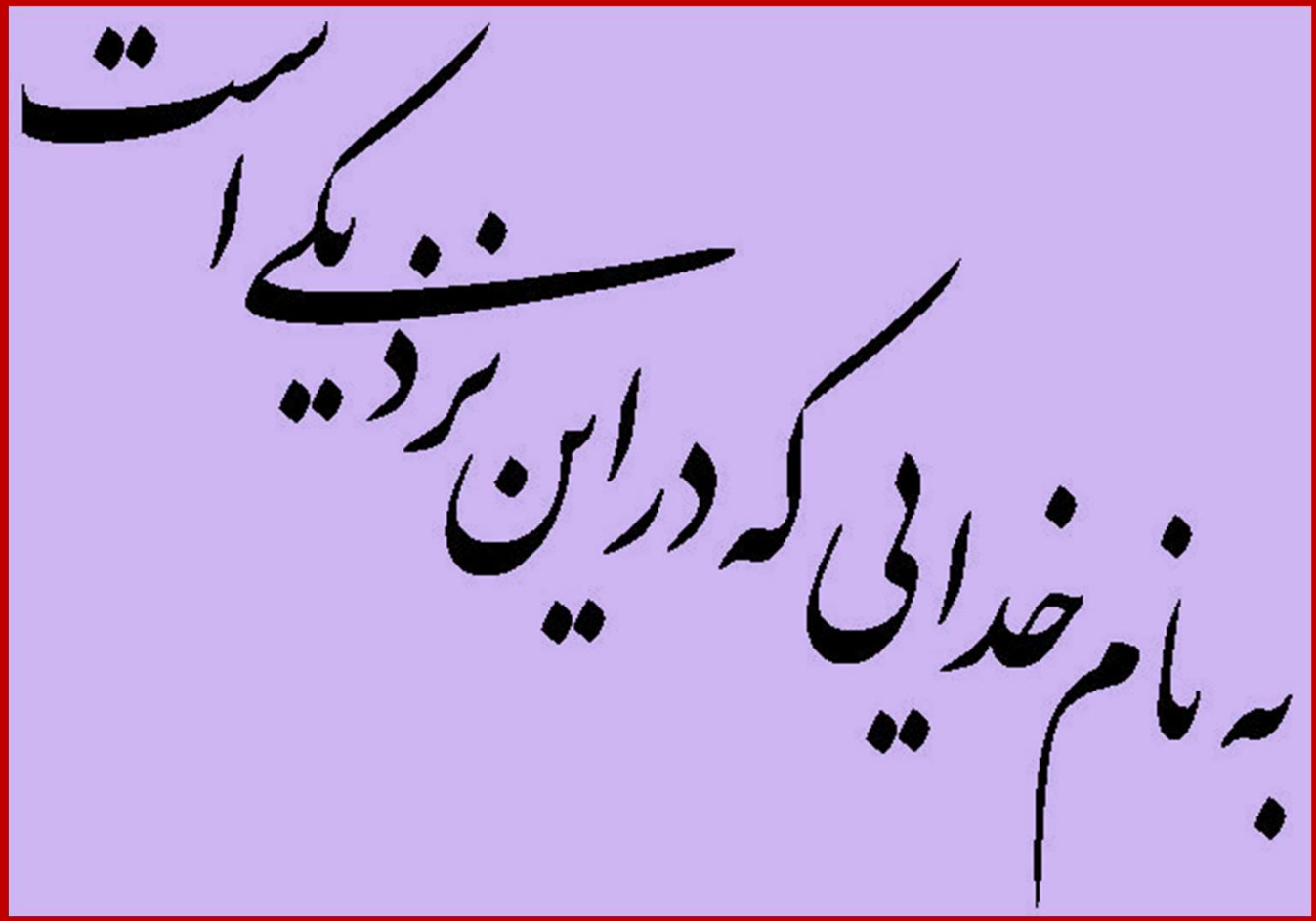

به نام خدایی که در این نزدیکی است

MEDIASTINAL TUMORS

Anatomy

Anatomically, the mediastinum is trapezoidal in shape and is essentially the center of the thoracic cavity.

It extends from the sternum anteriorly to the vertebral column posteriorly. The lungs and parietal pleurae are the lateral borders.

the diaphragm is the floor and the thoracic outlet of T1 , its rib and the manubrium form the roof of the mediastinum.

