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Anterior Mediastinal Mass

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10/06/11

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- 57M who fell on 6/19/11 while standing and had brief loss of consciousness and went to his PMD the following day who advised him to go to the local ER.
- PMH/SH: DM, HTN, BPH, hyperlipidemia
- Home meds: Janumet, Nateglinide, Metoprolol, Enalapril, Exforge, Vytorin, Flomax, ASA and Vit D.
- Allergies: NKDA
- Social Hx: 10 pack year ex-cigarette use
- Family Hx: non-contributory

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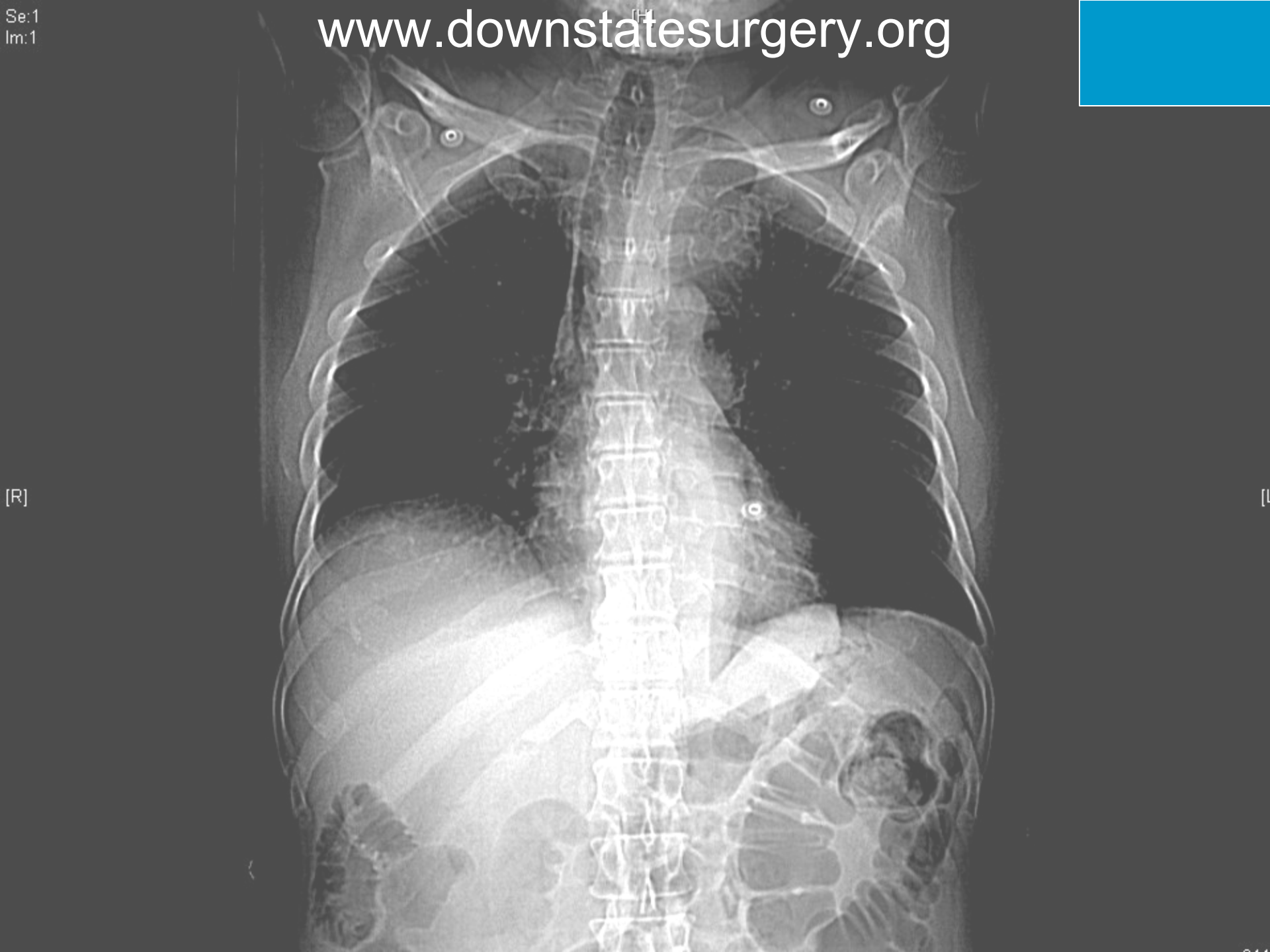
- Screening studies: Colonoscopy in 2011, negative. Stress test 1/2011, negative.
- Vitals: WT 75 kg, T 37.0 C, HR 65, BP 101/69, RR 16. O2 saturations 100% on room air.
- General: Healthy-appearing male, in no apparent distress.
- Lungs: Clear to auscultation bilaterally.
- Heart: Regular rate and rhythm without any murmurs, rubs or gallops.
- Labs: within normal limits.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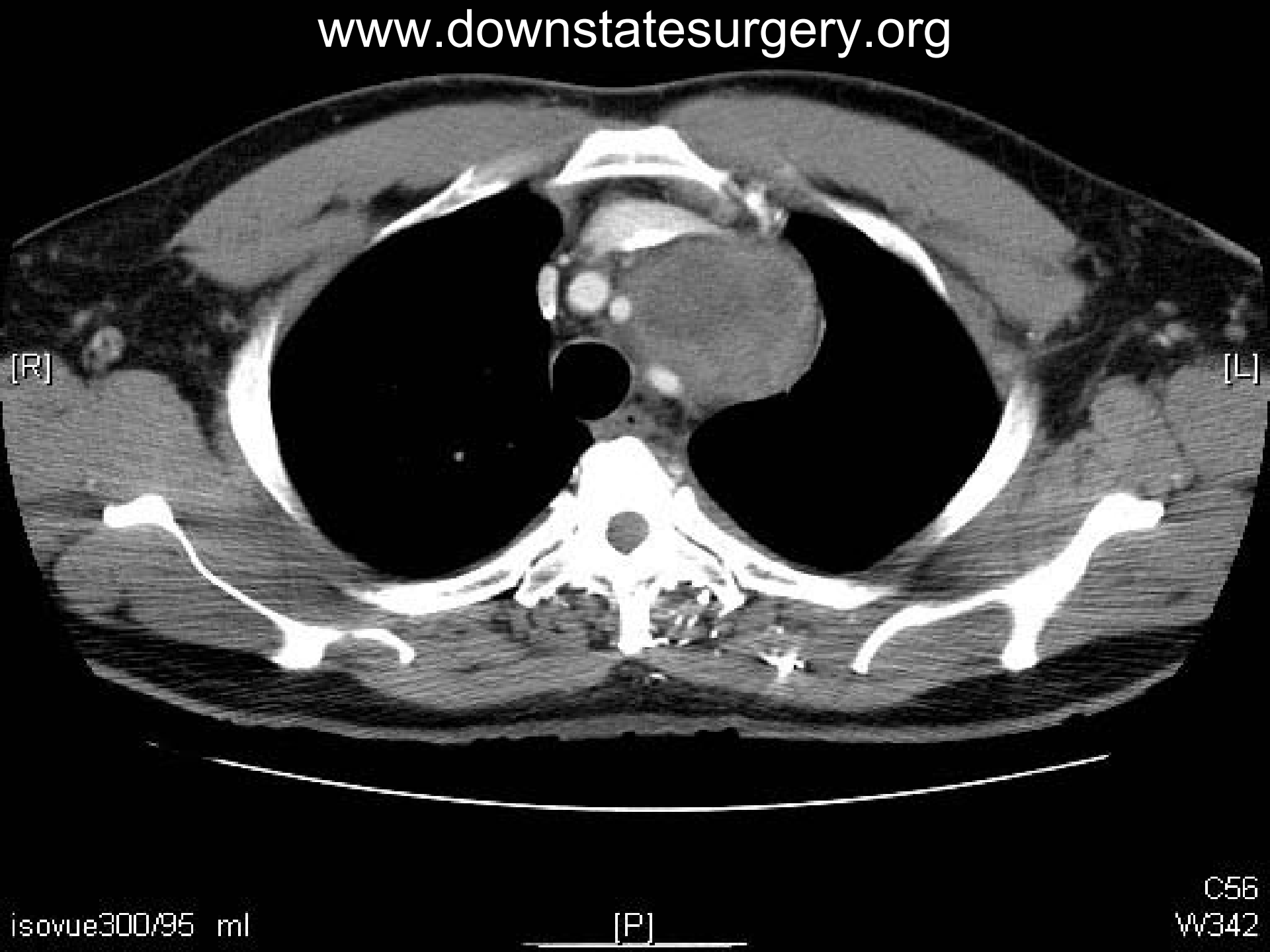

