Difficulties in the diagnosis and treatment of axillary malignant triton tumors: A case report

YANHUA ZHOU[1], LU LI[2], FEIFENG LAN[1], LI QIN[1] and DONGNING HUANG[1]

[1]Department of Oncology, The Liuzhou Worker's Hospital, Liuzhou, Guangxi Zhuang Autonomous Region 545005, P.R. China;
[2]Department of Radiology, The Liuzhou Worker's Hospital, Liuzhou, Guangxi Zhuang Autonomous Region 545005, P.R. China

Received September 10, 2024; Accepted December 6, 2024

DOI: 10.3892/ol.2025.14893

Abstract. Malignant triton tumor (MTT), a subtype of malignant peripheral nerve sheath tumor, is a rare soft-tissue sarcoma with a difficult diagnosis and poor prognosis. The course of MTT progression is rapid and the degree of malignancy is high. Patients with MTT can be treated with postoperative adjuvant radiotherapy and chemotherapy; however, treatment results are still poor. The present study describes a case of MTT of the axilla, which was diagnosed using histopathology with immunohistochemical staining and gene mutation detection. Complete surgical excision of the left axillary mass was performed in September 2023. Postoperative therapeutics included radiation therapy and deep hyperthermia; nine-field intensity-modulated radiation was delivered to the left axilla (46 Gy in 23 fractions over 5 weeks) and concurrent deep hyperthermia was performed three times per week for 5 weeks. In February 2024, the patient received oral anlotinib at a dose of 10 mg daily (before breakfast) for 2 weeks. It was demonstrated that a combination of surgery, radiation therapy, deep hyperthermia and targeted therapy may improve the survival of patients with MTT. After 1 month of comprehensive treatment, the patient's tumor had disappeared upon reexamination. As of the latest follow-up in October 2024, the patient had achieved a disease-free survival period of ~7 months, the patient was stable and remained on anlotinib treatment with good tolerance. With no standardized treatment recommendations available, the present study demonstrated that the combination of surgery, radiation therapy, deep hyperthermia and targeted therapy may provide a new strategy for the clinical treatment of MTT.

Correspondence to: Professor Dongning Huang or Professor Li Qin, Department of Oncology, The Liuzhou Worker's Hospital, 156 Heping Road, Liunan, Liuzhou, Guangxi Zhuang Autonomous Region 545005, P.R. China
E-mail: hdnliuzhou@163.com
E-mail: angelandy515@163.com

Key words: malignant triton tumor, malignant peripheral nerve sheath tumor, radiotherapy, tyrosine kinase inhibitors, hyperthermia

Introduction

Malignant peripheral nerve sheath tumors (MPNSTs) are rare soft-tissue sarcomas with an incidence of 0.001% in the general population as recorded in the Surveillance, Epidemiology, and End Results database (1). The global 5-year overall survival rate, 5-year event-free survival and local recurrence rate were reported to be 49, 37 and 38%, respectively (2). The primary risk factor for developing MPNST is neurofibromatosis type-1 (NF1), with ~10% of patients with NF1 experiencing this condition in their lifetime (3). In addition, ~5% of MPNST cases are induced by radiation (4). Originating from the sheaths of peripheral nerves, MPNST is a high-grade tumor made up of spindle cells (5), which is difficult to diagnose and relies on pathological results (6). According to World Health Organization standards, MPNST can be divided into several types, including low-grade MPNST, high-grade MPNST, epithelioid MPNST, perineurial MPNST and malignant melanotic schwannian tumors (7). Its differential diagnosis includes melanoma, clear cell sarcoma and epithelioid sarcoma (8). Le Guellec *et al* (9) reported that 29 tumors (18.1%) that were initially diagnosed as MPNST were reclassified on the basis of histological review, immunohistochemistry and molecular analysis. Goertz *et al* (10) studied a group of 65 cases of MPNST, for which the diagnosis of 32.3% of cases needed to be amended, indicating that the diagnosis of MPNST is challenging. Currently, there is no established treatment for MPNST, and most available options are derived from methods used to treat soft tissue tumors. Although surgery is the treatment of choice for MPNST, its aggressive nature makes achieving a full or wide resection challenging. The use of radiation, chemotherapy and targeted therapy for MPNST is still limited and uncertain, because of the lack of treatment methods with proven benefit (11).

MTT is a rare, highly aggressive subtype of MPNST with rhabdomyosarcomatous differentiation, and represents ~5% of all MPNST cases (1). To date, ~248 cases of MTT have been reported in the literature worldwide and the male-to-female incidence ratio is 1.5:1 (12). MTTs are more common in the head, neck, trunk and limbs (13), while mediastinal lesions are rarely observed. To date, ~20 cases of mediastinum MTT have been reported in studies published in English (14). MTTs are more common in middle-aged individuals and rare in children (15), with <50 cases in children reported

to date (16,17). Compared with MPNST, MTT has a higher degree of malignancy, is more invasive and is less common in clinical practice (18). The outcome of MTT remains poor after comprehensive surgical and chemoradiotherapy treatment (14). Owing to the rarity of this disease, no consensus exists for the treatment of MTT. The current study presents a case of an MTT of the axilla and describe the patient's clinical features, diagnosis and treatment. The purpose of the present study is to provide clinical strategies for the diagnosis and treatment of MTT.

Case report

A 60-year-old female patient presented at The Liuzhou Worker's Hospital (Liuzhou, China) in September 2023, reporting a tingling sensation in the axilla, secondary to a mass in the left axilla that had increased in size over the past 20 years. Physical examination demonstrated that the mass had a tough texture, clear boundaries with surrounding tissues and no local rupture; additionally, it was firm and accompanied by mild tenderness. Magnetic resonance imaging (MRI) demonstrated a left axillary lesion measuring 5.7x5.7x7.7 cm (Fig. 1), a clear boundary of the lump, low T1-weighted imaging (WI), high T2WI, uneven and significant enhancement on enhanced scanning and compression of the axillary arteries and veins. Therefore, a nerve sheath tumor was suspected. The patient's lactate dehydrogenase (LDH) level was within the normal range at 137 U/l (normal range, 120-250 U/l). Throughout the treatment process (from September 2023 to October 2024) the LDH level remained within the normal range, and routine blood and biochemical indicators were normal. Complete surgical excision of the left axillary mass was performed in September 2023. Grossly, the tumor measuring 5.0x4.7x6.5 cm had a capsular sheath with adhesion of the axillary artery and vein, and the ulnar and median nerves.