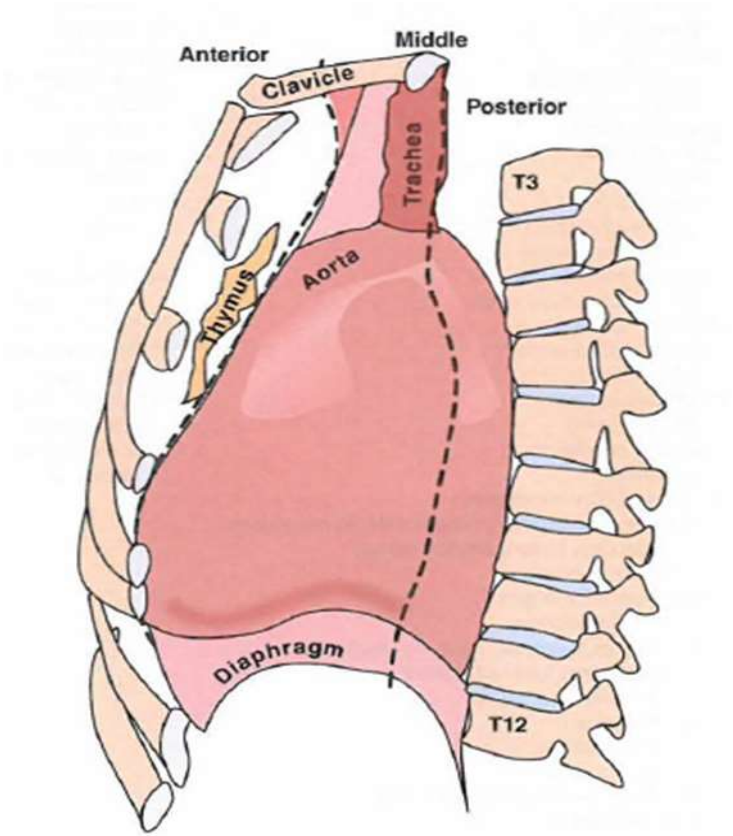
Conceptually, the mediastinum can be subdivided into three compartments. but no anatomic barriers physically separate the compartments

The anterior mediastinum is the space anterior to the pericardium and great vessels and is occupied by the thymus , lymph nodes and small vessels.

The middle mediastinum is comprised of the heart, proximal great vessels, Central airway structures and lymph nodes

The posterior mediastinum is posterior to the heart and great vessels and contains the sympathetic chain ganglia, vagus nerve, thoracic duct, and esophagus.

Adults generally develop thymic tumors and lymphomas, but they can also develop germ cell tumors and carcinomas.



Neurogenic tumors are usually seen in children.

THYMOMAS

The thymus gland is an irregular lobulated lymphoepithelial organ in the anterior mediastinum.

The blood supply is from the internal mammary arteries. The venous drainage is to innominate and internal thorasic veins.

The lymphatics drain to the lower cervical, internal mammary and hilar nodes.

Thymic tumors account for 50% of all anterior mediastinal masses. another 25%, are lymphomas and the remainder are various other tumors

The vast majority of thymic tumors are thymomas , 90% of which are found in the anterosuperior mediastinum

Thymomas are epithelial tumors with lymphoid component that are composed of immature cortical thymocytes

The thymoma incidence to be 0.15 per 100.000 person –years and are more common in men than in women.

For patients with associated myasthenia gravis, the peak age is in the fourth decade, but for patients without myasthenia gravis, the peak age is in the seventh decade or later

Diagnosis

Serum α -fetoprotein and B-HC*G* in men should be evaluated to rule out a germ cell tumor

CT scan often allows visualization of an anterior mediastinal mass

Magnetic resonance imaging (MRI) can provide more detail when needed, delineating the musculoskeletal anatomy and neurovascular structures of the mediastinum

Common features indicative of a high-grade tumor include low T2-signal foci within the mass. the presence of LAP, an incomplete capsule and inhomogenous enhancement.

Biopsy can be performed via a fine-needle aspiration, bronchoscopy, mediastinoscopy, video-assisted thoracoscopy, or open biopsy

Associated systemic disorders may be identified in 70% of patients with thymoma, including:

1) Myasthenia gravis that occurs in 30%-50% of patients

2) Red cell aplasia in 5% of patients with thymoma

3) Hypogammaglobulinemia in 5%-10% of thymoma patients

Staging

The most commonly used staging system for thymomas was published by Masaoka in 1981.