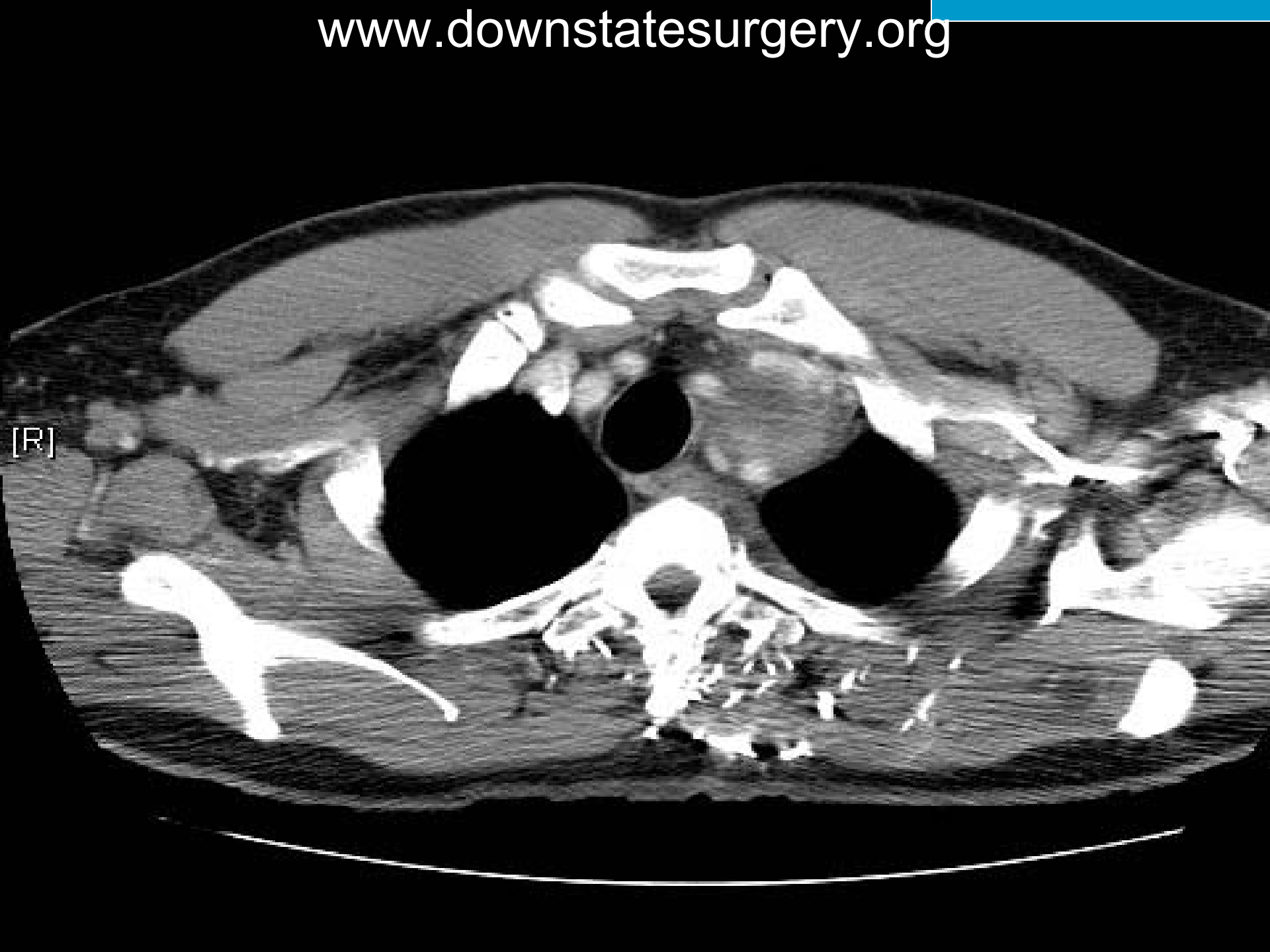

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- CT guided biopsy of the chest lesion (6/23/11):
  - Malignant epitheloid neoplasm, not otherwise specified. Differential diagnosis that includes seminoma and carcinoma.

- Immunohistochemical stains: 8/12/11
  - Both OCT4 and CD117 are negative.
  - Cam5.2 is negative as well.
  - In summary, no morphological or immunohistochemical evidence to suggest a tumor of germ cell origin.

- Testicular US (7/28/11): No suspicious testicular mass.

- Laboratories (7/28/11): Alpha-fetoprotein 6.9 (slightly elevated, it was 6.1 cutoff), beta hCG less then 2.0, and LDH 214.

- PET scan (8/4/11): Malignant disease likely at least 3 sites, the mediastinum at the level of the aortic arch; a retrocrural now a aortocaval lymph node approximately at the level of the renal vein, and a smaller node posterior to the aorta just above the bifurcation.

