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Radiotherapy in oncological emergencies. Is it still a mainstay?

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Case 1

- 71 year old male, retired, living alone

- Previous medical history:
  - CAD, post STE-ACS - 5 years prior, treated with primary PCI
  - COPD, no systemic steroid dependency
  - Hypertension treated with multiple medications
  - Superficial (non invasive) bladder cancer, treated with TURBT - 1 year prior, no signs of recurrence to date

Case 1

- 2 week history of:
  - shortness of breath
  - increased cough intensity
  - hoarseness
  - mildly elevated body temperature
- Treated with Amoxycyline+clavulonate for COPD exacerbation by his PCP – no improvement, progression of symptoms.

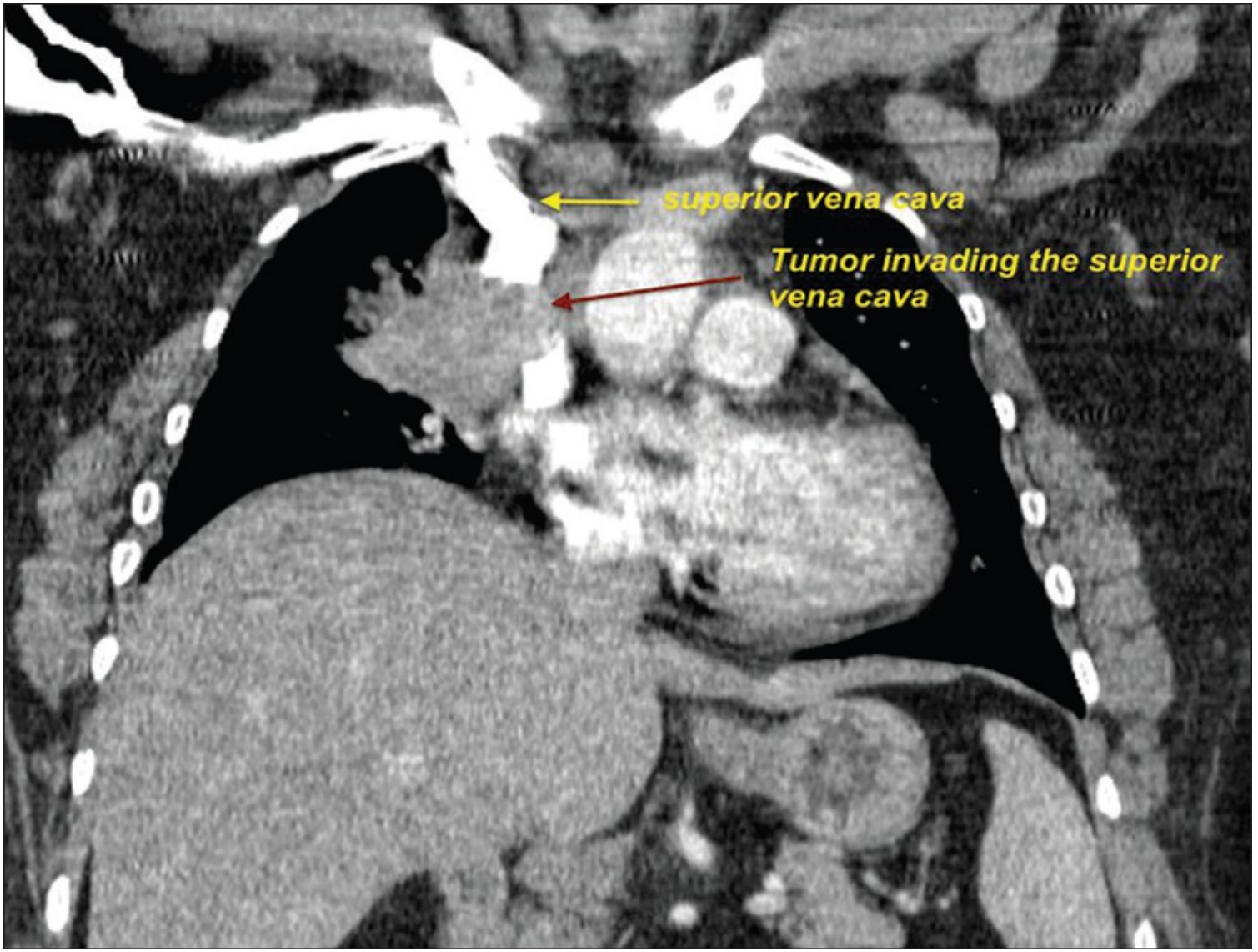
Case 1

- Physical examination
  - facial edema
  - distended jugular veins
  - tachypnoe
  - tachycardia
  - right-sided sibilant rhonchi (wheezing).

Case 1

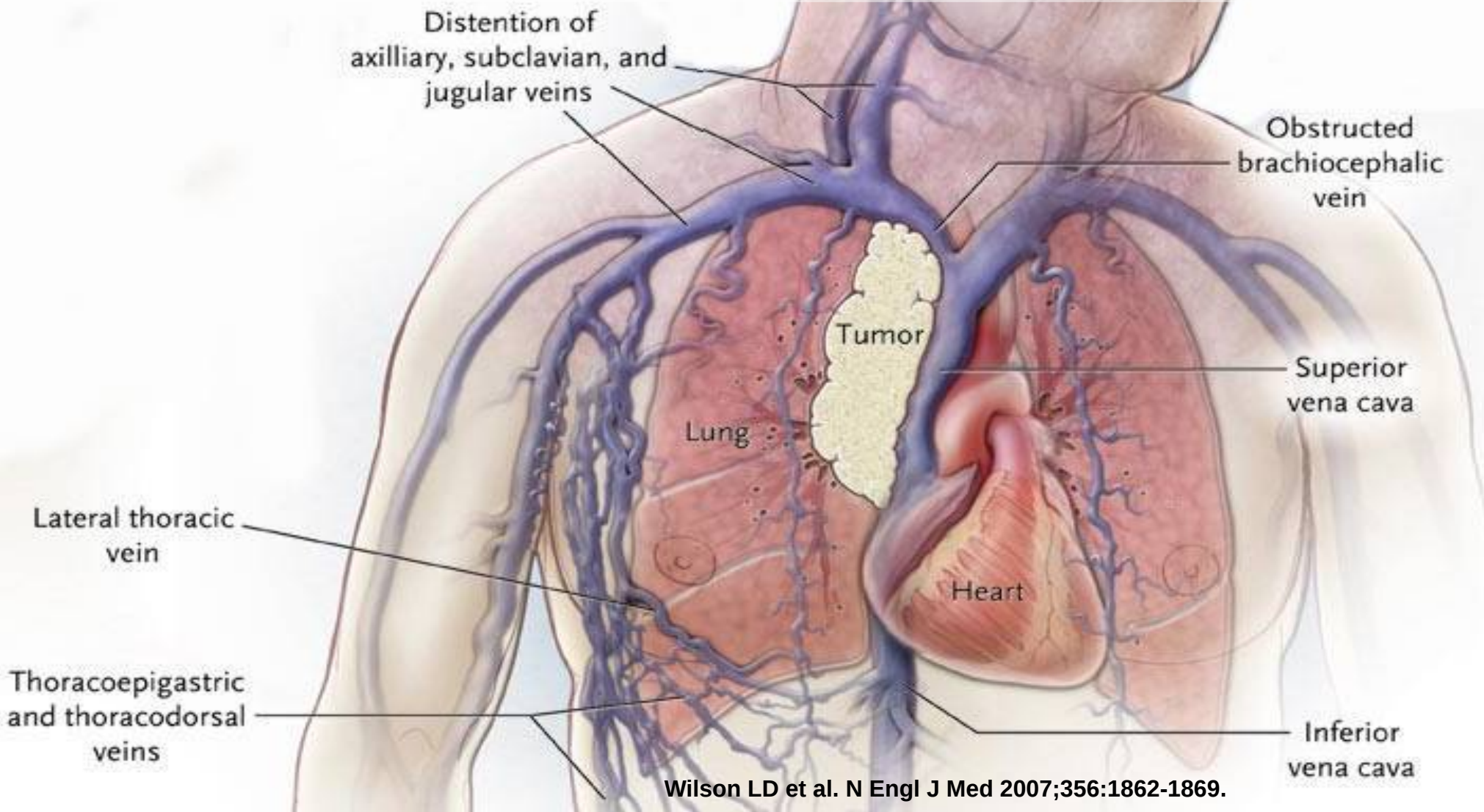
Diagnosis?