Stage		prescription
I		Macroscopically completely encapsulated, With no microscopic capsular Invasion
II	a	Microscopic invasion into the capsule
	b	Macroscopic invasion into surrounding medastinal fatty tissue or mediastinal pleura
III		Macroscopic Invasion into surrounding organs
IV	a	Pleural or pericardial implants/dissemination
	b	Lymphogenous or hematogenous metastases

Staging is based on the extent of either macroscopic or microscopic invasion into mediastinal structures at the time of surgery

The two factors that have consistently demonstrated prognostic value in multivariate analyses in large studies are disease stage and completeness of resection

In thymic carcinoma. patients with low levels of CD4+ and CD20+ lymphocytes with in the tumor stroma were found to have lower survival rates.

General Management

Surgical resection is the mainstay of treatment for thymomas. A *en-bloc surgical resection (R0) remains the treatment* of choice for all thymomas regardless of Invasiveness.

Recurrence rates for stage I thymomas after an R0 resection are so low that radiation is considered unlikely to offer improvement.

radiation therapy can be considered as an adjuvant treatment for patients with resected stage II and III thymomas.

The indication s for radiation are controversial, with:

1) Some recommending adjuvant radiation for all patients.

2) some recommending adjuvant radiation for stage II and III

3) others recommending radiation only after an incomplete resection

Radiation therapy alone has been used for patients who can not undergo surgery because of medical conditions or those for whom surgical resection is not possible.

Most recurrences (50% to 75%) are operable but 82% of these patient experienced a second recurrence

chemotherapy

The most promising use of chemotherapy is in the neoadjuvant setting.

Both single and combination chemotherapy demonstrated activity.

Drugs commonly used in chemotherapy include cisplatin, doxorubicin and cyclophosphamide.

Aside from cytotoxic agents. somatostatin analogs (e.g. octreotide) and high -dose corticosteroids have shown promise in thymomas

thymic carcinomas

A multimodality approach including surgery, **post op** **R**adiation and chemotherapy is recommended

THYMIC CARCINOID

Thymic carcinoid (neuroendocrine) tumors of the thymus are very rare. accounting for <5% of all neoplasms of the anterior mediastinum.

Most patients with thymic carcinoid are men aged 30 to 50 y

Half of thyroid carcinoids are associated with endocrine disorders such as MEN- 1 or secondary Cushing syndrome

The Masaoka staging system for thymoma has been used for staging thymic carcinoids.

Complete surgical resection is the preferred method of treatment.

Incomplete resections followed by adjuvant radiation, (chemotherapy) or both

Thymolipoma

Thymolipoma are composed of mature adipose and thymic tissue in anterior mediastin

Complete surgical resection is recommended treatment

Thymoliposarcoma

It grows by expansion and has a low risk of distant metastasis

Complete surgical resection with adjuvant radiation therapy has been used for local control.

Malignant Mediastinal germ cell tumors

Primary mediastinal extragonadal germ cell tumors account for 2% to 5% of all germ cell tumors and 50%-70% extragonadal GCT

The most of them occur in men between 20 and 40 years of age

Up to 20% of patients with mediastinal germ cell tumors were found to have the Klinefelter karyotype (47XXY)

Several unusual malignant processes are associated with nonsemtnomatous germ cell tumors Including:

1) acute myeloid leukemia
2) acute lymphocytic leukemia
3) acute megakaryocytic leukemia
4) myelodysplastic syndrome
5) malignant histiocytosis

primary germ cell tumors of the mediastinum are both more aggressive and have a poorer prognosis than gonadal tumor

Primary extra gonadal GCTs present with clinical symptoms in 90% to 100% of cases.

Dyspnea, chest pain, cough, fever, weight loss, vena cava occlusion syndrome and fatigue or weakness are the most common symptoms.

Like testicular tumors, mediastinal germ cell tumors Can be seminomatous or nonseminomatous.

Distant metastases from NSGCTs are much more common

Because primary gonadal GCTs can spread to retroperitoneum and mediastinum, the diagnostic workup must be thorough and meticulous to avoid overlooking an occult gonadal primary tumor.

