fig. 7).

Due to concern for airway obstruction as well as presence of mediastinal mass, cardiothoracic surgery (CT) and ear-nose-throat surgery were consulted. Both services suggested admission to the medical intensive care unit for airway observation, biopsy of the mass by interventional radiology, possible intubation if needed, and treatment with dexamethasone. In line with these recommendations, patient was admitted to the medical intensive care unit and on day three of hospitalization, interventional radiology performed an ultrasound guided core biopsy (Figs. 8 and 9) of the patient's mediastinal

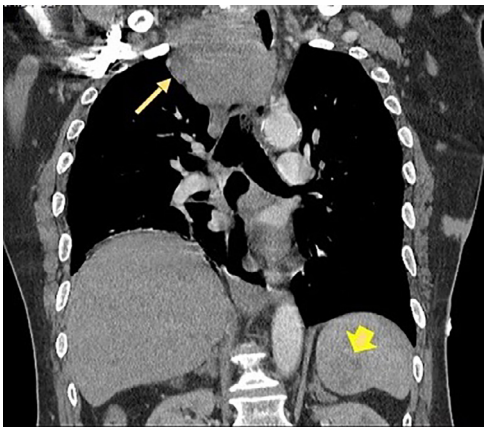

Fig. 4 – Axial and coronal CT images of the chest with contrast showing left chest wall mass (yellow dotted arrow), anterior mediastinal mass (yellow solid arrow), and splenic mass (yellow arrowhead) (color version of figure is available online.)

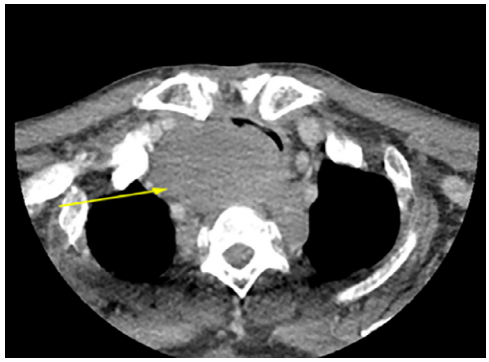

Fig. 6 – Axial CT showing large homogenous non-enhancing soft tissue mass at the level of the thoracic inlet (yellow arrow), extending inferiorly within the superior mediastinum, displacing the trachea, esophagus, and surrounding vascular structures without evidence of invasion or encasement (color version of figure is available online.)

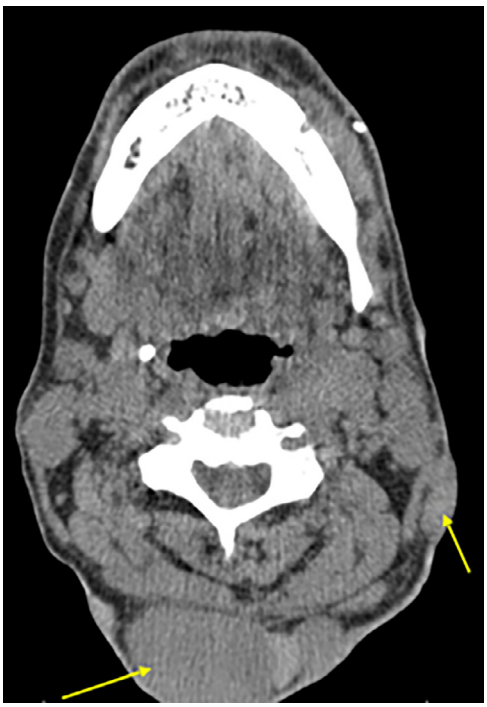

Fig. 5 – Axial CT soft tissue of the neck showing multiple masses seen throughout the soft tissues of the neck with the largest mass seen in the suboccipital region (yellow arrows) (color version of figure is available online.)

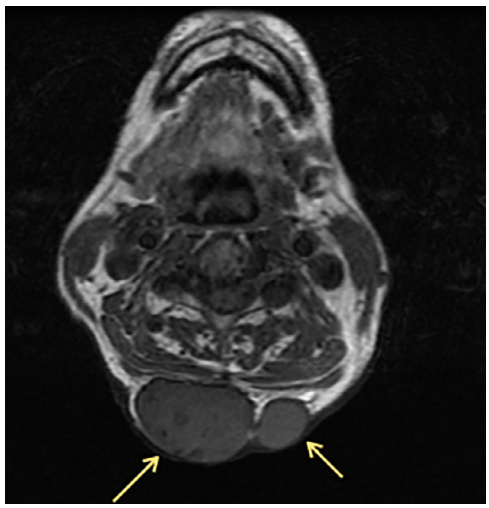

Fig. 7 – Axial T1-weighted MRI image showing soft tissue masses in posterior head and neck (yellow arrows) (color version of figure is available online.)

mass with four samples being sent for histologic evaluation.