Superior Vena Cava Syndrome



SVCS - overview

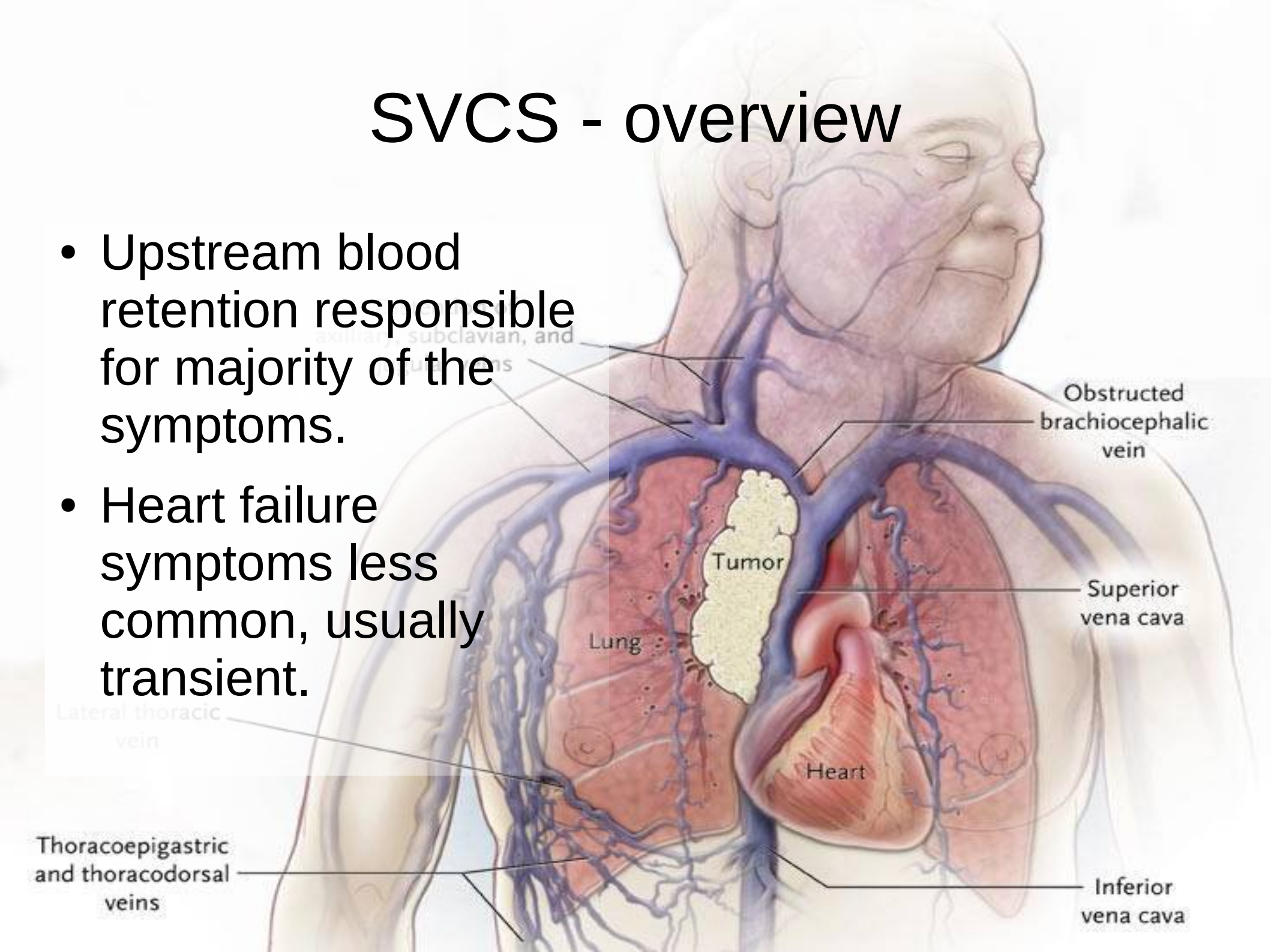
Clinical manifestation of blood flow obstruction (partial or complete) in vena cava superior.