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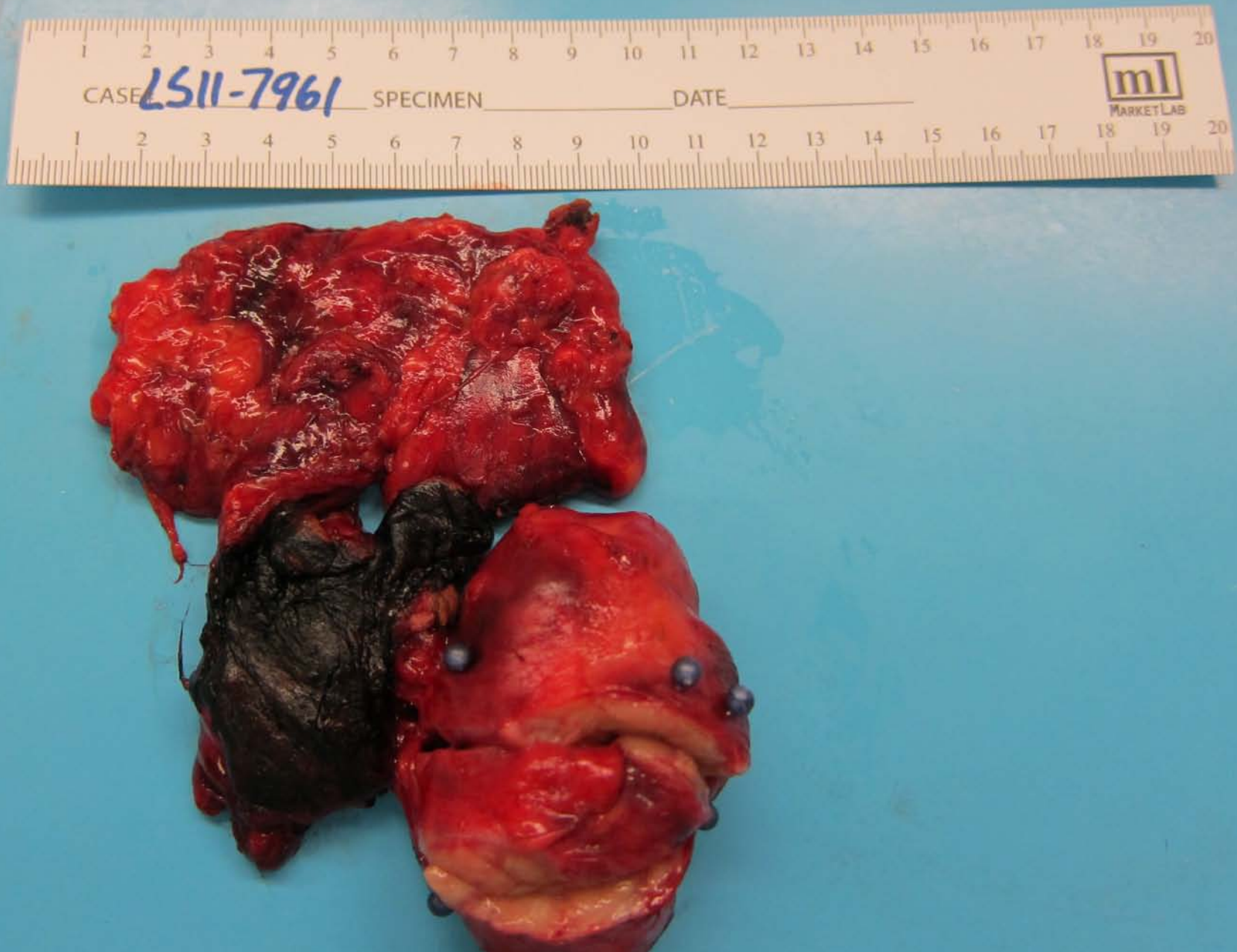
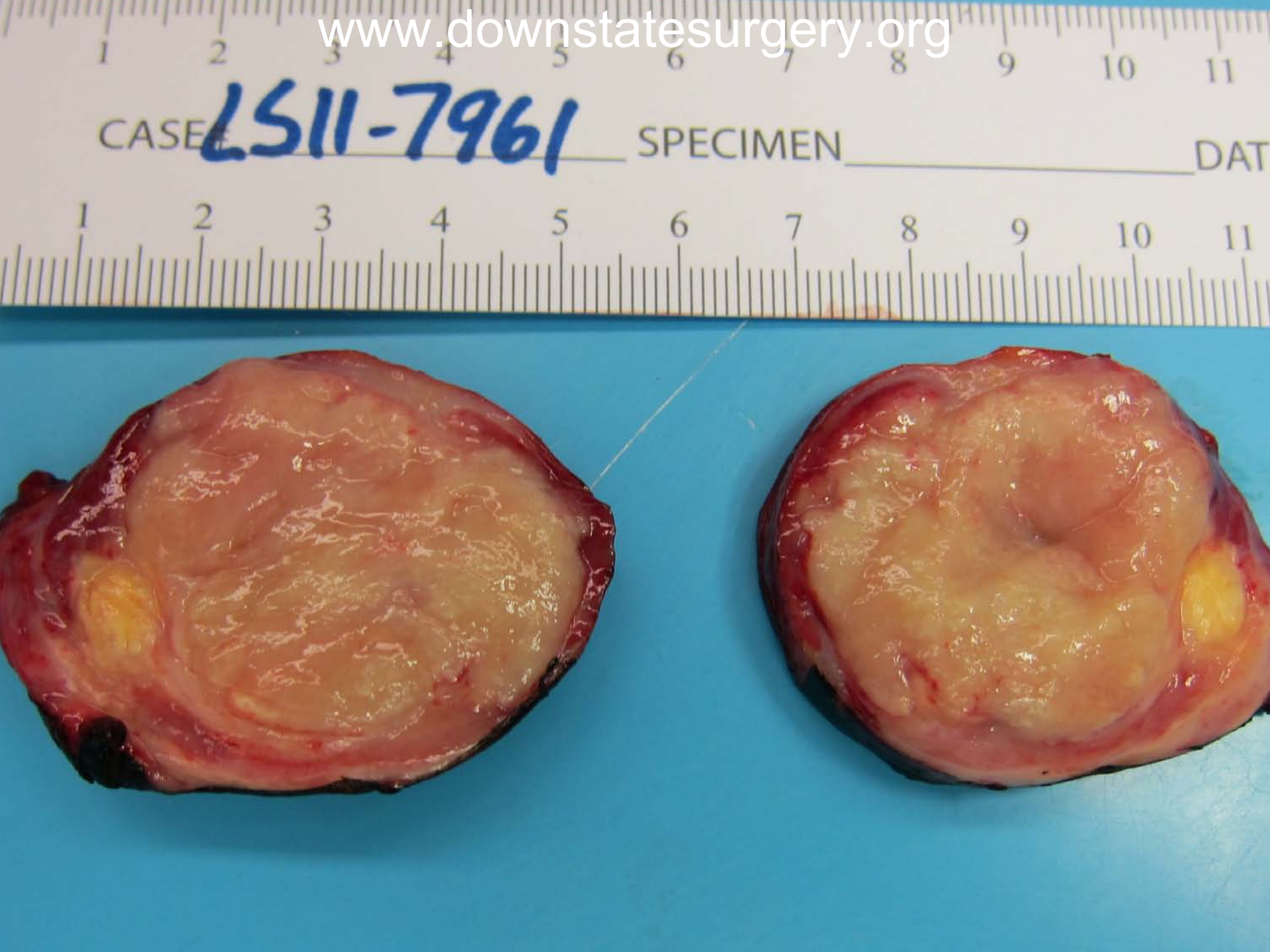
- Pulmonary function tests (8/4/11): FVC 4.05 (103% of predicted), FEV-1 3.39 (113% of predicted), DLCO 91% of predicted, DLCO/VA 106% of predicted.