Immunohistochemical analysis was performed using 5-μm paraffin-embedded tissue sections that had been fixed with 10% neutral formalin at room temperature for 24 h. The sections were baked at 65˚C for >2 h, dewaxed three times with xylene and then hydrated with a series of alcohol solutions. For antigen retrieval, sections were heated in EDTA buffer (pH 9.0) in a 100˚C water bath for 20 min and were then blocked with 3% hydrogen peroxide at room temperature for 10 min. The tissue sections were then incubated with a ready-to-use cytokeratin 20 antibody (Ks20.8; cat. no. Kit-0025), spectral cytokeratin antibody (AE1/AE3; cat. no. Kit-0009), vimentin antibody (MX034; cat. no. MAB-0735), H3K27Me3 antibody (RM175; cat. no. RMA-0843), S-100 antibody (4C4,9; cat. no. Kit-0007), Sox-10 antibody (EP268; cat. no. RMA-0726), desmin antibody (MX046; cat. no. RMA-0766), smooth muscle actin (SMA) antibody (1A4; cat. no. Kit-0006), Ki67 antibody (MXR002; cat. no. RMA-0731), integrase interactor 1 (INI-1) antibody (MRQ-27; cat. no. MAB-0696), programmed cell death-ligand 1 (PD-L1) antibody (MXR025; cat. no. RMA-1057), epithelial membrane antigen (EMA) antibody (E29; cat. no. Kit-0011), myogenin differentiation 1 (MYOD1) antibody (MX049; cat. no. MAB-0822), CD34 antibody (MX123; cat. no. MAB-1076), Bcl-2 antibody (MX022; cat. no. MAB-0711) and HMB-45 antibody (HMB45; cat. no. MAB-0098) (all from Fuzhou Maixin Biotechnology Development Co., Ltd.) for 1 h at room temperature, or with PBS (Fuzhou Maixin Biotechnology Development Co., Ltd.) as a negative control. Detection of primary antibody binding sites was carried out using the MaxVision™ HRP-Polymer anti-Mouse/Rabbit IHC Kit (cat. no. KIT-5030; Fuzhou Maixin Biotechnology Development Co., Ltd.) at room temperature for 1 h. DAB was used for color development. Hematoxylin counterstaining was also performed at room temperature for 2 min. The tissue sections were then sealed and observed under a light microscope (ECLIPSE Ci-L; Nikon Corporation). This process used a fully automated immunohistochemical staining instrument (Lumatas; Fuzhou Maixin Biotechnology Development Co., Ltd.). Hematoxylin and Eosin staining of the tumor sample was performed at room temperature for 45 min and was observed under a light microscope (ECLIPSE Ci-L; Nikon Corporation), which displayed a heterogeneously differentiated tumor consisting of spindle-shaped cells with a high mitotic index (Fig. 2A), gland-like epithelioid cells (Fig. 2B), focal necrosis and differentiated areas of rhabdomyosarcoma (Fig. 2C). Immunohistochemistry demonstrated that the neoplasm was positive for vimentin (Fig. S1A), EMA (Fig. S1B), MYOD1 (Fig. S1C), S-100 (Fig. S1D), Sox-10 (Fig. S1E), CD34 (Fig. S1F), Bcl-2 (Fig. S2A), desmin (Fig. S2B), SMA (Fig. S2C), INI-1 (Fig. S2D) and mosaic loss of H3K27me3 expression (Fig. 3A). The Ki-67 proliferation index was 75% (Fig. 3B). Markers such as pancytokeratin (CKpan; Fig. 3C), CK20 (Fig. 3D), HMB-45 (Fig. S2E) and (PD-L1 (Fig. 3E) were negative.

The VAHTS Universal DNA Library Prep Kit for Illumina V4 (cat. no. ND610-02; Nanjing Novozymes Biotech Co., Ltd.) was used to prepare the patient's surgical axillary tissue specimen DNA samples for sequencing. The Qsep 100 fully automated nucleic acid and protein analysis system (BiOptic, Inc.) was used to verify the quality/integrity of the processed samples. Next-generation sequencing (NGS) was then performed (paired end sequencing; nucleotide length, 150 bp) using the Novaseq X Series 10B Reagent Kit (300 cycles; cat. no. 20085594; Illumina, Inc.) or NovaSeq X Series 25B Reagent Kit (300 cycles; cat. no. 20104706; Illumina Inc.); the loading concentration of the final library was 150 pmol. Vardict 1.8.3 (19) was used to analyze the data (open source). NGS (Fig. 3F) demonstrated the presence of mutations in the NF1 tumor suppressor gene (NF1: exon 30 c.4084C>T p.R1362, with a mutation abundance of 2.40%).

To further exclude the diagnosis of synovial sarcoma, tumor cells underwent fluorescence *in situ* hybridization (FISH) detection according to the instructions of the SS18 gene two-color breakage probe kit (cat. no. FP-055; Wuhan Kanglu Biotechnology Co., Ltd.,). The FISH interpretation criteria were as follows: The normal negative signal pattern consisted of two yellow signals fused with red and green, while the typical positive signal pattern cosisted of a separated signal of one yellow, one red and one green (with a red green signal separation diameter of ≥2 signal points). A total of 100 tumor cells from at least two tumor regions were counted, and the proportion of positive signal cells ≥13% was defined as SS18 gene rearrangement positive. FISH (Fig. 3G) for the SS18/SYT gene rearrangement was negative. On the basis of aforementioned findings, the patient was diagnosed with MPNST with rhabdomyosarcomatous differentiation, also known as MTT.

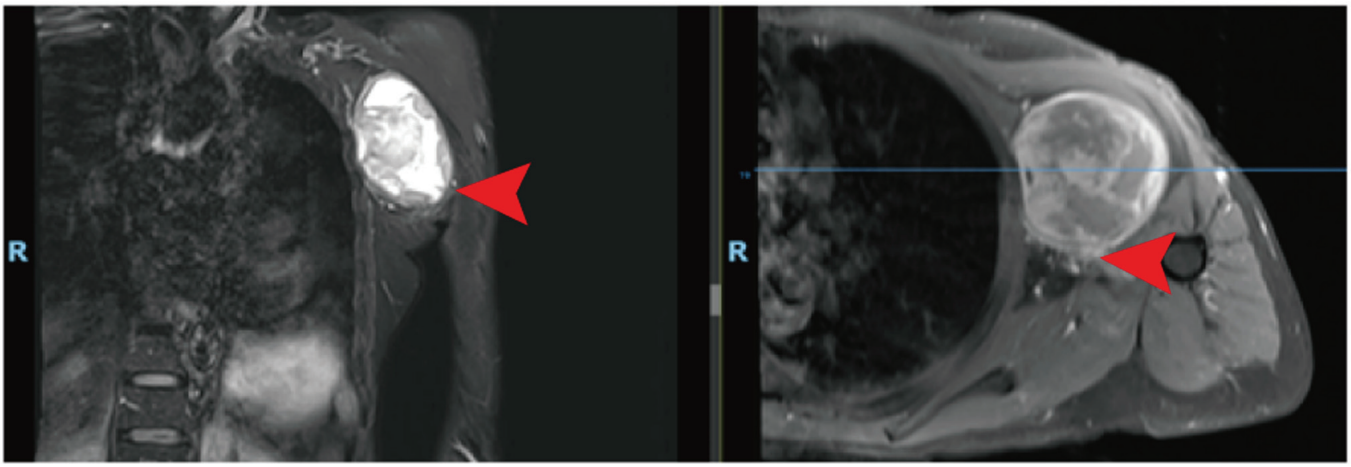

Figure 1. Magnetic resonance imaging was used to identify a left axillary lesion measuring 5.7x5.7x7.7 cm, from which a diagnosis of a nerve sheath tumor was initially suspected; the arrows indicate the tumor.