Wilson LD et al. N Engl J Med 2007;356:1862-1869.

SVCS - overview

- Upstream blood retention responsible for majority of the symptoms.
- Heart failure symptoms less common, usually transient.

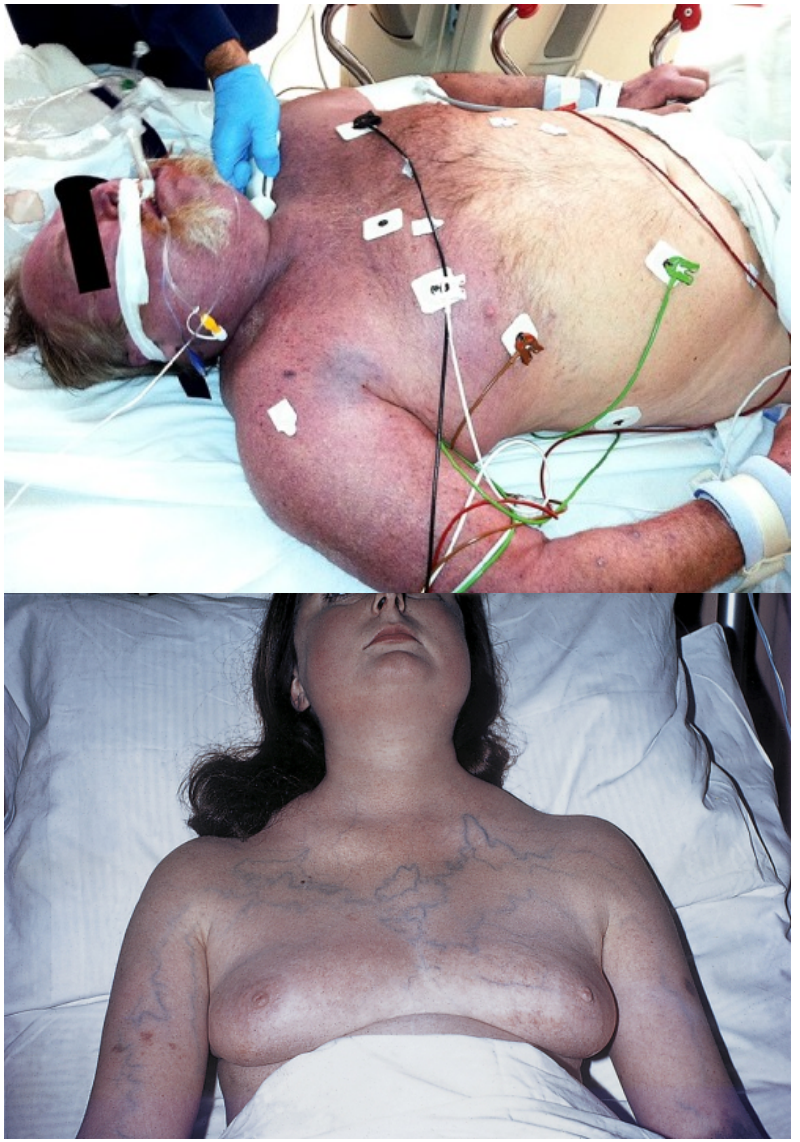


SVCS – symptoms

Table 2. Symptoms and Signs Associated with the Superior Vena Cava Syndrome.*

Sign or Symptom	Frequency	Range
	percent	
Facial edema	82	60–100
Arm edema	46	14–75
Distended neck veins	63	27–86
Distended chest veins	53	38–67
Facial plethora	20	13–23
Visual symptoms	2	0–3
Dyspnea	54	23–74
Cough	54	38–70
Hoarseness	17	15–20
Stridor	4	0–5
Syncope	10	8–13
Headaches	9	6–11
Dizziness	6	2–10
Confusion	4	0–5
Obtundation	2	0–3

