

A case of primary mediastinal Ewing's sarcoma/primitive neuroectodermal tumor presenting with initial compression of superior vena cava

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Abstract:

Ewing's sarcomas and peripheral primitive neuroectodermal tumors (ES/PNETs) are high grade malignant neoplasms. These malignancies are characterized by a chromosome 22 rearrangement, arise from bone or soft tissue, predominantly affect children and young adults, and are grouped in the Ewing family of tumors. Multimodality treatment programs are the treatment of choice. Primary localization of ES/PNET in the mediastinum is extremely rare. We describe a case of ES/PNET presenting as a mediastinal mass with tracheal compression and initial signs of superior vena cava in a 66-year-old woman.

Key words:

Ewing's sarcoma, extraosseous, extraskeletal, peripheral primitive neuroectodermal tumor

Ewing's sarcomas are high grade relatively rare malignant bone neoplasms that predominantly affect children and young adults and involves the major long bones, pelvis, and ribs. Extraskeletal sites of Ewing's sarcomas (EES) such as chest wall, lower extremities, retroperitoneum and paravertebral region have been observed in about 15% of cases. These tumors are aggressive with a high incidence of local recurrence and distant metastases. Primary mediastinal Ewing's sarcoma and peripheral primitive neuroectodermal tumor (ES/PNET) is extremely rare. Multimodality treatment programs achieve event-free survival rates of 60%.

Case Report

We describe the case of a 66-year-old no smoking woman admitted to our Hospital with dyspnea for tracheal compression, dysphagia, retrosternal pain and signs of initial extrinsic compression of superior vena cava (SVC).

A computed tomography (CT) scan showed multiple lymph nodes extended from the left supraclavicular region to the anterior-superior mediastinum, with encasement of the anonymous arch. The patient was initially submitted to CT guided fine-needle aspiration that failed to obtain adequate tissue for cytopathologic evaluation. In this case, diagnosis can be reached with less invasive and cost-effective procedures (i.e. endobronchial ultrasound-guided transbronchial needle aspiration), but due to unavailable

of technology for endobronchial ultrasound in our hospital, thoracic surgeon performed diagnostic mediastinoscopy.^[1,2] Due to initial signs of SVC, radiotherapy (RT) consultation was required from medical oncologists. Due to the clinical presentation, we planned a primary RT regarding palliation of respiratory symptoms. Before the start of RT we received the result on histopathologic examination that showed small and round blue cells with round nuclei, small nucleoli and scanty cytoplasm. Immunohistochemical analysis revealed positive staining for CD99, vimentin, S-100 and NSE and negative staining for chromogranin A, MELAN-A, thyroid transcription factor-1, DESM, panCK, cytokeratin 7, CK 20 and CEA. Based on these findings, an ES/PNET was diagnosed.

After a multidisciplinary decision-making approach, we delayed the planned RT and the patient received 6 cycles primary chemotherapy in according to Italian Sarcoma Group.^[3]

Restaging CT scan after four cycles demonstrated a partial response [Figure 1a and b]. Chemotherapy was administered with safely profile. After a thoracic surgery consultation, the tumor was considered unresectable.

One month after the end of systemic therapy the patient underwent mediastinal three-dimensional conformal RT. Treatment planning was based on CT scan with 5-mm section

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thickness obtained in the treatment position. Dose-prescription was according to the International Commission of Radiation Unit report 62. The clinical target volume (CTV) and the planning target volume (PTV) were defined using the post-chemotherapy diagnostic CT scan. PTV was obtained with an isotropic expansion of 1 cm of CTV, to include setup error and organ motion. RT was delivered with four individually shaped non coplanar fields to include the entire PTV in the isodose 100% (range, 95%–107%) area, using 6 MV photon beam produced by a linear accelerator (Synergy Platform; Elekta). Total RT dose was 60 Gy administered with daily standard fractionation schedule of 2 Gy.

The maximum dose to the spinal cord was 40 Gy, the percentage of total lung volume exceeding 20 Gy (V_{20}) was 23%; the percentage of esophagus volume exceeding 55 Gy (V_{55}) was 59% [Figure 2a and b].