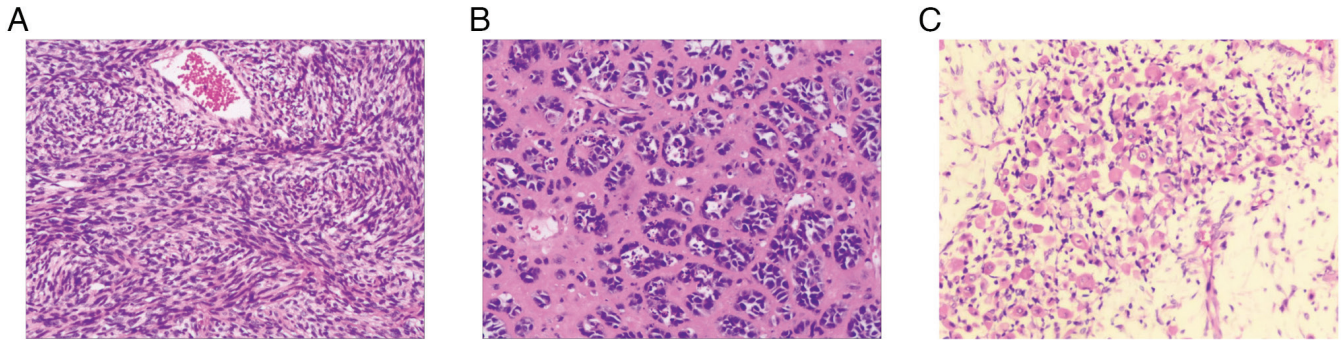

Figure 2. Representative histological images of the tumor sample. (A) Pathological examination demonstrated areas of the tumor comprising spindle-shaped cells arranged in a staggered bundle pattern (H&E; magnification, x10). (B) Partial tumor areas exhibited epithelial-like cell differentiation, with a visible glandular arrangement (H&E; magnification, x10). (C) Differentiation area of rhabdomyosarcoma (H&E; magnification, x10).

The patient was staged as pT2N2M0 or IIIA according to the staging criteria of the 8th edition of the American Joint Committee on Cancer Staging System (20), combined with preoperative MRI and postoperative pathology.

A whole-body ^{18}F-fluorodeoxyglucose-positron emission/computed tomography (^{18}F-FDG PET/CT; Fig. 4) scan was performed 40 days after surgery and showed an FDG-avid lesion 3.6x3.4x3.4 cm in size in the left axilla, which was interpreted as early local recurrence. Secondary surgery could not be considered, as due to the involvement of the axillary artery and vein there was a risk of bleeding. Postoperative therapeutics included radiation therapy and deep hyperthermia; nine-field intensity-modulated radiation was delivered to the left axilla (46 Gy in 23 fractions over 5 weeks; Fig. 5) and concurrent deep hyperthermia was performed three times per week for 5 weeks. Later, in January 2024, reexamination via MRI confirmed the reduction of tumor size (2.8x1.1x1.1 cm; Fig. 6A). In February 2024, the patient received oral anlotinib at a dose of 10 mg daily (before breakfast) for 2 weeks. An MRI reexamination of the left upper arm indicated that the tumor had entirely disappeared after 1 cycle (included 2 weeks of being on the regimen and 1 week off) of tyrosine kinase inhibitor (TKI)-targeted therapy (Fig. 6B). The patient developed hypertension following the first cycle of TKI-targeted administration, which was well controlled after antihypertensive treatment (nifedipine controlled-release tablets 30 mg orally, once daily). As of the latest follow-up in October 2024, the patient was stable and remained on anlotinib treatment with good tolerance, with follow-up occurring every 2-3 months.

Discussion

First described by Masson (21) in 1932, MTT is a rare, highly aggressive subtype of MPNST with rhabdomyosarcomatous differentiation (22). The etiology of MTT remains elusive, but there is an association with NF1 mutations (23). In a systematic literature review of 34 patients and a retrospective, single-center study of 16 patients, Marcel *et al* (24) demonstrated that primary MTTs were large, lobulated tumors with necrotic areas, low T1WI, high T2WI and heterogeneous enhancement, features which were suggestive but non-specific, and that they were difficult to distinguish from other types of MPNSTs on the basis of imaging alone. S-100 and Sox-10 are specific protein markers of Schwann cells. However, a study by Karamchandani *et al* (25) examining protein expression levels of Sox-10 and S-100 markers in 1,012 specimens, which included 78 cases of MPNST, demonstrated that the sensitivities of Sox-10 and S-100 protein for the detection of MPNSTs