* Data are from Armstrong et al.,[1] Yellin et al.,[4] Schraufnagel et al.,[5] Chen et al.,[13] Rice et al.,[15] and Urruticoechea et al.[18]



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SVCS - etiology

- 75% cases secondary to malignancies
- Other causes: infections, benign tumors or benign lymphadenomegaly, thrombi, fibrosis.
- mixed etiology frequent (ie. thrombus secondary to vein compression or infiltration)
- Interesting etiology evolution over time
  - Majority of cases were secondary to infections in the pre-antibiotic era
  - Malignancies responsible for up to 90% in the 80's
  - Rising incidence of SVCS due to thrombosis secondary to indwelling devices

Malignant SVCS - etiology

Table 1. Malignant Causes of the Superior Vena Cava Syndrome.*

Tumor Type	Proportion	Suggestive Clinical Features	
	% *(range)*		
Non–small-cell lung cancer	50 (43–59)	History of smoking; often age >50 yr	2-4% of NSCLC patients
Small-cell lung cancer	22 (7–39)	History of smoking; often age >50 yr	10% of SCLC patients
Lymphoma	12 (1–25)	Adenopathy outside the chest; often age <65 yr	2-4% of NHL patients
Metastatic cancer†	9 (1–15)	History of malignant condition (usually, breast cancer)	
Germ-cell cancer	3 (0–6)	Usually, male sex and age <40 yr; elevated levels of β human chorionic gonadotropin or alpha-fetoprotein are common	
Thymoma	2 (0–4)	Characteristic radiographic appearance on the basis of the location of the thymus; frequently associated with the parathymic syndromes (e.g., myasthenia gravis and pure red-cell aplasia)	
Mesothelioma	1 (0–1)	History of asbestos exposure	
Other cancers	1 (0–2)		

* Data are from Armstrong et al.,[1] Yellin et al.,[4] Schraufnagel et al.,[5] Chen et al.,[13] Rice et al.,[15] Nicholson et al.,[16] and Detterbeck and Parsons.[17]

† Approximately two thirds of the patients who have metastatic cancers have breast cancer.

Wilson LD et al. N Engl J Med 2007;356:1862-1869.

SVCS – symptoms dynamics

Depends on:

- obstruction mechanism:

  infiltration vs compression vs thrombus

- obstruction dynamics
- potential for collaterals recruitment (bypass circulation)

SVCS - workup

- Plain RTG – indirect findings:
  mediastine distension, evident tumor, pleural effusion.
- Duplex USG – compression beyond reach of the scan - indirect findings:
  upstream veins dilatation, flow spectrum abnormalities.
- Laboratory findings – vary widely:
  - hints suggesting malignancy: thrombocytosis (very common finding in cancer patients), anemia, hypoalbuminemia, hyponatremia.
  - Circulating cancer biomarkers (ie. CEA, Ca125, Ca19-9 etc.) are **not** reliable for diagnosis.
  - Elevated D-dimer level does **not** confirm thrombus.

SVCS - workup

- Cross-sectional imaging (CT, MRI, preferably contrast enhanced):
  - identification of underlying cause
  - localization of obstruction level and extent
- Contrast enhanced fluoroscopy (“superior vena cavogram”):
  - best for identifying exact location and extent of the obstruction as well as assessing the collaterals
  - rarely gives out the etiology
  - not always available

Malignant SVCS - workup

- Identifying the malignancy
  - Attempt to secure a tissue sample.
  - Cytology sample (ie. sputum, effusion, bronchoalveolar lavage) may be enough especially if time is short and tissue sample is hard to obtain.
  - Consider the easiest access. Search for lesions that are superficial or available via endoscopy.
  - Always weigh the impact of invasive procedures on future clinical course against the need of exact pathological diagnosis.