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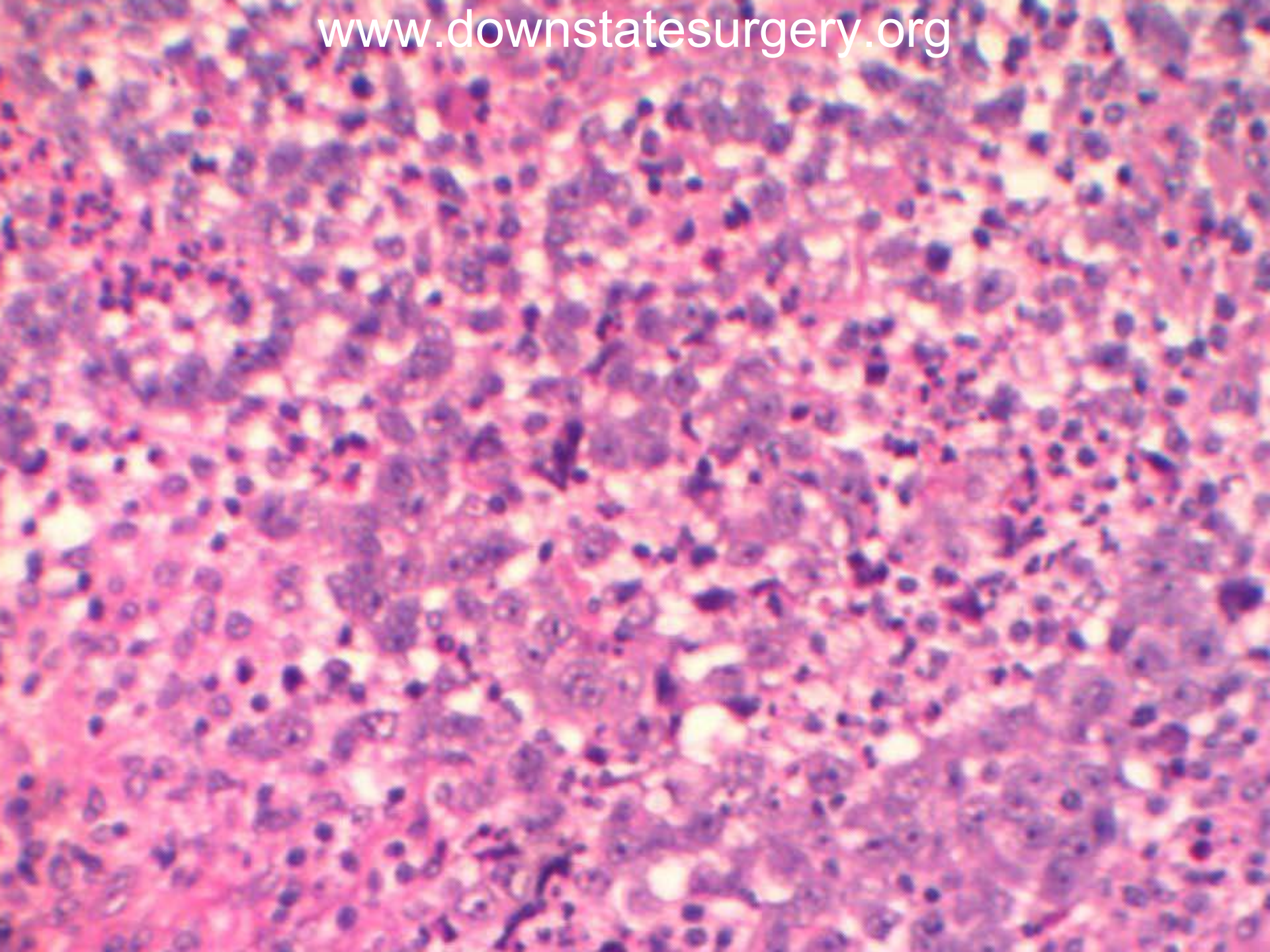
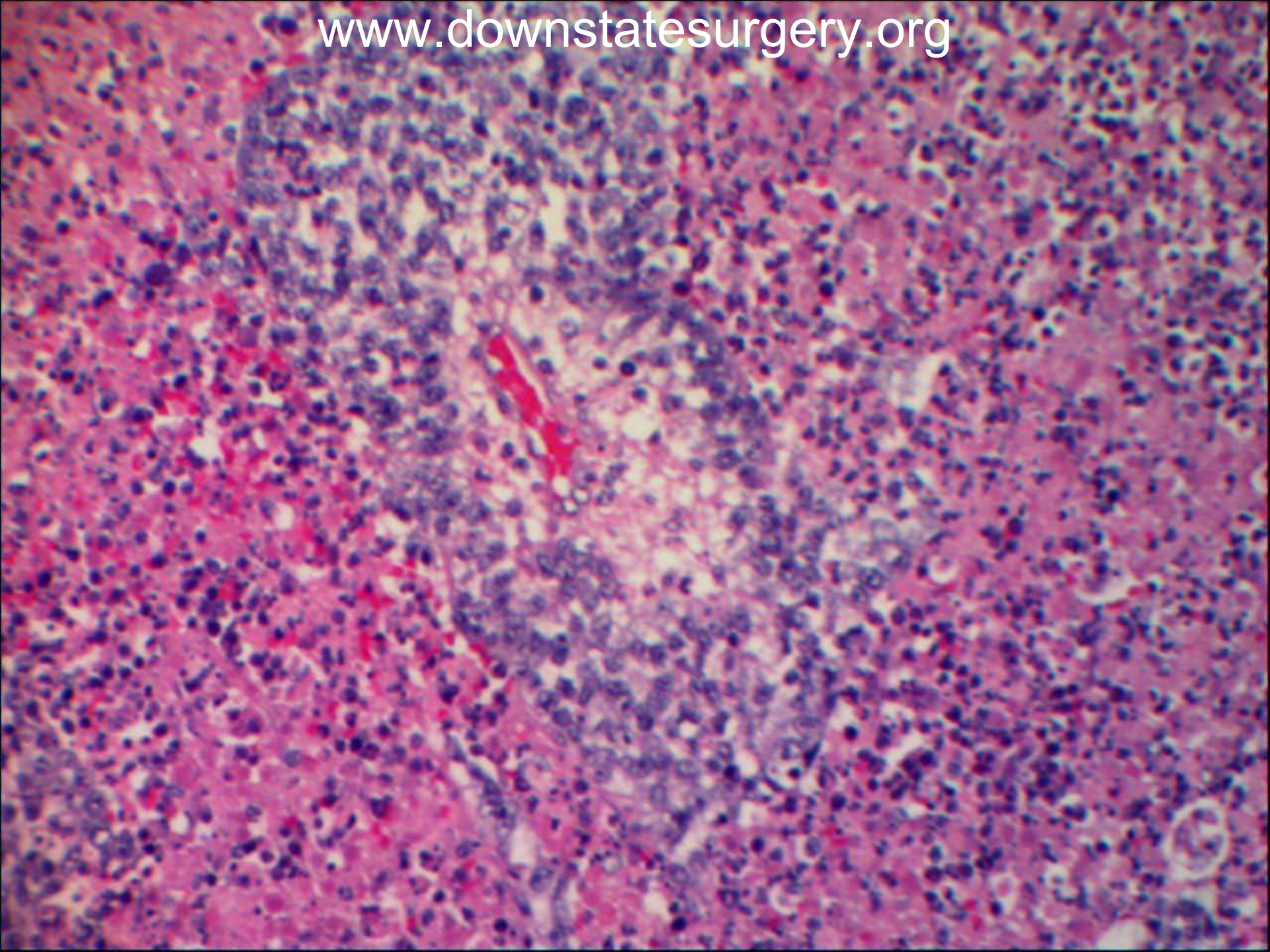
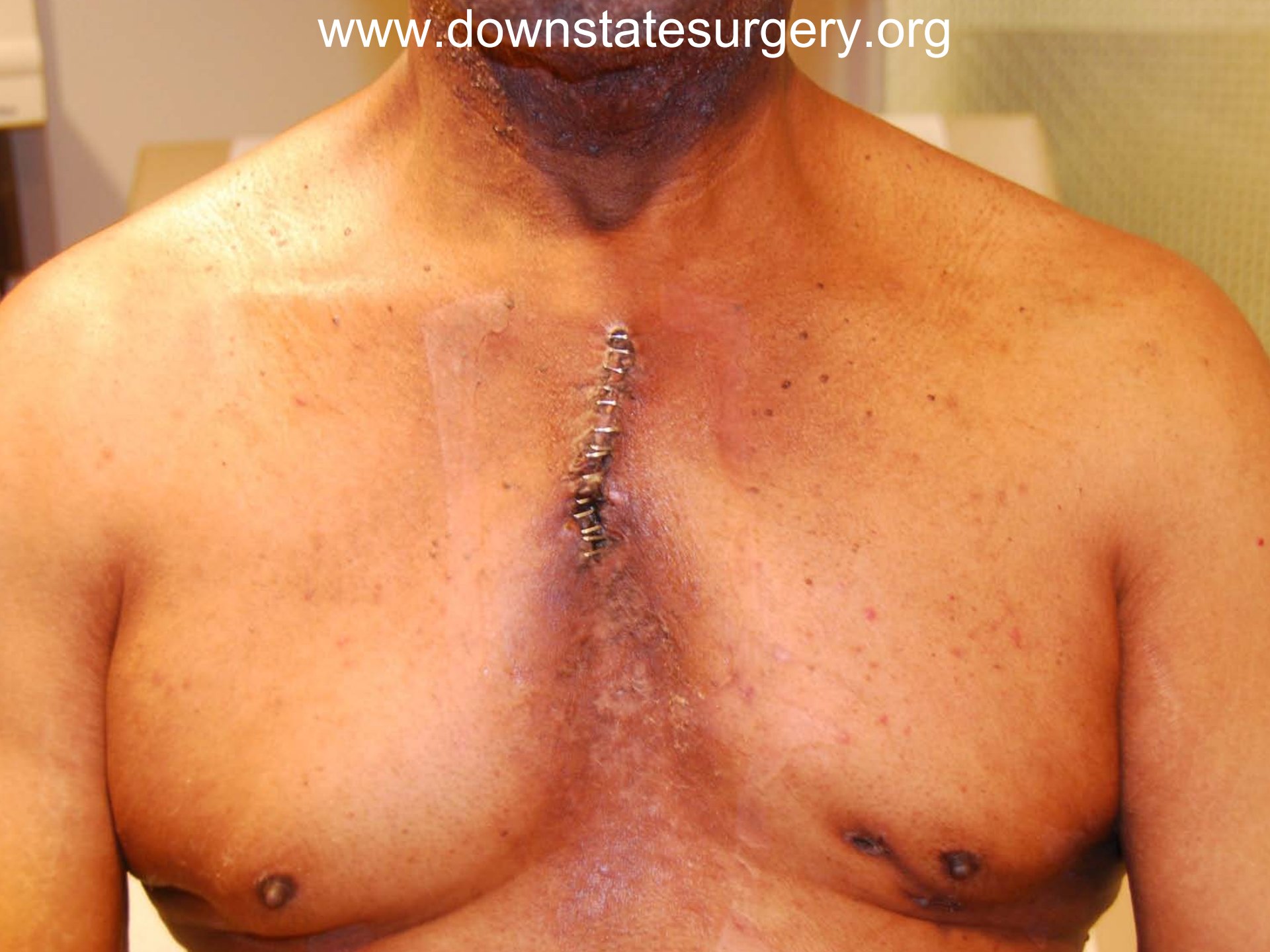
- Yolk sac tumor 6.8 cm, encapsulated, composed of pleomorphic cells, trabecular and endodermal sinus patterns with Shiller-Duval bodies.
- Immunostains: tumor cells are positive for SALL4, GPC3 and negative for CD117 and OKT4;
- Positive for the cytokeratin stains CAM5.2 and AE 1-3.
- Inked markers negative for tumor.
- Lymph nodes:
  - seventeen reactive lymph nodes, negative for tumor (0/17).
- Flow cytometry negative for B-cell or T-cell lymphoma.