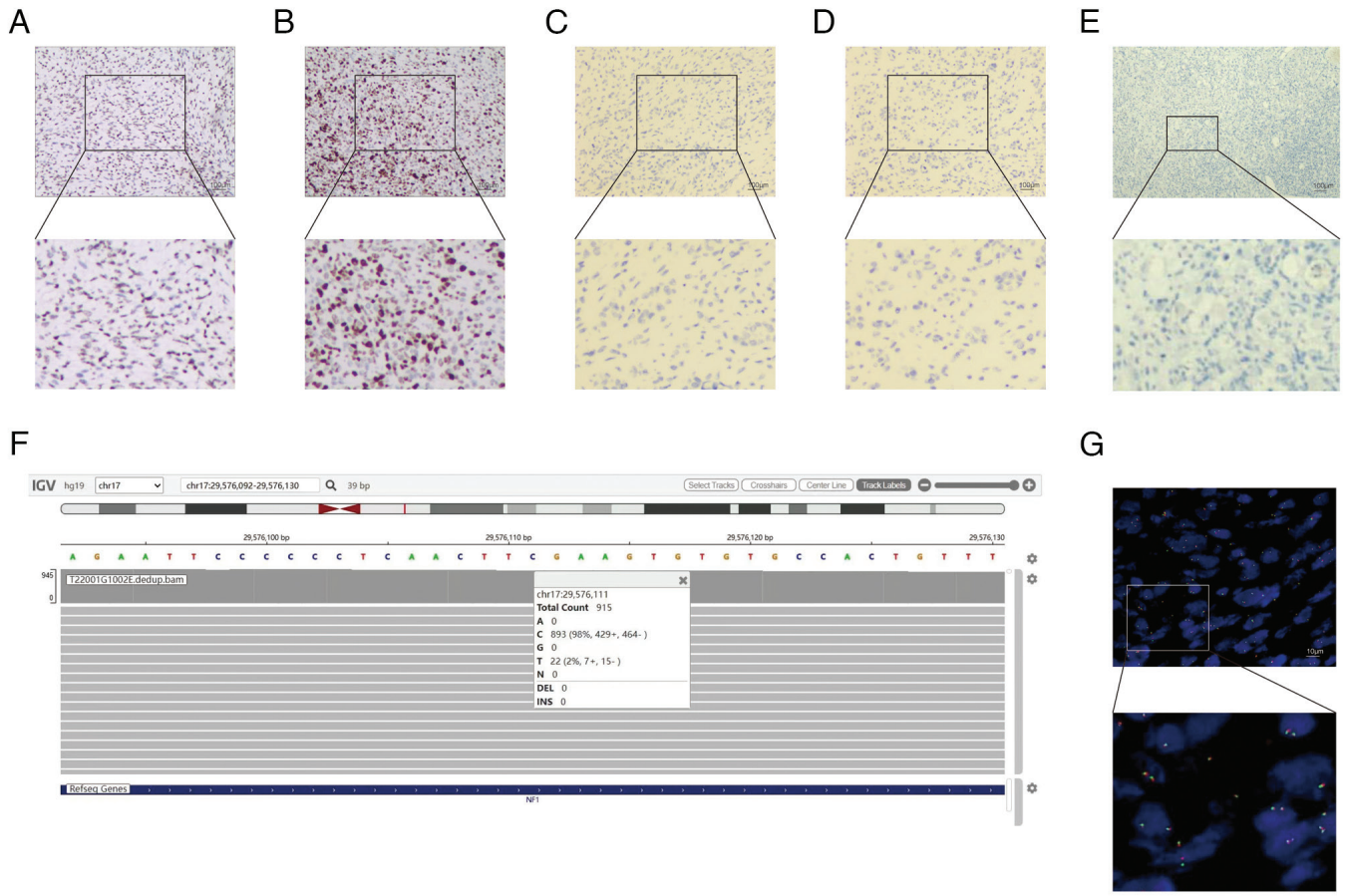

Figure 3. Representative immunohistochemistry images of the tumor sample. Immunohistochemistry showed (A) mosaic loss of H3K27me3 expression (magnification, x10; magnification in subpart, x4.44) and (B) a Ki-67 proliferation index of 75% (magnification, x10; magnification in subpart, x4.44). Immunohistochemistry was negative for (C) pancytokeratin (magnification, x10; magnification in subpart, x4.44), (D) CK20 (magnification, x10; magnification in subpart, x4.44) and (E) programmed cell death-ligand 1 (magnification, x10; magnification in subpart, x4.44). (F) Next-generation sequencing identified mutations present in the NF1 tumor suppressor gene (915 reads were sequenced, 789 of which were normal base C, and 22 mutated to T, denoted as c4084C>T). (G) Fluorescence *in situ* hybridization for SS18/SYT gene rearrangement was negative (magnification, x100; magnification in subpart, x2.74).

were 27 and 40%, respectively. The loss of H3K27me3 expression is a sensitive marker for MTT, with H3K27me3 negativity found in 95% of cases (26).

In the present case, the patient's LDH level was 137 U/l, which is a normal level that may indicate that the patient could achieve a good prognosis if they actively cooperated with treatment. Jurisic *et al* (27) reported that the intracellular characteristics of LDH enzymes are sensitive indicators of the cellular metabolic state, aerobic or anaerobic direction of glycolysis, activation status and malignant transformation, and that analysis of LDH activity is useful for the early diagnosis and treatment of tumors. The patient of the present study had no medical history of the condition NF1 or radiation therapy. MRI revealed a left axillary lobulated mass measuring 5.7x5.7x7.7 cm, with low T1WI, high T2WI and heterogeneous enhancement. Pathological examination suggested that certain tumor areas exhibited epithelial-like cell differentiation, with a visible glandular arrangement. Essentially, these areas are sarcoma cells, some poorly differentiated cell sarcomas often exhibit epithelioid cells (28). The immunohistochemical markers CKpan and CK20 in the patient's epithelium were negative, which can exclude an epithelial origin (29,30). These findings validated the diagnosis of a sarcoma and the presence of such cells indicated glandular elements, which are exceedingly rare (31). The results of immunohistochemistry demonstrated positive Sox-10 and S-100 staining, and mosaic loss of H3K27me3 expression, suggesting a diagnosis of MTT. However, the diagnosis of synovial sarcoma could be fully ruled out, due to the focal and weak expression of EMA (32). Further genetic testing was therefore necessary for the present patient. FISH conducted for the SS18/SYT gene rearrangement was negative, in conjunction with mutation of the NF1 tumor suppressor gene, which are consistent with the diagnosis of MTT (32).

MTT is a rare, highly aggressive disease with a poor prognosis, and no standardized treatment recommendations are currently available. At present, the treatment of MTT is primarily surgery, supplemented with radiotherapy and chemotherapy (12,14). A meta-analysis reported that the 5-year survival rate of patients with MTT was 14%, with a median overall survival time of 13 months (15). Complete surgical resection and local adjuvant radiotherapy are reported to improve patient prognosis (33,34). However, radiotherapy processes vary from center to center, including the choice of radiotherapy technology and the way radiation doses are segmented. The commonly used chemotherapeutic agents include ifosfamide, vincristine, carboplatin and dactinomycin, but there is currently no consensus on the optimal chemotherapy treatment (35). Angel *et al* (36) reported that