Mediastinal GCTs are usually readily detected on chest x-rays, with most masses noted in the anterosuperior mediastinum

CT scans of the chest, abdomen and pelvis are essential to evaluate the mass and to screen for metastases and LAP

A careful physical examination and testicular sonography should be performed

The determination of baseline tumor-marker levels both before treatment and after treatment completion is essential

Levels of tumor markers such as α-fetoprotein, β-HCG and LDH can be helpful for diagnosis, for evaluating treatment efficacy and for monitoring recurrence

Biopsy samples should be obtained whenever possible because both choice of treatment and prognosis depend greatly on histology

Prognostic Factors

The most important prognostic factor for MGCT is histology.

Seminomas are highly curable, but nonseminomatous GCT are associated with poor progression-free and overall survival.

The presence of metastases with tumors of either histologic type is also associated with adverse PFS and overall survival

In nonseminomatous tumors, elevated β-HCG levels are associated with inferior overall survival.

General Management

teratoma

Treatment of a mature mediastinal teratoma consists of complete surgical resection

For teratomas with a malignant component (immature) , adjuvant cisplatin-based combination chemotherapy is recommended

Chemotherapy includes (four cycles of cisplatin, etoposide, and bleomycin) or (vinblastine, ifosfamide, and cisplatin).

Seminomatous Tumors

Seminomas are quite sensitive to both radiation therapy and chemotherapy.

All patients with tumors of seminomatous histology should be treated with curative intent even in the presence of widely metastatic disease

Most patients should be initially treated with chemotherapy.

Some clinicians have advocated surgical resection or biopsy of all postchemotherapy masses larger than 3cm. others recommend close follow-up in such cases.

In F/U approach, if the mass enlarges on chest x-ray or CT scan then intervention perforemed with resection, radiation, or salvage chemotherapy.

For patients who are not candidates for chemotherapy, definitive radiation has produced local tumor control rates of 89% to 100% and long-term survival rates of 60% to 80%.

Nonseminomotous GCTs

The primary treatment for nonseminomatous GCT is intensive cisplatin-based chemotherapy.

Surgical resection of all residual masses after first-line chemotherapy is recommended

Nonseminomatous GCTs are also radiation sensitive, but they require higher doses than seminomntous tumors, and doses of 60 Gy or more may be necessary to achieve control

Radiation may be useful for unresectable residual masses.

long-term survival rates for patients with relapsed mediastinal germ cell tumors are <10%

MESENCHYMAL TUMORS

Mediastinal mesenchymal tumors compose 2% to 8% of all primary mediastinal tumors

1) Lipoma are most common mesenchymal mediastinal tumor
They should be referred for surgical resection

2) Liposarcoma: optimal treatment consists of surgical resection and adjuvant radiation therapy

3) Lymphangiomas: Surgical resection Or RT (if unresectable)

4) Hemangioma: Surgery remains the mainstay of therapy and should not be treated with radiation

5) Hemangiopericytoma: Surgical resection ± RT (optional)

NEUROGENIC TUMORS

they are the most common cause of a posterior mediastinal mass and account for one-quarter of mediastinal neoplasms.

Neurogenic tumors of the thorax are generally classified by their neural cell of origin, including:

1) nerve sheath (schwannomas and neurofibromas) that are the most common neurogenic tumors in adults are benign and often presenting in the setting of NF type-I

2) Autonomic ganglion (ganglioneuroma and neuroblastoma)

3) paraganglion (paragangliomas and pheochromocytomas)

Individuals with NF-1 are also at increased risk of developing malignant peripheral nerve sheath tumors (MPNSTs), most MPNSTs arise within pre-existing plexiform neurofibromas.

High-resolution CT is essential, as is MRI to evaluate the neural and spinal anatomy

Surgical resection is the mainstay of therapy. An R0 resection should be attempted

As is true for the treatment of soft tissue sarcomas. adjuvant radiation is part of the treatment of localized MPNSTs

For patients with unresectable disease, radiation delivered either alone or with chemotherapeutic agents

Few agents are effective for MPNSTs, and treatment regimens usually include doxorubicin or ifosfamide.