Pathologic examination of the samples was significant for a high-grade spindle cell sarcoma with a focal fascicular pattern and myxoid stroma containing numerous large pleomorphic cells with eccentric nuclei and abundant eosinophilic cytoplasm consistent with rhabdomyoblasts.

Immunohistochemistry was positive for S-100, desmin, myogenin, and CD57 and negative for SOX-10 and MART-1 (Figures A-I). In light of these findings in the setting of neurofibromatosis, pathology indicated a diagnosis of malignant peripheral nerve sheath tumor with rhabdomyoblastic differentiation, also known as malignant Triton tumor.

In light of patient's dysphagia, a barium swallow was performed on day seven to evaluate for obstruction, revealing severe stenosis of the proximal esophagus secondary to mass effect but no evidence for invasion. Considering the aggressive nature of this type of tumor, on day eight of hospitalization CT surgery performed a median sternotomy with resection of mediastinal mass and radical excision of cervical mass. Surgically negative margins were not able to be obtained through the majority of the masses were excised. Post-surgery, the patient's diet was eventually advanced from clear liquids to a regular diet, which was tolerated, and he was discharged in

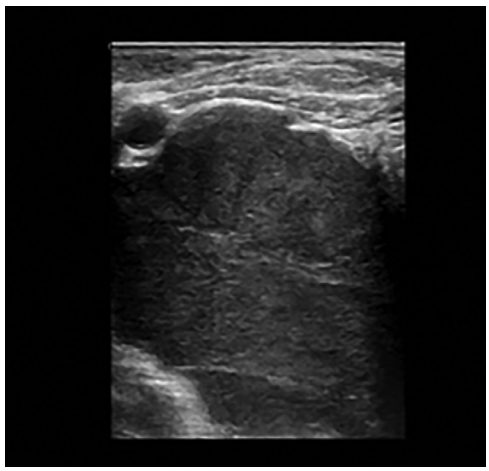

Fig. 8 – Ultrasound-guided biopsy of right anterior mediastinal mass. (A) Hematoxylin and Eosin (H&E) 200x, (B) H&E 400x, (C) S100 100x (Positive), (D) S100 200x (Positive), (E) Desmin 200x (Positive), (F) Myogenin 200x (Positive), (G) CD57 200x (Positive), (H) SOX-10 200x (Negative), (I) MART-1 100x (Negative).

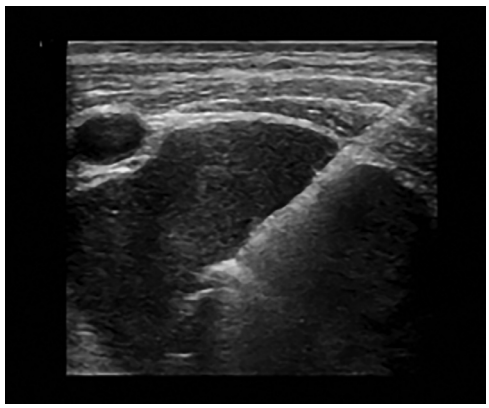

Fig. 9 – Ultrasound-guided biopsy of right anterior mediastinal mass. (A) Hematoxylin and Eosin (H&E) 200x, (B) H&E 400x, (C) S100 100x (Positive), (D) S100 200x (Positive), (E) Desmin 200x (Positive), (F) Myogenin 200x (Positive), (G) CD57 200x (Positive), (H) SOX-10 200x (Negative), (I) MART-1 100x (Negative).

stable condition on day fourteen to a rehabilitation facility. Given lack of surgically negative margins, the aggressive nature of this tumor and the presence of likely metastases, referrals were made for the patient to see radiation oncology for outpatient follow-up.

The patient subsequently underwent a course of adjuvant radiotherapy over the next two months. Approximately four months after surgical resection of his tumor, a CT scan of the thorax with contrast was performed to assess treatment response. This demonstrated new and enlarging masses including 2.9 cm and 3.5 cm lesions anterior to the sternum (Fig. 10), a persisting mass in the superior mediastinum extending into the posterior mediastinum measuring 4.5 cm (previously 3.8

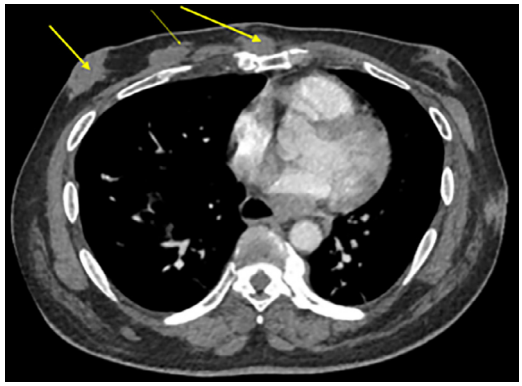

Fig. 10 – Axial CT of the thorax showing new and enlarging masses anterior to the sternum (yellow arrows) (color version of figure is available online.)