RT was well tolerated, with relief of persistent mild dyspnea and retrosternal pain.

However, restaging CT scan performed at one month after RT showed a disease progression and the appearance of multiple intraparenchymal lungs metastases.

Then, the patient underwent a second line chemotherapy, interrupted for severe hematologic and gastrointestinal toxicity. Following vertigo and mental changes the patient was submitted to a brain MRI that showed multiple supra and subtentorial metastases. Due to the systemic progression, palliative supportive care was prescribed.

Discussion

Ewing's sarcoma is an uncommon malignant, tumor disease that usually arises in bones or in soft tissues and most commonly affects children and young adults. ES/PNETs are rare and aggressive soft tissue neoplasms, part to Ewing's family, characterized by the presence of the traslocation $t(11;22)(q24;q12)$.

Several studies demonstrated the prognostic impact of tumor stage, size, site and age at diagnosis, with the majority of reports focused on Ewing sarcoma of the bone. As reported in few clinical trials, the outcomes of skeletal Ewing sarcoma are at least similar to that of ES/PNET.^[4]

Only a few published series have reported on Ewing's family in adults; the incidence of ES/PNET is quite variable, but relatively more common in adults, ranging from 9 to 47%.

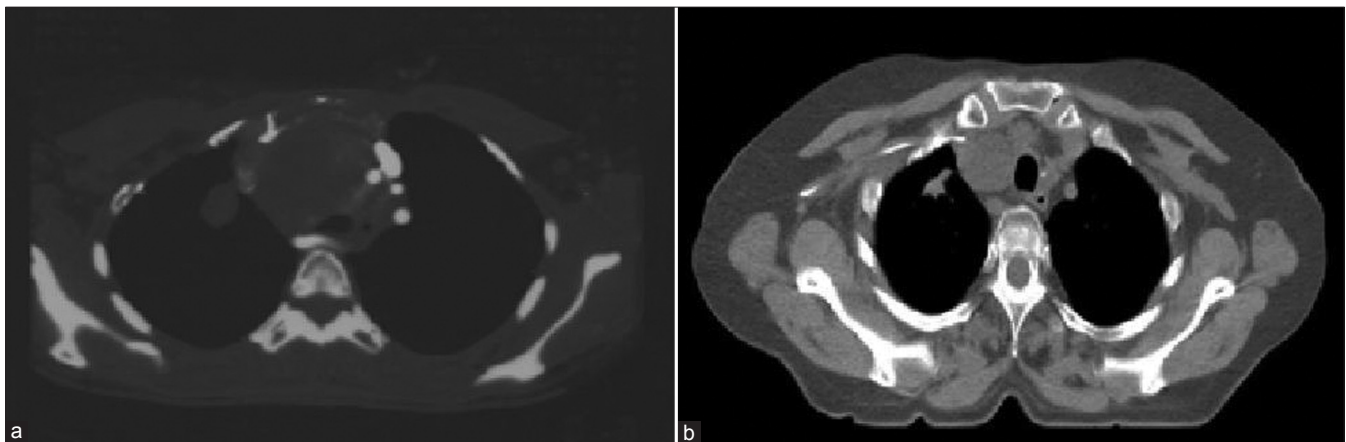


Figure 1: Chest diagnostic CT image in the axial plane pre-chemotherapy (a) and post-chemotherapy (b)