TRACHEAL CARCINOMAS

The trachea is a fibrocartilaginous tube with 12 cm length; its diameter is larger in men (2.3 cm) than in women (2.0 cm)

The upper border lies around the sixth or seventh cervical vertebra, and the lower border around the fourth (full expiration) or sixth (full inspiration) thoracic vertebra .

The posterior aspect or the trachea is membranous and is intimately associated with the esophagus

Each centimeter of trachea contains two cartilaginous rings

Tracheal neoplasms are quite rare, contributing to fewer than 0.5% of all tumors

Natural History

the most prevalent histology worldwide is squamous cell (60% to 90%),

Adenoid cystic carcinoma (cylindromas) seems to be more common among nonsmokers.

SCC variants typically present during the sixth decade of life, whereas adenoid cystic carcinomas seem to present at younger ages

Tracheal carcinomas can present with a variety or symptoms, including cough, dyspnea, dysphagia, and hemoptysis.

Bhattacharyya proposed a staging system that was used by Webb in evaluating the experience at MD Anderson Cancer Center

T	prescription
T1	Primary tumor confined to trachea; size <2cm
T2	Primary tumor confined to trachea; size ≥2m
T3	Spread outside the trachea but not to adjacent organs
T4	Spread to adjacent organs or structures

N	prescription
N0	No evidence of regional nodal disease
N1	Positive regional nodal disease

Stage	T	N
I	T1	N0
II	T2	N0
III	T3	N0
IV	T4	ANY
IV	ANY	N1

General Management

Bronchoscopy is essential for diagnosis of tracheal malignancies and for preoperative surgical planning

Esophagoscopy is suggested for all patients to rule out esophageal invasion.

A CT scan of the chest is indicated to aid in evaluation of tumor extension, resectability, involvement of lymph nodes, and pulmonary metastasis

The optimal management strategy seems to be a combined-modality approach including surgical resection and postop RT

Radiation in mediastinum

Thymomas& Thymic carcinoma

The exact indications for radiation are controversial:

1) Some authors recommend adjuvant radiation for all patients. (especially **thymocarcinomas**)

2) Others recommend adjuvant radiation for stage II and III thymomas.

3) others recommend radiation only in the circumstance of incomplete resection.

In summary:

1) Adjuvant radiation should be considered for any residual disease or incomplete resection regardless of stage.

2) for stage I patients, the recurrence rates are low enough that the benefit from radiation is marginal.

Radiation has been suggested for use in the neoadjuvant setting with the intent of reducing tumor burden and improving resectability,

especially in the setting of gross invasion of critical structures:
1) Trachea 2) Aorta 3) Spine

Radiation Dose

Radiation doses range from 45 to 70 Gy with standard fractionation (1.8 to 2.0 Gy).

1) Postoperatively, the dose delivered is 45 to 54 Gy and higher for (+) margins or frank invasion

2) In definite Radiation, the dose delivered is 60 to 70 Gy

The treatment volume for a thymoma should encompass the entire thymus, but not **Lymph nodes**

Malignant Mediastinal Germ Cell Tumors

Seminomas are very sensitive to both **radiation therapy** and **chemotherapy**

all patients with a seminomatous histology should be treated with curative intent

Doses as low as 30 Gy to as high as 50 Gy have been recommended.

Doses should be adjusted based on the size of the lesion, the history of chemotherapy exposure. and entire mediastinum should be encompassed in fields

The primary treatment for nonseminomatous germ cell tumor is intensive cisplatin-based combination **chemotherapy**.

Radiation may have a role for unresectable residual masses given the high rate of persistent viable tumor and the poor rates of salvage therapy

Nonseminomatous germ cell tumors require higher doses than seminomatous tumors. Doses of 60 Gy or more may be necessary to achieve control.

Tracheal Carcinomas

After resection, postoperative radiation is recommended.

In unresectable tumors, radiation has been used alone. The best results have come from studies where doses >60 Gy have been given.

For resected patients, 1 to 1.5 months of healing time should be allowed before beginning postoperative radiotherapy.

External beam doses should be limited to 60 Gy.

An intraluminal boost (Brachy therapy) technique allows increasing dose with minimal added acute or late side effects.

Yet if mediastinal or cervical nodes are discovered at surgery or by CT, radiation to these regions is warranted.

Given the low proclivity of lymphatic spread for most Tracheal Carcinomas, elimination of elective nodal irradiation is sometimes reasonable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