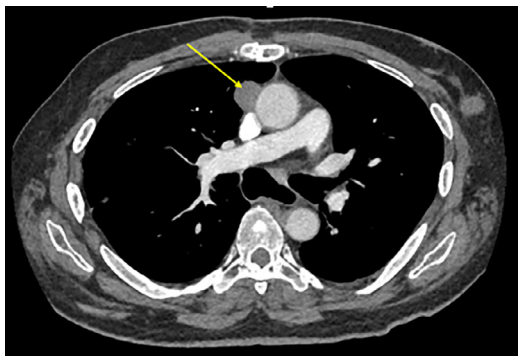

Fig. 11 – Axial CT of the thorax showing enlarging anterior mediastinum nodule adjacent to the ascending aorta (yellow arrow) (color version of figure is available online.)

cm) with smaller surrounding lesions, an enlarging anterior mediastinum nodule adjacent to the ascending aorta (Fig. 11) measuring 19 mm (previously 7 mm), and new small nodules measuring 5 and 7 mm in the left and right lower lung lobes, respectively (Fig. 12). In addition to these findings suggestive of growing malignancy and new metastases, there was a new focus of airspace disease in the anterior basal segment of the right lower lobe. Due to findings suggestive of cancer progression, the patient was referred to medical oncology for chemotherapy as well as palliative care for end-of-life discussions. The patient ultimately passed away approximately seven months after his initial presentation.

Discussion

MPNSTs are exceptionally rare tumors, occurring at an incidence rate of 0.001% within the general population; however, in patients with NF-1, their incidence is much higher at 4.6% [5]. MTTs are even rarer, accounting for 5% of MPNSTs [2,5]. While MPNSTs imply that the tumor arises from peripheral nerve sheaths or coverings, this is not definitively defined and the actual cell of origin may have multiple sources [6]. MPN-

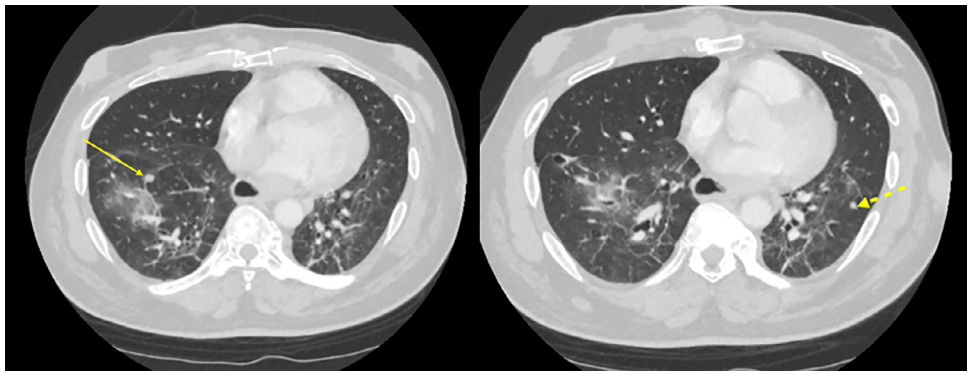

Fig. 12 – Axial CT of thorax showing new small modules measuring 7 mm in the right lower lung lobe (solid yellow arrow) and 5 mm in left lower lung lobe (dashed yellow arrow) (color version of figure is available online.)

STs usually occur in the third to sixth decade of life but can occur earlier in the setting of NF-1; given that NF-1 patients already have multiple peripheral nerve sheath tumors, they are at increased risk for malignant transformation, especially in deeper plexiform neurofibromas [6]. Our patient, despite having NF-1, presented with a MTT at a later age than what is usually observed.

MTTs are a subtype of MPNSTs with rhabdomyoblastic differentiation. The term MTT was first used in 1973 and a set of diagnostic criteria were defined: a) the tumor arises along a peripheral nerve or in the setting of NF-1 b) the cells have a growth pattern similar to that of Schwann cells c) rhabdomyoblasts are present and occur independently of an extrinsic rhabdomyosarcoma [7]. Immunohistochemical staining is often used to aid the identification of tumor cells. S-100 and CD57 positivity is seen as an indication of nerve sheath differentiation whereas desmin, actin, and myogenin positivity is used to evaluate for the presence of rhabdomyoblastic differentiation [3,8,9]. SOX-10 is a transcription factor vital in neural crest cell differentiation and is commonly expressed in melanomas as well as tumors with Schwann cell differentiation [10]. MART-1 is a melanocytic marker used to differentiate non-melanocytic tumors from primary or metastatic melanoma [11]. Our patient's tumor, in being positive for S-100, CD57, desmin and myogenin but negative for SOX-10 and MART-1, was suggestive of a nerve sheath tumor with rhabdomyoblastic differentiation.