SVCS - grading

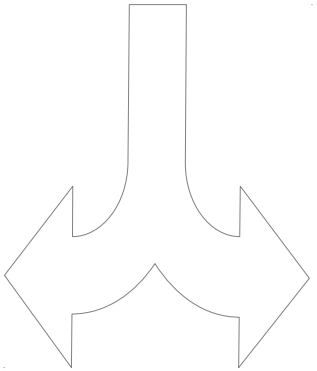
TABLE 2. Proposed Grading System for Superior Vena Cava Syndrome

Grade	Category	Estimated Incidence (%)	Definition[a]
0	Asymptomatic	10	Radiographic superior vena cava obstruction in the absence of symptoms
1	Mild	25	Edema in head or neck (vascular distention), cyanosis, plethora
2	Moderate	50	Edema in head or neck with functional impairment (mild dysphagia, cough, mild or moderate impairment of head, jaw or eyelid movements, visual disturbances caused by ocular edema)
3	Severe	10	Mild or moderate cerebral edema (headache, dizziness) or mild/moderate laryngeal edema or diminished cardiac reserve (syncope after bending)
4	Life-threatening	5	Significant cerebral edema (confusion, obtundation) or significant laryngeal edema (stridor) or significant hemodynamic compromise (syncope without precipitating factors, hypotension, renal insufficiency)
5	Fatal	<1	Death

[a] Each sign or symptom must be thought due to superior vena cava obstruction and the effects of cerebral or laryngeal edema or effects on cardiac function. Symptoms caused by other factors (e.g., vocal cord paralysis, compromise of the tracheobronchial tree, or heart as a result of mass effect) should be not be considered as they are due to mass effect on other organs and not superior vena cava obstruction.

Yu et al. Journal of Thoracic Oncology Aug 2008

SVCS – treatment decision



Life threatening, high dynamics:

- Stabilization (possibly ICU)
- Essential diagnostics
- Rapid treatment focused on SVC decompression

Non life threatening, low dynamics:

- Symptoms management
- Extended diagnostics
- Customized therapeutic plan

MSVCS – treatment modalities

- Radiotherapy – feasible in most malignancies
- Chemotherapy – chemosensitive malignancies (lymphoma, small cell lung cancer, germ cell cancers).
- Stent – ad hoc decompression until accurate diagnosis and appropriate treatment (best option for dynamic, life threatening SVCS) or palliative option combined with best supportive care (patients not feasible for causative treatment).
- Surgical bypass – rare
- Supportive care: glicocorticosteroids, antitussiva, heart failure treatment etc.