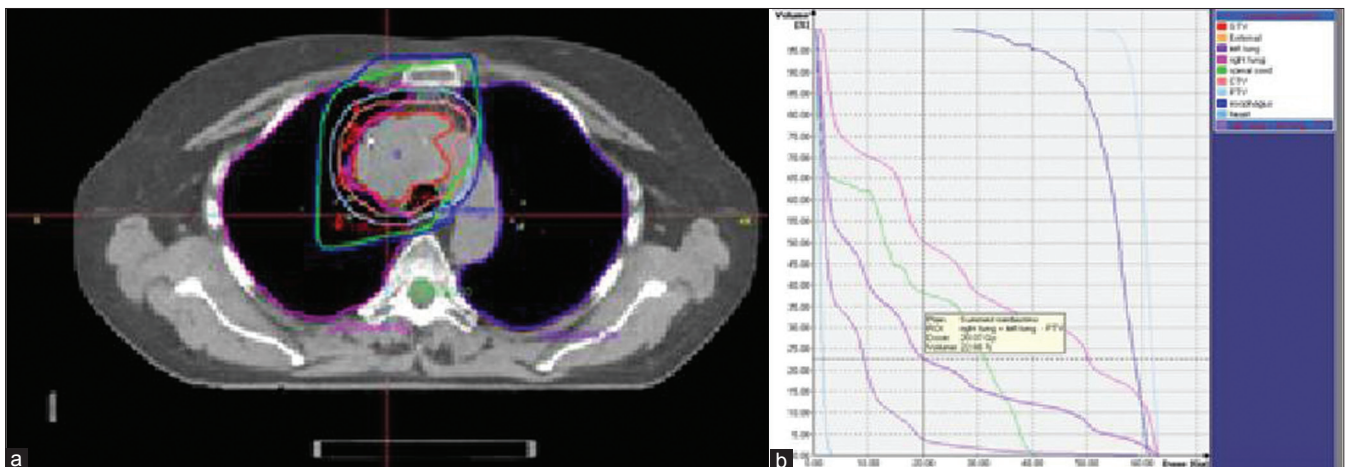


Figure 2: Planning CT (a) and dosimetric values (b)

The clinical features, treatment and prognostic factor of ES/PNET are different and limited to few reports reflecting the rarity of this disease.

In a recent report, Applebaum *et al.* investigated whether patients' characteristics differ from skeletal and EES. EES was also more likely to have a histological classification of PNET *vs* Ewing sarcoma. Patients with EES had a higher mean age compared with patients with bone tumors. Axial location was the most frequent site and there were no differences in tumor size or metastatic status. Five-year overall survival was superior for localized EES compared with localized skeletal tumors.^[5]

The treatment of ES/PNET involves combined modality therapy with chemotherapy and local therapy offered by surgical resection, radiation or both.

The consistent use of more effective chemotherapy regimen in the treatment of localized Ewing's sarcomas during the past two decades increased the rate of 5- and 10-year survival rates until 50 to 60%.

Although Ewing tumors are radiosensitive malignancies, RT does not seem to be curative as a primary local treatment.

There are no randomized studies about the advantage on local control of combined surgery plus RT *vs* surgery alone. However, data from literature suggest a better local control rate when RT is administered after complete surgical resection instead to irradiation alone. Definitive RT with dose ranging from 50 to 60 Gy is the treatment of choice when tumor is unresectable or negative surgical margins cannot be achieved.

ES/PNET arising from mediastinum is extremely rare and only few cases are reported in literature.^[6-8]

Manduch *et al.* described a case of a woman presented with ES/PNET of the posterior mediastinum with extension into the spinal canal, submitted to T3-T5 laminectomy with subsequent multi-drugs chemotherapy regimen.^[9]

Kuzucu *et al.* reported a case of a patient with multifocal intrathoracic mass lesions involving the mediastinum diagnosed as ES/PNET submitted to surgical resection, adjuvant chemotherapy and RT.^[10]

In our report we describe a case of a woman with a large upper mediastinal mass with tracheal compression and progressive dyspnea with initial signs of extrinsic compression of SVC.

In this clinical and radiological setting, the most common malignant causes are non-small-cell lung cancer (approximately 50%), small-cell lung cancer (approximately 25%), lymphoma, and metastatic lesions (each approximately 10%). Germ cell cancer, thymoma, mesothelioma and other cancers are rare. The

location of the tumor and the presentation of acute respiratory distress can change the timing of therapeutic approach. In our patient the initial respiratory symptoms allowed to delay immediate RT and chemotherapy was administered first. Surgical debulking without the intention of achieving clear surgical margins is not recommended and RT was the treatment of choice. Rapid progression of mediastinal mass and the appearance of metastatic brain spread define the aggressiveness of this family of tumors, with still low local control and overall survival rates.

Although ES/PNET arising from mediastinum is extremely rare, it should be considered in the differential diagnosis of SVC in adult patients and may benefit from an aggressive multimodality treatment.

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