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Tumors of the Anterior Mediastinum

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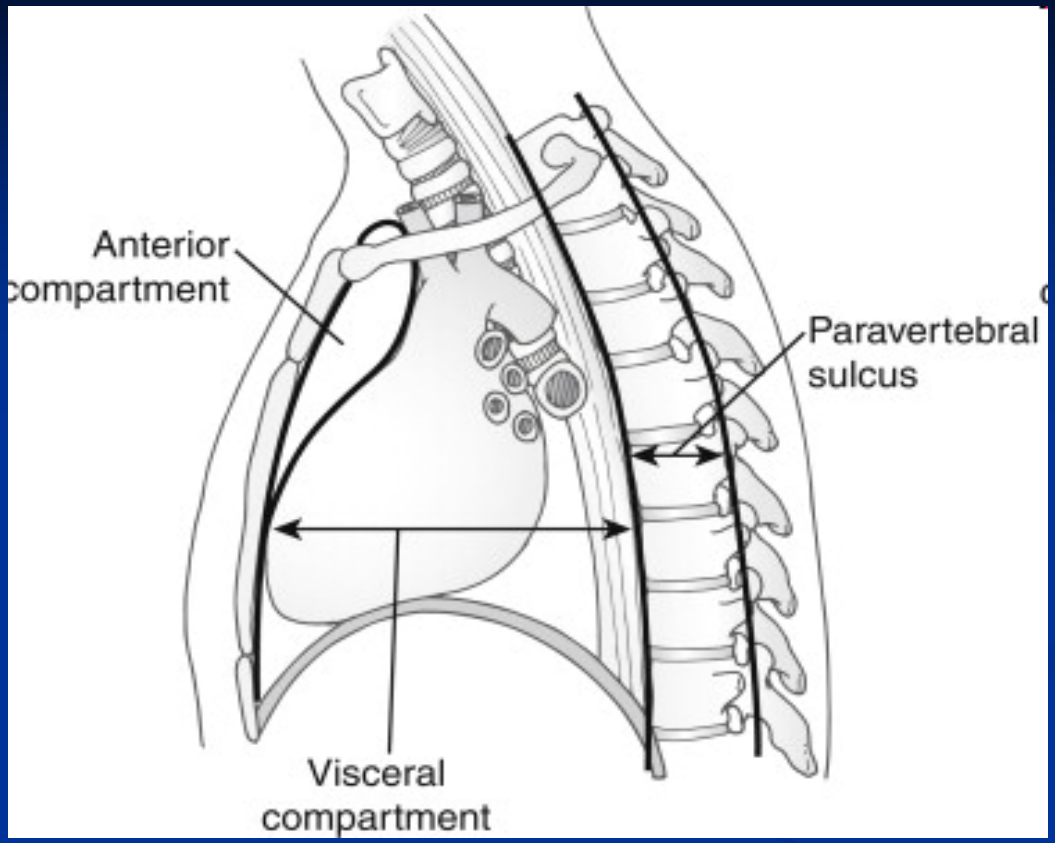

Three-compartment division of the mediastinum as proposed by Shields.
(From Shields TW. General thoracic surgery. 2nd ed. Philadelphia: Lea & Febiger; 1983, with permission.)

Components of Mediastinal Compartments* as Proposed by Shields

Anterior	Visceral (middle)	Paravertebral (posterior)
Thymus	Pericardium/heart	Sympathetic chain
Internal thoracic vessels	Great vessels	Proximal intercostals: nerve, artery, and vein
Internal thoracic lymph nodes	Trachea	Posterior paraesophageal lymph nodes
Prevascular lymph nodes	Proximal right and left main-stem	Intercostal lymph nodes
Fat and connective tissue	Esophagus	
	Phrenic nerve Thoracic duct Proximal azygos vein Pretracheal lymph nodes (levels 2, 4, and 7) Pleuropericardial lymph nodes Fat and connective tissue	

**The nodal basin draining the anterior chest wall and female breast lie in the anterior compartment, whereas the majority of those draining the lung and important in lung cancer staging lie in the visceral compartment.*

From Shields TW. General thoracic surgery. *2nd ed. Philadelphia: Lea & Febiger; 1983, with permission.*

TABLE 75.3. Usual Location of Mediastinal Lesions.

	Mediastinal compartment		
Type of lesion	***Anterior***	***Visceral***	***Paravertebral sulci***
Primary			
More common	Thymoma Benign and malignant germ cell tumors Lymphoma	Foregut cyst Pleuropericardial cyst Lymphoma Mediastinal granuloma	Neurilemoma (schwannoma) Neurofibroma Neuroblastoma Malignant schwannoma Ganglioneuroma Ganglioneuroblastoma Foregut cyst Paraganglioma
Less common	Mesenchymal tumors Thymic cyst Parathyroid adenoma	Paraganglioma Neurenteric cyst Thoracic duct cyst	Pheochromocytoma Mesenchymal tumors Lymphoma Extramedullary hematopoiesis
Secondary	Thyroid goiter Bony tumors	Thyroid goiter Metastatic carcinoma Foramen of Morgagni hernia Hiatal hernia Pancreatic pseudocyst	Bony tumors

Source: Adapted from Shields,[78] with permission.

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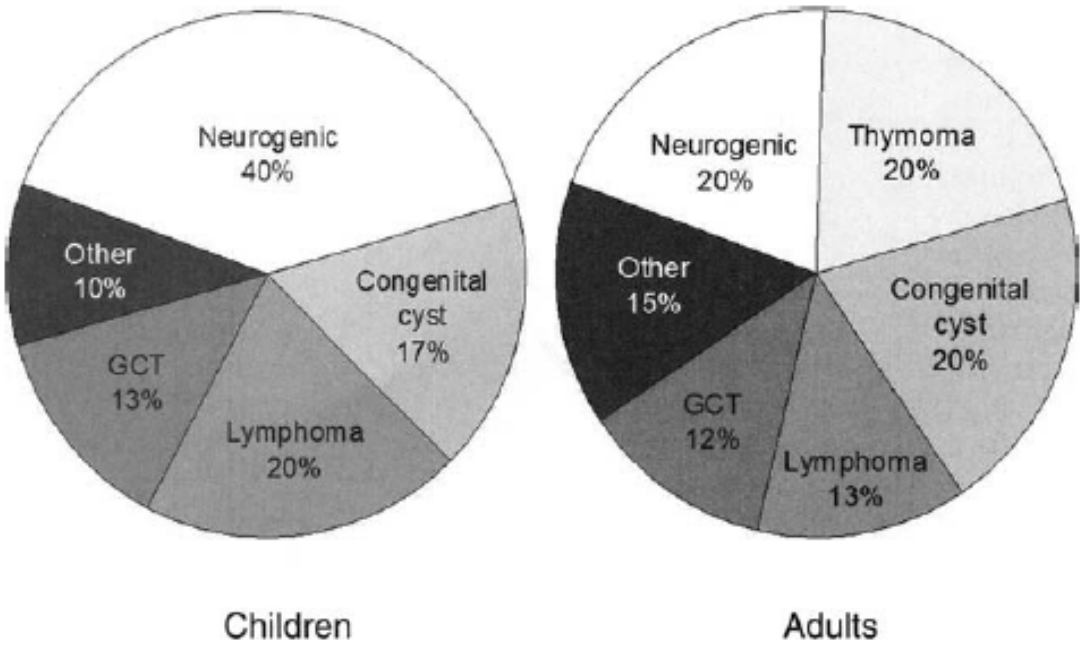