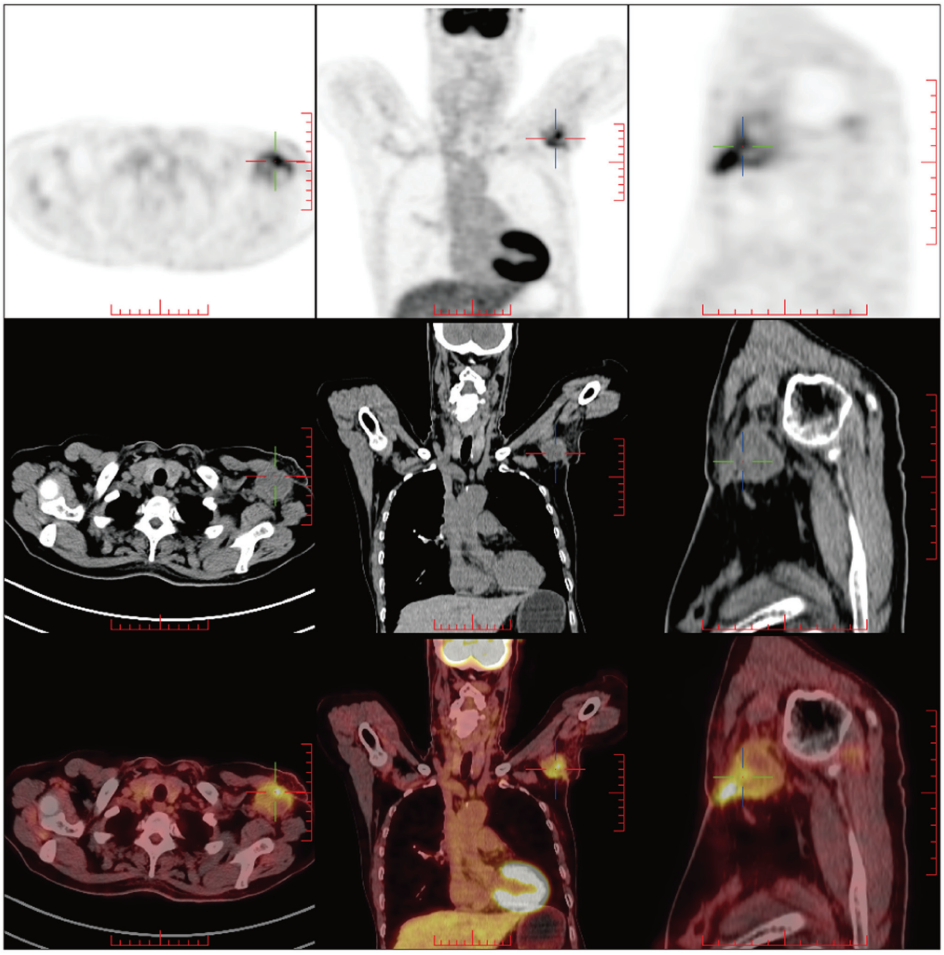

Figure 4. ^{18}F-FDG-positron emission/computed tomography demonstrated an FDG-avid lesion that measured 3.6x3.4x3.4 cm. ^{18}F-FDG, ^{18}F-fluorodeoxyglucose.

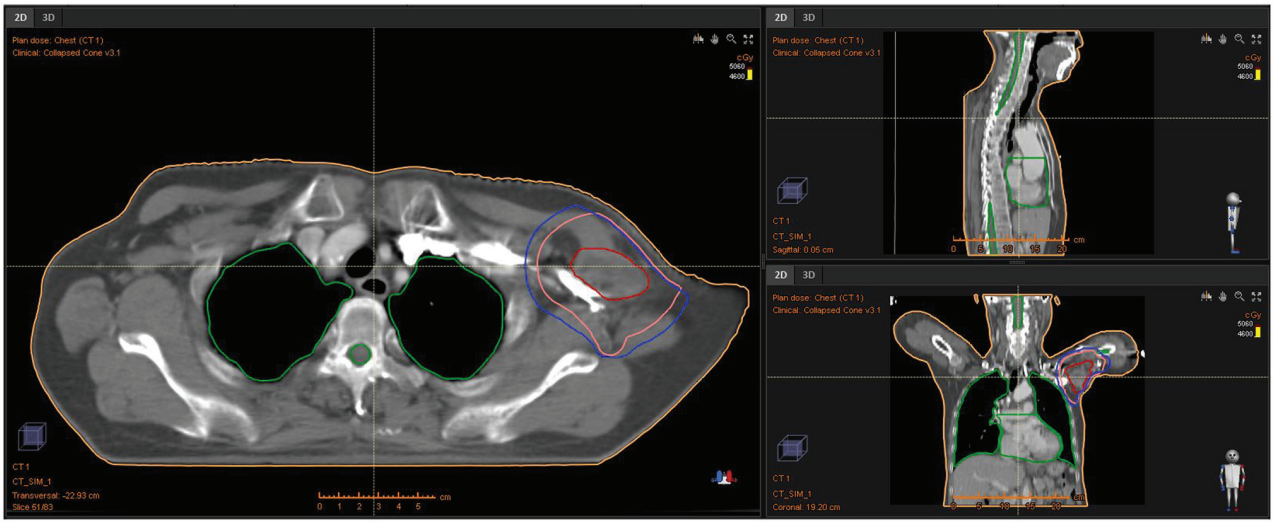

Figure 5. The 64-row computed tomography images indicated the target area range of postoperative therapeutics, including nine-field intensity-modulated radiotherapy targeted to the left axilla.

neoadjuvant chemotherapy followed by surgical resection and adjuvant chemotherapy is also a treatment option for MTT. A number of studies have been conducted ranging from bench work to clinical trials on hyperthermia combined with chemoradiotherapy and targeted therapy to improve the treatment effects on tumors, which confirmed the positive effects of hyperthermia as an adjunctive therapy for treating tumors (37-41).

MTT has an aggressive clinical course; the patient in the present study was diagnosed with early local recurrence via