The head, neck, and trunk regions are reported to be common areas of MTT occurrence, with 20% of MTTs reported in the head and neck, 32% in the trunk, and 24% in the extremities; occurrence in the mediastinum, heart, or lungs is rare and occurs in <10% of cases [2,12].

Chaudry et al. report that, as of 2018, only thirteen cases of mediastinal MTTs have been reported in the literature, of which only five were noted in the anterior mediastinum [12]. The prognosis of MTTs is very poor with a five-year survival rate of only 5%-15% in comparison to MPNSTs, where it is 50%-60% [4]. A literature review done by Ducatman et al. of 120 cases of MPNSTs suggests that large tumor size, the presence of neurofibromatosis, and incomplete resection are negative prognostic factors [5]. Other studies have indicated the following as prognostic factors: tumor size >10 cm at diagnosis, metastases, as well as location [12,13].

Prognosis appears to be better when the head, neck, or extremities are involved [12]. On the other hand, prognosis is more guarded with mediastinal, retroperitoneal, buttock, or trunk involvement [12,14]. Our patient had a mediastinal tumor with metastases at presentation as well as coexisting NF-1. Furthermore, he had incomplete resection of his tumor likely due to the difficulty of attaining tumor free margins within the mediastinum, contributing to a poor prognosis. In a case series done by Chaudhry et al., of thirteen cases involving mediastinal Triton tumors, ten developed recurrences after treatment, demonstrating the aggressive nature of this malignancy in the mediastinum [12].

Ultimately, the diagnosis of MTT requires a biopsy to differentiate between benign and malignant tumors, as conventional imaging is not a reliable indicator [6]. However, Ahlawat et al. suggest that magnetic resonance imaging (MRI) using diffusion-weighted index/apparent diffusion coefficient (DWI/ADC) mapping can be used to accurately differentiate between benign and malignant peripheral nerve sheath tumors [15]. There are some findings that may suggest malignancy on conventional CT or MRI though, such as tumor size >5 cm, invasion of fat planes, heterogeneous character, irregular margins, and edema [16]. A number of case reports in the literature describe the following as imaging findings associated with MTTs: large size, irregular margins, heterogeneity, isodense T1 and long T2 signals on MRI, heterogenous contrast enhancement after gadolinium administration, and heterogenous diffusion restriction in diffusion-weighted MRI and ADC map [17–20]. Li et al. indicate some features common to MTTs and MPNSTs, such as ill-defined margins, intratumoral lobulation, surrounding edema, calcifications, and destruction of surrounding bone. At the same time, they highlight some features specific to MTTs including the presence of a mass-like shadow and a septum within the mass accompanied by possible hemorrhagic, necrotic, and cystic changes [21].

As noted, before, our patient presented with a MTT at a later age than what is usually observed given his NF-1 status. Patients with NF-1 who develop MTTs tend to be male and younger whereas those who have sporadic occurrences tend

to be female and older [22]. This is only the sixth case, as far as we know, of an anterior mediastinal MTT. There has only been one case of mediastinal MTT presenting at a later age but this was in a female patient without NF-1 [22].

Ultimately, this case represents a highly unusual occurrence considering the patient's age, the tumor's location, and the rarity of the tumor itself.

Conclusion

MTTs, as a result of being a rare phenomenon, pose a lot of questions regarding diagnosis and treatment. While some studies have indicated types of diagnostic imaging or features found on studies that may suggest MTT over other types of tumors, biopsy and pathological classification remains the definitive diagnostic methodology. An effective treatment algorithm remains elusive. Even with total resection and adjuvant radiation therapy, recurrence rates remain high especially in mediastinal tumors. Our patient had a rare mediastinal presentation of an already rare disease; his coexisting NF-1 combined with the location of his tumor contributed to a poor prognosis.

More research is needed to help delineate between MTTs and benign tumors on imaging and evaluate the value of imaging as a screening tool for MTT in NF-1 patients, considering their heightened risk for malignant transformation.

Ethics approval

This is a retrospective case report not requiring ethics approval.

Patient consent

All patient data has been removed and no informed consent is required to participate.

Consent for publication

All patient data has been removed and no informed consent is required to publish.

Authors' contribution

All authors contributed to writing this manuscript. All authors read and approved the final manuscript.

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