FIGURE 75.3. Common primary mediastinal lesions by patient age. Note that almost half of mediastinal lesions in children are neurogenic tumors, and that thymomas, among the most common in adults, are rare in children. Neurogenic tumors in children under 2 years are most likely neuroblastomas; in children aged 2 to 10 years they are most likely to be ganglioneuromas; and in adults they are most often neurilemomas. GCT, germ cell tumor. (Reprinted from Block,[195] with permission.)

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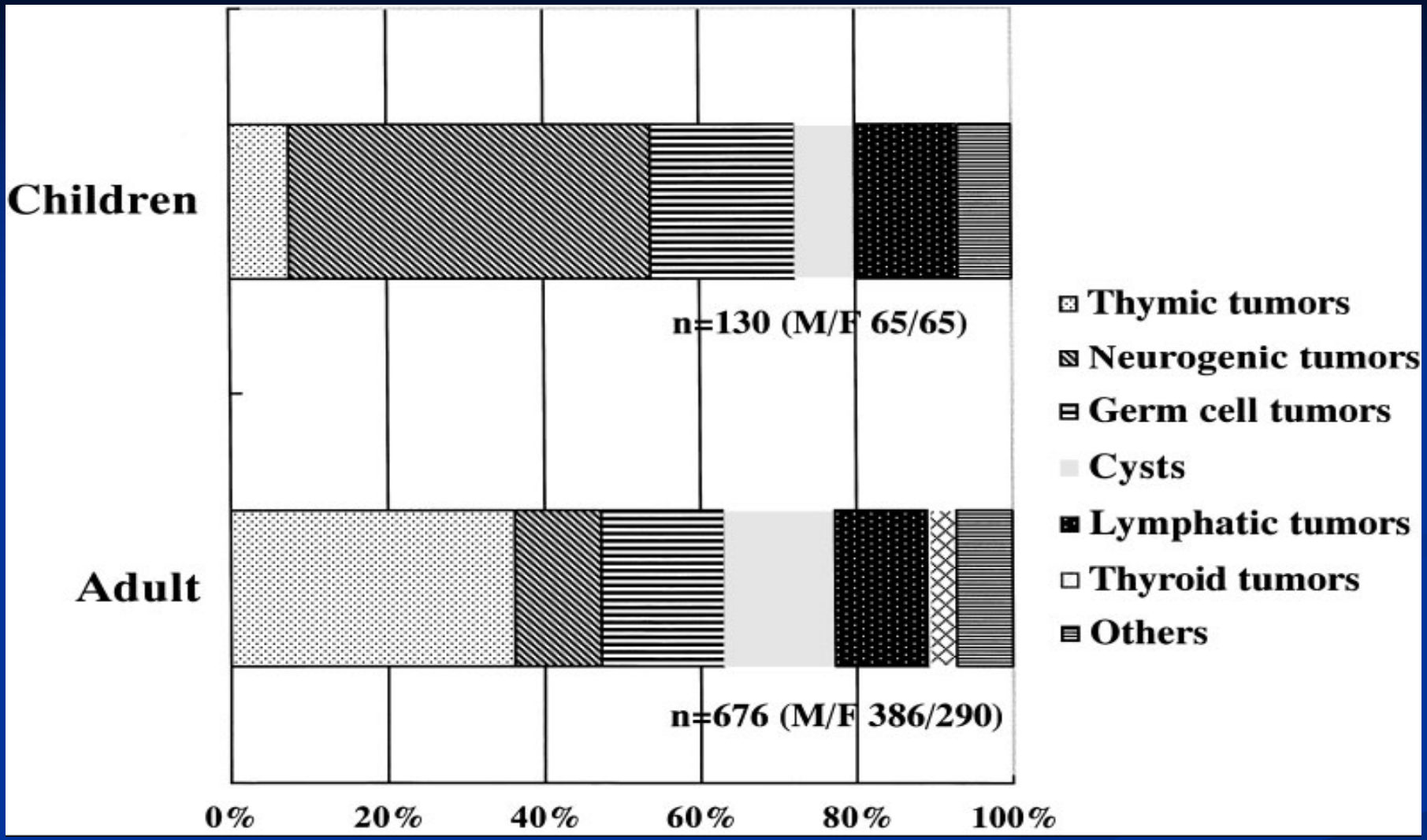

Comparison of adult vs. children for histologic types of mediastinal tumors.
Shin-Ichi Takeda and all., Clinical Spectrum of Primary Mediastinal Tumors: A Comparison of Adult and Pediatric Population sat a Single Japanese Institution; Journal of Surgical Oncology 2003;83:24–30

- Mediastinal lesions are symptomatic in 50%-75% of patients.
- 50% of all mediastinal lesions are incidental discoveries on chest x-ray or CT scan.
- Symptoms can be caused by local mass effects, systemic effects of tumor derived hormones and peptides, or infection.

TABLE III. Symptoms With Reference to Malignancy (Adults vs. Children)

Symptom	Adults 676 cases			Children 130 cases			*P* value (adults vs. children)
	Benign 361	Malignant 315	Total 676	Benign 82	Malignant 48	Total 130	
Asymptomatic	244	78	322	56	13	69	0.88
Symptomatic	117	237	354	26	35	61	0.88
Chest pain	35	37	72	9	2	11	0.56
Dyspnea	4	25	29	7	13	20	<0.01
Cough	10	19	29	6	9	15	<0.02
SVC syndrome	2	42	44	0	3	3	0.07
Chest oppression	7	16	23	0	3	3	0.42
Fever	11	4	15	2	5	7	<0.05
Hoarseness	7	24	31	0	0	0	<0.02
Horner	0	4	4	1	2	3	0.54
MG	38	69	108	0	0	0	<0.0001
Others	5	3	8	3	15	18	<0.0001

SVC, superior vena cava; MG, myasthenia gravis.

TABLE 75.4. Mediastinal Tumors and Associated Clinical Syndromes.

Tumor	*Syndrome*
Thymoma	Autoimmune and immune deficiency
	Myasthenia gravis
	Red blood cell aplasia
	White blood cell aplasia
	Aplastic anemia
	Hypogammaglobulinemia
	Polymyositis
	Dermatomyositis
	Progressive systemic sclerosis
	Hemolytic anemia
	Systemic lupus erythematosus
	Rheumatoid arthritis
	Collagen vascular disease
	Endocrine disorders
	Panhypopituitarism
	Addison's disease
	Hyperthyroidism
	Miscellaneous
	Megaesophagus
	Myocarditis
Lymphoma	Anemia
	Myasthenia gravis
Neurofibroma	von Recklinghausen's disease
Thymic carcinoid	Multiple endocrine neoplasia (I and II)
Neurenteric cysts	Vertebral anomalies
Nonseminomatous germ cell tumors	Klinefelter's syndrome

Source: Adapted from Davis et al.,[77] with permission.

TABLE 75.5. Syndromes Caused by Tumor-Derived Products.