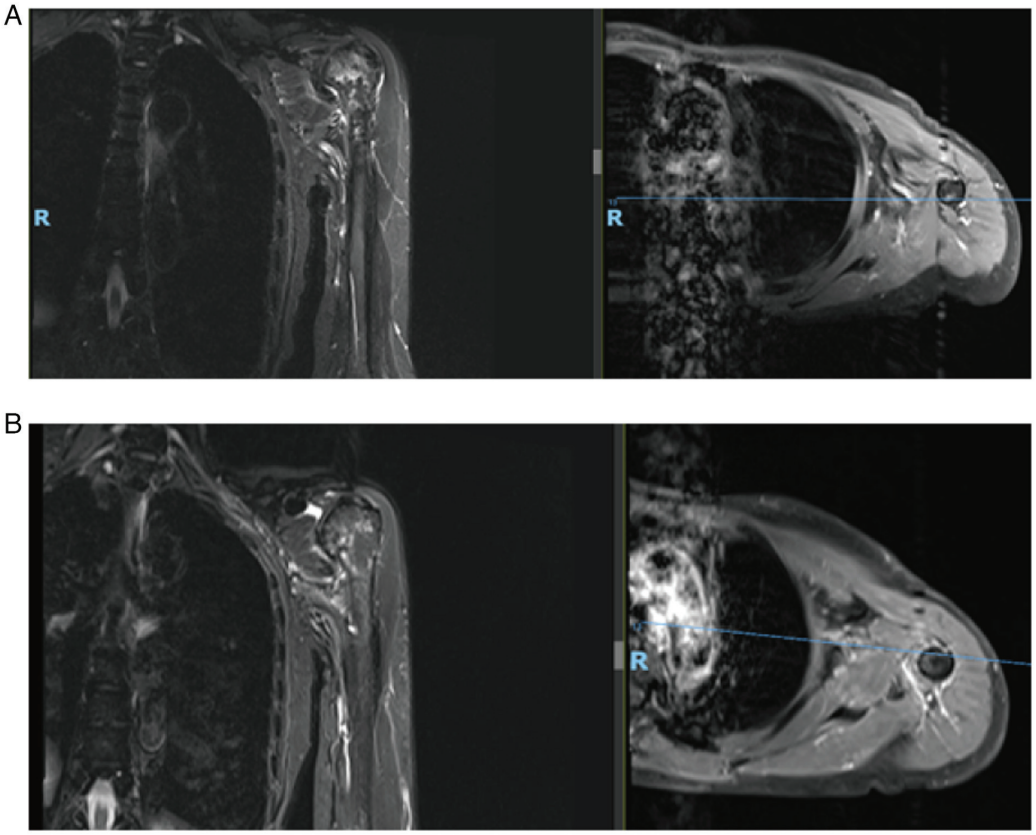

Figure 6. Reexamination of MRI after patient treatment. (A) Reexamination using MRI after radiation confirmed the reduction in the size of the tumor to 2.8x1.1x1.1 cm. (B) Reexamination using MRI after 1 cycle of tyrosine kinase inhibitor-targeted therapy indicated that the tumor had completely disappeared. MRI, magnetic resonance imaging.

^{18}F-FDG PET/CT 40 days after surgery. Following multidisciplinary discussion, the postoperative therapeutics included radiation therapy and deep hyperthermia, followed by TKI-targeted therapy. TKIs are used to treat various tumors with positive EGFR mutations, but TKIs also have adverse effects. Obradovic *et al* (42) reported that rashes and diarrhea are common side effects of TKI therapy in patients with non-small cell lung cancer, and examined the association between EGFR polymorphisms and TKI-associated toxicities. This previous study revealed that out of nine EGFR single-nucleotide polymorphisms related to TKI side effects, rs11568315, rs712829 and rs712830 were associated with skin toxicity. NSCLC carriers of long CA repeats (rs11568315, SL + LL) were revealed to be more likely to develop TKI-associated skin toxicity than short CA repeats (rs11568315, SS). Anlotinib (43) is a novel multitarget TKI that inhibits VEGFR2/3, fibroblast growth factor receptor 1-4, platelet-derived growth factor receptor α/β and stem cell factor receptor (cKit). The most common adverse event observed was hypertension and other common adverse reactions included hypothyroidism, hypertriglyceridemia, diarrhea and hand-foot syndrome.

The primary treatment for MTT is surgery, with adjuvant radiotherapy and chemotherapy, but the efficacy of these treatments is currently unclear (16,17). There is no unified standard for radiation therapy dosage. Previous studies (12,44) reported cases treated with 52 Gy of radiotherapy. In the present case, considering that the tumor was located in the axilla and that high-dose radiotherapy may affect the patient's limb movement and lymphatic return, a radiation dose of 46 Gy was used, which was proven to be safe and effective. PET/CT was used to guide the precise delineation of the target area. Immunotherapy (IO) has shown efficacy in the treatment of various tumor types (45-48), and PD-L1 expression is associated with immune therapy efficacy and prognosis. Compared with low PD-L1 expression levels, high PD-L1 expression levels are associated with a shorter survival time in lung cancer (49). The National Comprehensive Cancer Network (50) guidelines recommend IO combined with or without chemotherapy for patients with advanced lung cancer, which has high expression of PD-L1. Zhou *et al* (51) reported the case of a patient who was misdiagnosed with hepatocellular carcinoma, who received transcatheter arterial chemoembolization combined with lenvatinib and pembrolizumab for 3 months. The patient subsequently underwent surgery and was ultimately diagnosed with MTT using postoperative pathology and immunohistochemistry. This was the first application of PD-1 inhibition in MTT. In the present study, the expression levels of PD-L1 were first detected to guide treatment. As PD-L1 was negative, the TKI anlotinib was used to treat the disease instead of IO, which was the first reported application of anlotinib therapy in MTT.

To the best of our knowledge, the present case was the first application of deep hyperthermia for MTT. Radiation therapy and deep hyperthermia were well tolerated by the patient without significant adverse effects. The patient developed hypertension following the first cycle of TKI-targeted

administration, which was well controlled after antihypertensive treatment (nifedipine controlled-release tablets 30 mg orally, once daily). An MRI reexamination indicated that the tumor had entirely disappeared after 1 cycle of TKI-targeted therapy. Currently, the patient remains on anlotinib treatment with good tolerance. The present study reported the use of TKI-targeted therapy with MTT, and focused on its efficacy and adverse reactions. As of the latest follow-up in October 2024, the patient had achieved a disease-free survival (DFS) period of ~7 months, the patient was stable and remained on anlotinib treatment with good tolerance .The issue of the treatment duration with anlotinib and whether maintenance therapy should be continued should be further examined.

In summary, MTT is a rare, highly aggressive disease with a poor prognosis that is difficult to diagnose using radiological imaging only. The present study reported the case of a 60-year-old patient diagnosed with MTT by the clinical features, MRI, histopathology [e.g. Sox-10(+), S-100(+)] and genetic testing (NGS of NF1 mutations and FISH) results, which demonstrated that the tumor was PD-L1-negative. Following multidisciplinary discussions, surgeons did not consider a second surgery. The patient achieved a DFS of ~7 months and good tolerance after undergoing PET/CT-guided moderate-dose radiotherapy, anlotinib-targeted therapy and deep hyperthermia following surgical recurrence. With no standardized treatment recommendations available, the present study demonstrated that the combination of surgery, radiation therapy, deep hyperthermia and targeted therapy may provide a new strategy for the clinical treatment of MTT.

Acknowledgements

Not applicable.

Funding

The present study was a self-funded research project supported by the Autonomous Region Health Commission(grant nos. Z-B20231444 and Z-B20241428).

Availability of data and materials

The data generated in the present study may be requested from the corresponding author. The data generated in the present study using high-throughput next-generation sequencing may be found in the National Center for Biotechnology Information Sequence Read Archive under accession number PRJNA1182037 or at the following URL: https://www.ncbi.nlm.nih.gov/sra/?term=PRJNA1182037.

Authors' contributions

YZ, LL and FL collected the data, including medical images and clinical information, and wrote the original draft. YZ advised on patient treatment. LL and FL analyzed patient data. DH and LQ made substantial contributions to study conception and design, and reviewed and edited the manuscript. YZ and LQ confirm the authenticity of all the raw data All authors read and approved the final version of the manuscript.

Ethics approval and consent to participate

The present study was conducted in accordance with the guidelines of The Declaration of Helsinki and was approved (approval no. KY2024521) by the Ethics Committee of The Liuzhou Worker's Hospital (Liuzhou, China) to ensure that patient information was not misused and privacy information was not leaked, in order to protect the rights and interests of the patient. Written informed consent was obtained from the patient.

Patient consent for publication

Written informed consent was obtained from the patient for publication of the data and the images in this case report.

Competing interests

The authors declare that they have no competing interests.

References

1. Knight SWE, Knight TE, Santiago T, Murphy AJ and Abdelhafeez AH: Malignant peripheral nerve sheath Tumors-A comprehensive review of pathophysiology, diagnosis, and multidisciplinary management. Children (Basel 9): 38, 2022.
2. Cai Z, Tang X, Liang H, Yang R, Yan T and Guo W: Prognosis and risk factors for malignant peripheral nerve sheath tumor: A systematic review and meta-analysis. World J Surg Oncol 18: 257, 2020.
3. Ferner RE and Gutmann DH: International consensus statement on malignant peripheral nerve sheath tumors in neurofibromatosis. Cancer Res 62: 1573-1577, 2002.
4. Riad S, Biau D, Holt GE, Werier J, Turcotte RE, Ferguson PC, Griffin AM, Dickie CI, Chung PW, Catton CN, *et al*: The clinical and functional outcome for patients with radiation-induced soft tissue sarcoma. Cancer 118: 2682-2692, 2012.
5. Widemann BC: Current status of sporadic and neurofibromatosis type 1-associated malignant peripheral nerve sheath tumors. Curr Oncol Rep 11: 322-328, 2009.
6. Okada K, Hasegawa T, Tajino T, Hotta T, Yanagisawa M, Osanai T, Nishida J, Seki K and Itoi E: Clinical relevance of pathological grades of malignant peripheral nerve sheath tumor: A multi-institution TMTS study of 56 cases in Northern Japan. Ann Surg Oncol 14: 597-604, 2007.
7. Louis DN, Ohgaki H, Wiestler OD, Cavenee WK, Burger PC, Jouvet A, Scheithauer BW and Kleihues P: The 2007 WHO classification of tumours of the central nervous system. Acta Neuropathol 114: 97, 2007.
8. Rodriguez FJ, Folpe AL, Giannini C and Perry A: Pathology of peripheral nerve sheath tumors: Diagnostic overview and update on selected diagnostic problems. Acta Neuropathol 123: 295-319, 2012.
9. Le Guellec S, Decouvelaere AV, Filleron T, Valo I, Charon-Barra C, Robin YM, Terrier P, Chevreau C and Coindre JM: Malignant peripheral nerve sheath tumor is a challenging diagnosis: A systematic pathology review, immunohistochemistry, and molecular analysis in 160 patients from the French sarcoma group database. Am J Surg Pathol 40: 896-908, 2016.
10. Goertz O, Langer S, Uthoff D, Ring A, Stricker I, Tannapfel A and Steinau HU: Diagnosis, treatment and survival of 65 patients with malignant peripheral nerve sheath tumors. Anticancer Res 34: 777-783, 2014.
11. Bradford D and Kim A: Current treatment options for malignant peripheral nerve sheath tumors. Curr Treat Options Oncol 16: 328, 2015.
12. Li G, Liu C, Liu Y, Xu F, Su Z, Wang Y, Ren S, Deng T, Huang D, Tian Y and Qiu Y: Analysis of clinical features and prognosis of malignant triton tumor: A report of two cases and literature review. Oncol Lett 10: 3551-3556, 2015.
13. Kamran SC, Howard SA, Shinagare AB, Krajewski KM, Jagannathan JP, Hornick JL and Ramaiya NH: Malignant peripheral nerve sheath tumors: Prognostic impact of rhabdomyoblastic differentiation (malignant triton tumors), neurofibromatosis 1 status and location. Eur J Surg Oncol 39: 46-52, 2013.