Syndrome	*Tumor product*	*Tumor*
Cushing's syndrome	ACTH	Carcinoid
Palpitations/ hypertension	Norepinephrine Epinephrine (rare)	Paraganglioma Pheochromocytoma Chemodectoma Ganglioneuroma Neuroblastoma
Hypoglycemia	Insulin-like hormone	Mesothelioma Teratoma Fibrosarcoma Neurosarcoma
Diarrhea	Vasoactive intestinal polypeptide	Ganglioneuroma Neuroblastoma Neurofibroma
Hypercalcemia	PTH Parathyroid-like hormone	Parathyroid adenoma Hodgkin's disease
Thyrotoxicosis	Thyroid hormone	Substernal thyroid
Gynecomastia	β-HCG	Nonseminomatous germ cell tumor
Precocious puberty	Testosterone	Nonseminomatous germ cell tumor

Source: Adapted from Davis et al.,[17] with permission.

- Fewer than 5% of all germ cell tumors are found in the mediastinum.
- Arise from primordial germ cells that migrate from the urogenital ridge into the mediastinum and thymus gland during embryogenesis
- Almost all are found in the anterior compartment.

- 50% of all mediastinal germ cell tumors are benign (teratomas);
  - peak incidence during the second through fourth decades of life.

- Benign tumors are classified as epidermoid cysts, dermoid cysts (teratodermoids), or mature teratomas.
  - Pluripotent stem cells
  - Contain multiple tissue elements derived from one or more of the three embryonic germ cell layers.

- Malignant tumors are further classified as:
  - Seminomas or nonseminomatous lesions
  - Much more common in men than women.
- 30% to 50% of malignant mediastinal germ cell tumors are seminomas.

- Seminomas:
  - almost exclusively found in men between the ages of 20 and 40 years
  - extensive local invasion.
- Extrathoracic disease is uncommon, with metastatic spread occurring first through regional lymphatics.
- Definitive diagnosis is made by FNA or open biopsy.

- NSGCT includes embryonal cell carcinomas, teratocarcinomas, choriocarcinomas, and yolk sac (endodermal sinus) tumors.
  - aggressive, are more likely to metastasize to extrathoracic sites
  - less sensitive to therapy.
- Most NSGCTs produce -HCG, AFP, or both, and more than 90% of patients have elevated levels in their serum.
- Primary therapeutic modality is platinum-based chemotherapy.

Table 13.3. Staging of mediastinal germ cell tumors

Stage I	Distinct tumor without direct or microscopic invasion of surrounding structures
Stage II	Tumor within the mediastinum with direct and/or microscopic invasion of surrounding structures
Stage IIIA	Tumor with intrathoracic metastases
Stage IIIB	Tumor with extrathoracic metastases

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Tissue diagnosis is often, but not always, required before proceeding with therapy.

Circumstances in which biopsy is indicated include:

(1) suspicion of a tumor that is treated primarily with nonoperative therapy (e.g., lymphoma, NSGCT, or seminoma);

(2) Evidence of local invasion that would require resection and reconstruction of vital structures (e.g., involvement of the SVC by a large anterior mediastinal mass);

(3) evidence of metastatic disease rendering resection inappropriate.

Surgical approaches to biopsy:

1. Chamberlain Procedure (Anterior Mediastinotomy)
2. Transcervical biopsy (Cervical Mediastinotomy)
3. Thoracoscopic Biopsy
4. Extended Mediastinoscopy

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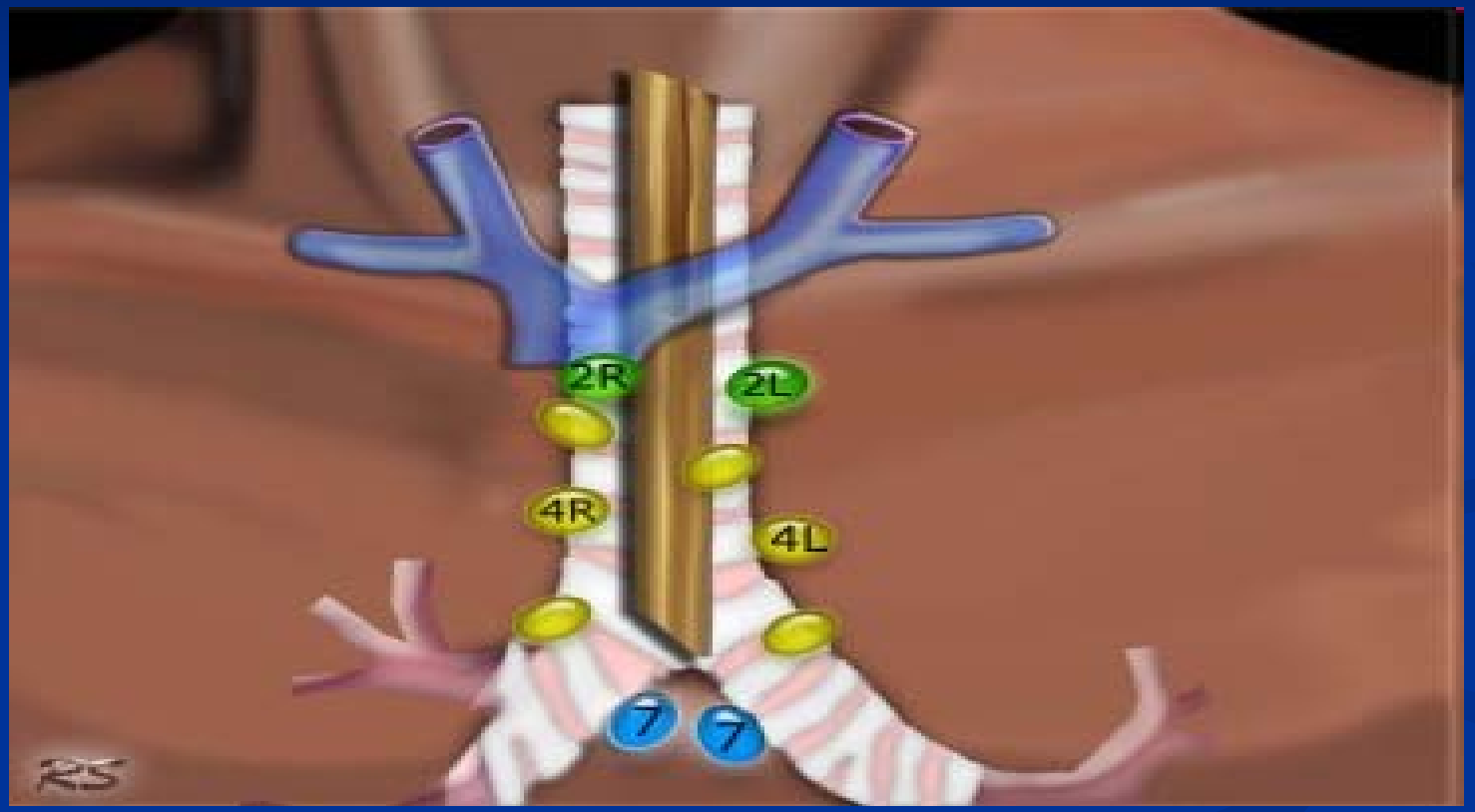
Conventional mediastinoscopy