14. Tsimpinos M, Pigadiotis E, Kontaxis V and Lioulias A: Giant malignant triton tumour of the posterior mediastinum. Interact Cardiovasc Thorac Surg 33: 657-659, 2021.
15. McConnell YJ and Giacomantonio CA: Malignant triton tumors-complete surgical resection and adjuvant radiotherapy associated with improved survival. J Surg Oncol 106: 51-56, 2012.
16. Bins RB, Pinzon CE, da Silva Pereira LD, Bertuol M, Isolan P and Takamatu EE: Malignant triton tumor of the kidney in a child: A case report. Int J Surg Case Rep 85: 106252, 2021.
17. Zhao A, Ding D, Li X and Wang J: Malignant triton tumor in a child: Case report and literature review. Cancer Manag Res 11: 10759-10766, 2019.
18. Stasik CJ and Tawfik O: Malignant peripheral nerve sheath tumor with rhabdomyosarcomatous differentiation (malignant triton tumor). Arch Pathol Lab Med 130: 1878-1881, 2006.
19. Lai Z, Markovets A, Ahdesmaki M, Chapman B, Hofmann O, McEwen R, Johnson J, Dougherty B, Barrett JC and Dry JR: VarDict: A novel and versatile variant caller for next-generation sequencing in cancer research. Nucleic Acids Res 44: e108, 2016.
20. Amin MB, Greene FL, Edge SB, Compton CC, Gershenwald JE, Brookland RK, Meyer L, Gress DM, Byrd DR and Winchester DP: The eighth edition AJCC cancer staging manual: Continuing to build a bridge from a population-based to a more 'personalized' approach to cancer staging. CA Cancer J Clin 67: 93-99, 2017.
21. Masson P: Recklinghausen's neurofibromatosis, sensory neuromas and motor neuromas. libman anniversary New York, 1932.
22. Woodruff JM, Chernik NL, Smith MC, Millett WB and Foote FW Jr: Peripheral nerve tumors with rhabdomyosarcomatous differentiation (malignant 'Triton' tumors). Cancer 32: 426-439, 1973.
23. de Traux de Wardin H, Dermawan JK, Vanoli F, Jiang SC, Singer S, Chi P, Tap W, Wexler LH and Antonescu CR: NF1-Driven rhabdomyosarcoma phenotypes: A comparative clinical and molecular study of NF1-Mutant rhabdomyosarcoma and NF1-associated malignant triton tumor. JCO Precis Oncol 8: e2300597, 2024.
24. Marcel AD, Aleksandar M, Rainer H, Grüneisen JS, Haubold J, Opitz MK, Bauer S, Umutlu L, Forsting M and Schaarschmidt BM: Impact of CT and MRI in the diagnostic workup of malignant triton tumour-a monocentric analysis and review of the literature. Br J Radiol 97: 430-438, 2024.
25. Karamchandani JR, Nielsen TO, van de Rijn M and West RB: Sox10 and S100 in the diagnosis of soft-tissue neoplasms. Appl Immunohistochem Mol Morphol 20: 445-450, 2012.
26. Otsuka H, Kohashi K, Yoshimoto M, Ishihara S, Toda Y, Yamada Y, Yamamoto H, Nakashima Y and Oda Y: Immunohistochemical evaluation of H3K27 trimethylation in malignant peripheral nerve sheath tumors. Pathol Res Pract 214: 417-425, 2018.
27. Jurisic V, Radenkovic S and Konjevic G: The actual role of LDH as tumor marker, biochemical and clinical aspects. Adv Exp Med Biol 867: 115-124, 2015.
28. Judith VMGB: Jason L. Hornick: Practical soft tissue pathology: A diagnostic approach, 2nd edition. Virchows Arch 473: 785-786, 2018.
29. Mokhtari M, Safavi D, Soleimani N, Monabati A and Safaei A: Carcinoma of unknown primary origin: Application of immunohistochemistry with emphasis to different cytokeratin 7 and 20 staining patterns. Appl Immunohistochem Mol Morphol 30: 623-634, 2022.
30. Tuffaha MMSA, Guski H and Kristiansen G: Immunohistochemistry in Tumor Diagnostics, 2017.
31. Yurina M and Khin T: Malignant peripheral nerve sheath tumor with divergent glandular differentiation. Int J Surg Pathol 25: 310-313, 2017.
32. Who WHO: WHO Classification of Tumours of Soft Tissue and Bone: WHO Classification of Tumours, vol. 5. WHO classification of tumours of soft tissue and bone, 2013.
33. AlAli B and Amr S: Malignant glandular triton tumor arising in the radial nerve with prolonged survival: A case report and review of the literature. Case Rep Pathol 2021: 4614185, 2021.
34. Yasuda M, Muto Y, Kuremoto T, Murakami K, Onisihi T, Koida A, Inui T and Hisa Y: A case of recurrent malignant triton tumor successfully treated with radiotherapy. Auris Nasus Larynx 43: 710-714, 2016.
35. Ailing Z, Daling D, Xueqin L and Jiangtao W: Malignant triton tumor in a child: Case report and literature review. Cancer Manag Res 11: 10759-10766, 2020.
36. Angel G, Jose Luis P, David R and Francisco B: Malignant triton tumor of the kidney. New location not previously reported. Urol Int 99: 121-123, 2015.
37. Ba MC, Long H, Cui SZ, Gong YF, Yan ZF, Wang S and Wu YB: Mild hyperthermia enhances sensitivity of gastric cancer cells to chemotherapy through reactive oxygen species-induced autophagic death. Tumour Biol 39: 1010428317711952, 2017.
38. Ohguri T, Harima Y, Imada H, Sakurai H, Ohno T, Hiraki Y, Tuji K, Tanaka M and Terashima H: Relationships between thermal dose parameters and the efficacy of definitive chemoradiotherapy plus regional hyperthermia in the treatment of locally advanced cervical cancer: Data from a multicentre randomised clinical trial. Int J Hyperthermia 34: 461-468, 2017.
39. Wang Y, Zou L, Qiang Z, Jiang J, Zhu Z and Ren J: Enhancing targeted cancer treatment by combining hyperthermia and radiotherapy using Mn-Zn ferrite magnetic nanoparticles. ACS Biomater Sci Eng 6: 3550-3562, 2020.
40. Yang H, Li M and Mei T: Survival benefit of thermal ablation combined with chemotherapy for the treatment of stage IV nonsmall cell lung cancer: A propensity-matched analysis. Int J Hyperthermia 39: 348-357, 2022.
41. Zhou Y, Zhong Q, Huang D, Qin L, Huang J, Wang C, Chen B, Chen M, Li Y and Liu W: The efficacy of adding hyperthermia to the treatment of advanced NSCLC patients based on the states of EGFR. Aging (Albany NY) 14: 5223-5232, 2022.
42. Obradovic J, Todosijevic J and Jurisic V: Side effects of tyrosine kinase inhibitors therapy in patients with non-small cell lung cancer and associations with EGFR polymorphisms: A systematic review and meta-analysis. Oncol Lett 25: 62, 2023.
43. Si X, Zhang L, Wang H, Zhang X, Wang M, Han B, Li K, Wang Q, Shi J, Wang Z, *et al*: Management of anlotinib-related adverse events in patients with advanced non-small cell lung cancer: Experiences in ALTER-0303. Thorac Cancer 10: 551-556, 2019.
44. Chaudhry I, Algazal T, Cheema A, Al Faraj A, Al Malki N, Mutairi H, Abbas A and Amr S: Mediastinal malignant triton tumor: A rare case series and review of literature. Int J Surg Case Rep 62: 115-119, 2019.
45. Chow LQM, Haddad R, Gupta S, Mahipal A, Mehra R, Tahara M, Berger R, Eder JP, Burtness B, Lee SH, *et al*: Antitumor activity of pembrolizumab in Biomarker-unselected patients with recurrent and/or metastatic head and neck squamous cell carcinoma: Results from the phase Ib KEYNOTE-012 expansion cohort. J Clin Oncol 34: 3838-3845, 2016.
46. Liu SV, Reck M, Mansfield AS, Mok T, Scherpereel A, Reinmuth N, Garassino MC, De Castro Carpeno J, Califano R, Nishio M, *et al*: Updated overall survival and PD-L1 subgroup analysis of patients with extensive-stage small-cell lung cancer treated with atezolizumab, carboplatin, and etoposide (IMpower133). J Clin Oncol 39: 619-630, 2021.
47. Overman MJ, Lonardi S, Wong KYM, Lenz HJ, Gelsomino F, Aglietta M, Morse MA, Van Cutsem E, McDermott R, Hill A, *et al*: Durable clinical benefit with nivolumab plus ipilimumab in DNA mismatch Repair-Deficient/microsatellite Instability-high metastatic colorectal cancer. J Clin Oncol 36: 773-779, 2018.
48. Amin S and Lin C: Immunotherapy plus chemoradiation improves overall survival in stage IV esophageal cancer: A cohort study. Gastro Hep Adv 3: 302-310, 2024.
49. Brody R, Zhang Y, Ballas M, Siddiqui MK, Gupta P, Barker C, Midha A and Walker J: PD-L1 expression in advanced NSCLC: Insights into risk stratification and treatment selection from a systematic literature review. Lung Cancer 112: 200-215, 2017.
50. Ettinger DS, Wood DE, Aisner DL, Akerley W, Bauman J, Chirieac LR, D'Amico TA, DeCamp MM, Dilling TJ, Dobelbower M, *et al*: Non-small cell lung cancer, version 5.2017, NCCN clinical practice guidelines in oncology. J Natl Compr Canc Netw 15: 504-535, 2017.
51. Zhou B, Zhan C, Tian Y, Gao Z and Yan S: Primary hepatic malignant triton tumor mimicking hepatocellular carcinoma by demonstrating arterial-phase hypervascularity and subsequent washout on dynamic contrast-enhanced imaging: A case report and literature review. Front Med (Lausanne) 11: 1361690, 2024.