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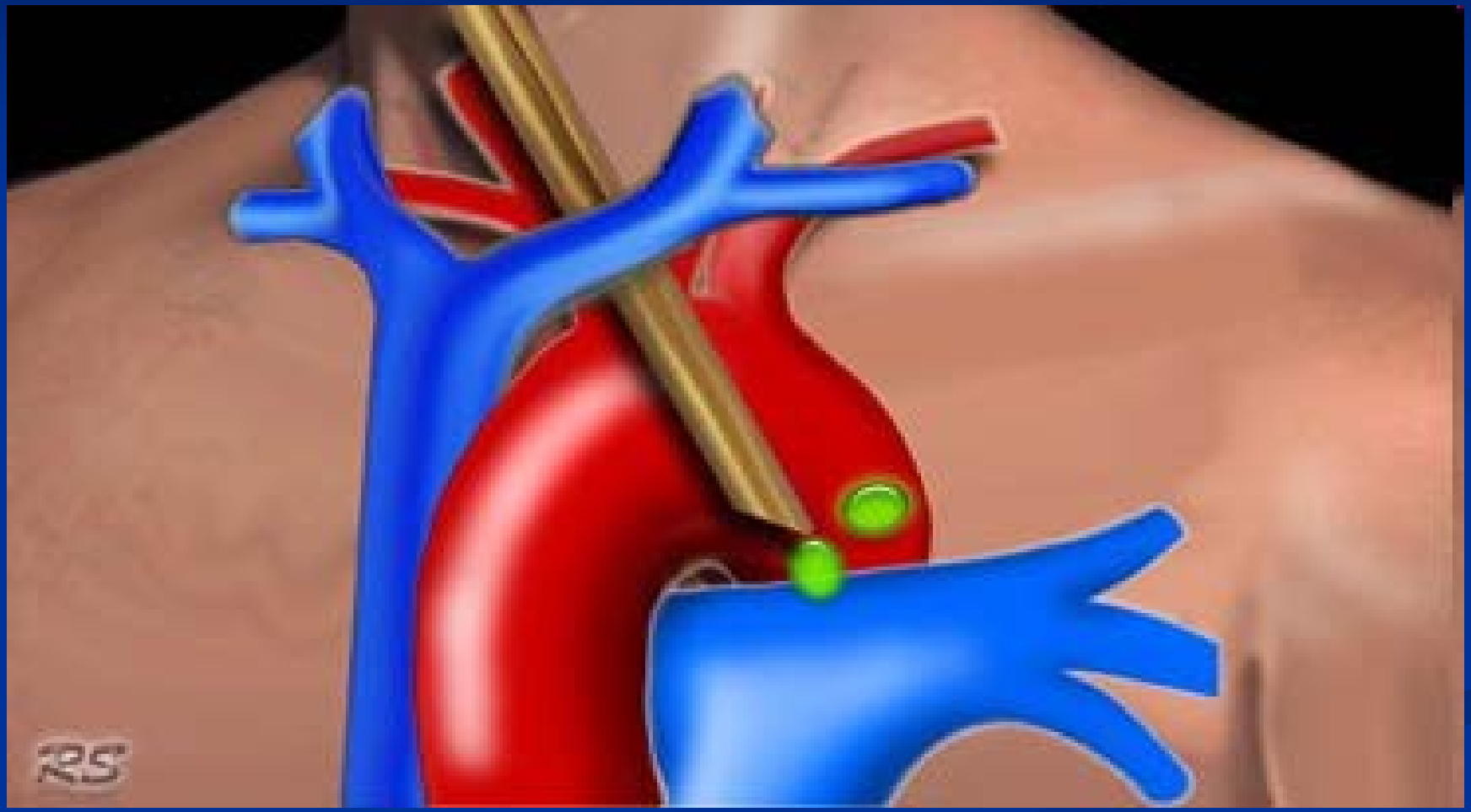
Extended mediastinoscopy is an alternative for the anterior-second interspace mediastinotomy which is more commonly used for exploration of mediastinal nodal stations.



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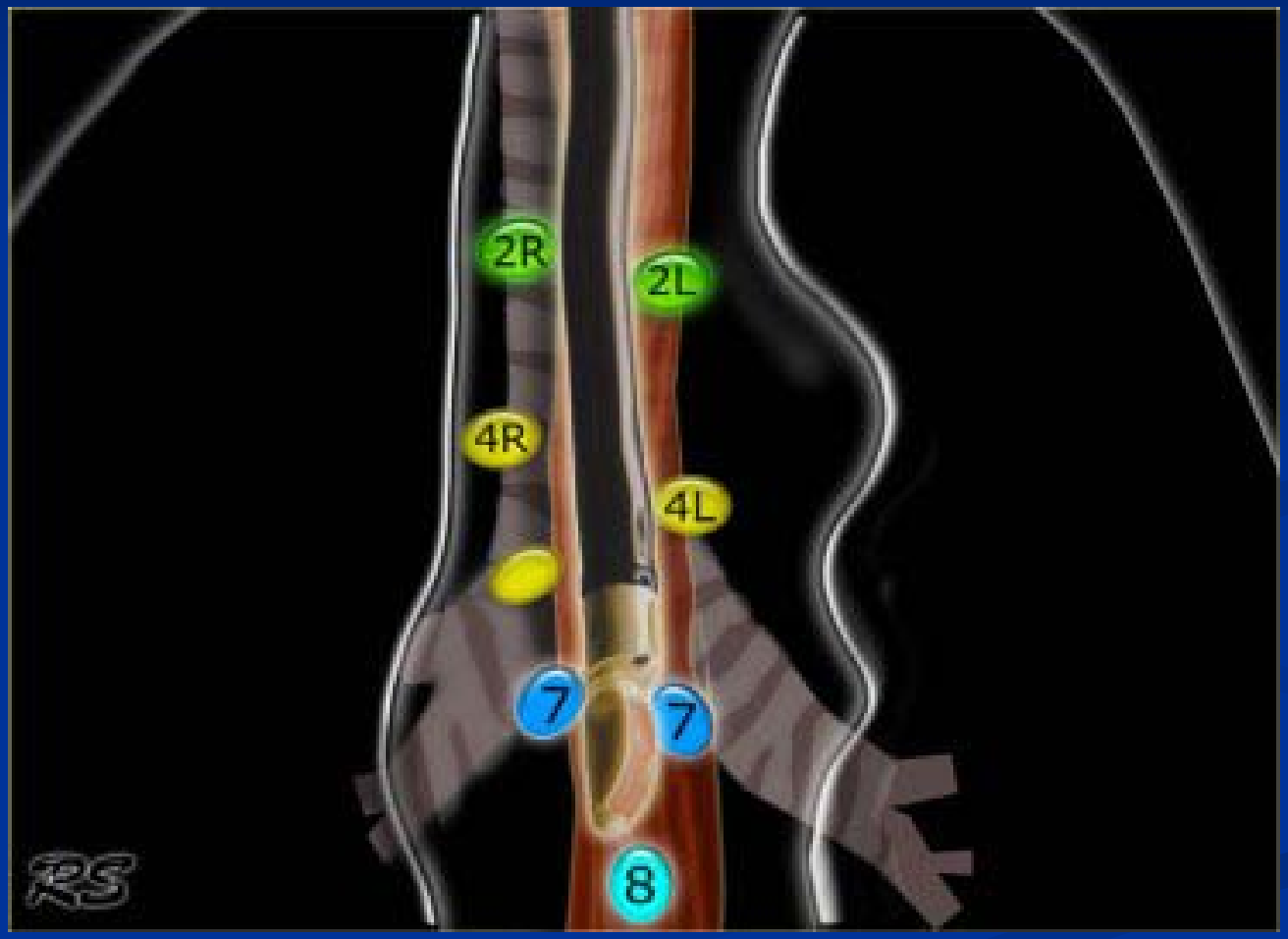
Endoscopic Ultrasound with Fine Needle

Aspiration



- The pure mediastinal germ cell seminomas are extremely radiosensitive and are treated with radiation therapy.
  - After radiation, about 80% of patients with pure seminoma are cured.
  - Residual masses greater than 3 cm should be resected.

- Nonseminomas usually treated with three-drug chemotherapy (bleomycin, etoposide, and cisplatin).
  - Surgical resection is reserved for a residual mass after treatment, with normalization of serum markers.

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Indiana University reviewed their 25-year experience with treated mediastinal nonseminomatous germ cell tumors in 158 patients. With a median follow-up of 34 months, they reported a 62% overall survival.

Kesler KA, Rieger KM, Hammoud ZT, et al. A 25-year single institution experience with surgery for primary mediastinal nonseminomatous germ cell tumors. *Ann Thorac Surg* 2008;85:371-8.

Long-term disease-free survival was achieved in 54% of patients with mediastinal NSGCT, most commonly by using induction chemotherapy followed by consolidation surgery.

Rodney AJ, Tannir NM, Siefker-Radtke AO, Liu P, Walsh GL, Millikan RE, Swisher SG, Tu SM, Pagliaro LC. Urol Oncol. 2010 Oct 6.