MSVCS – therapeutic approach

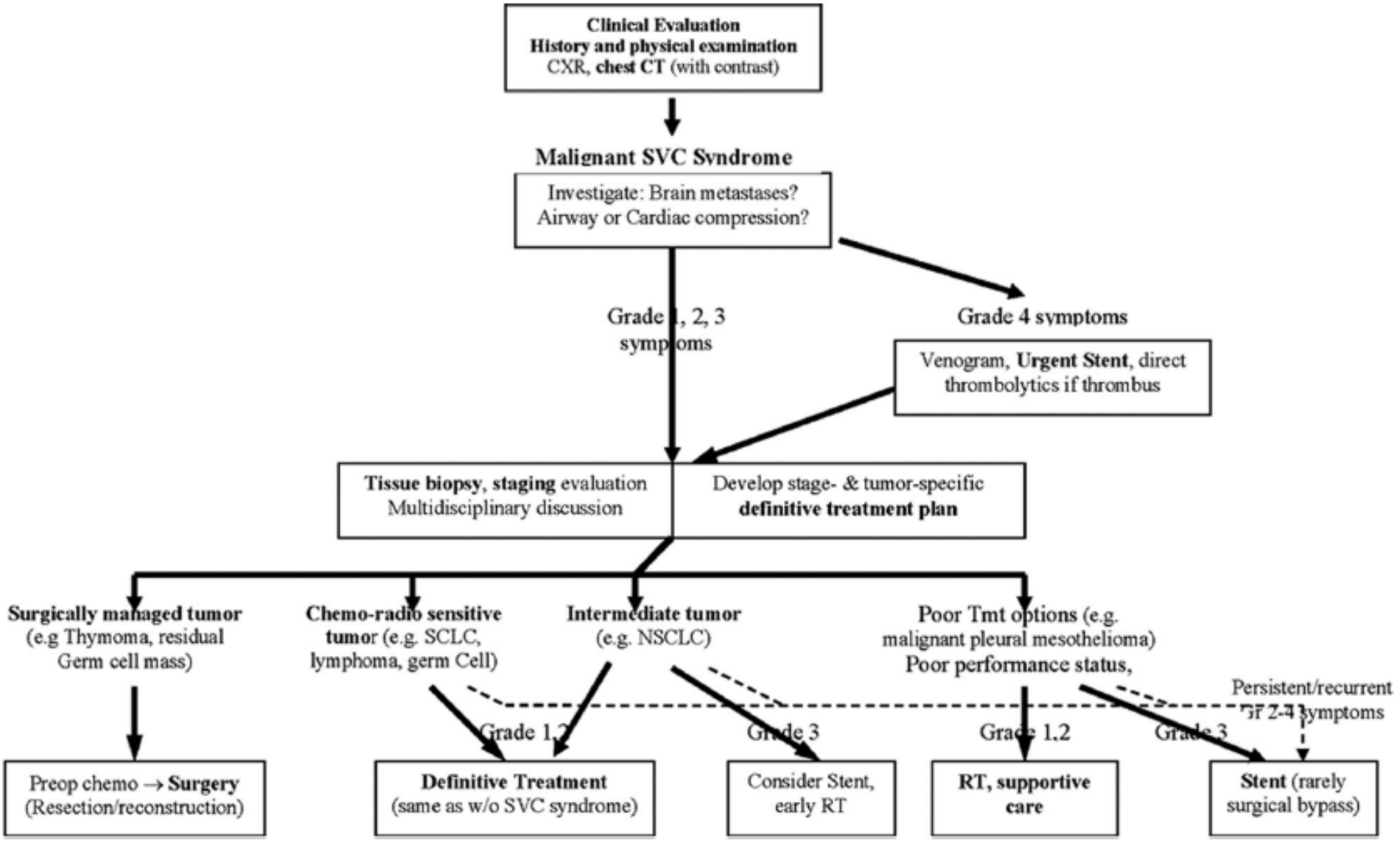
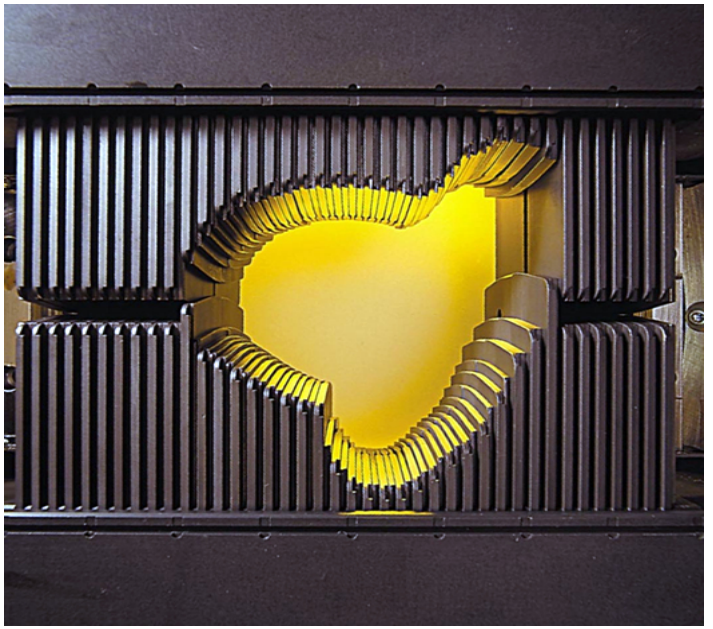


FIGURE 1. Proposed management algorithm.

MSVCS - radiotherapy

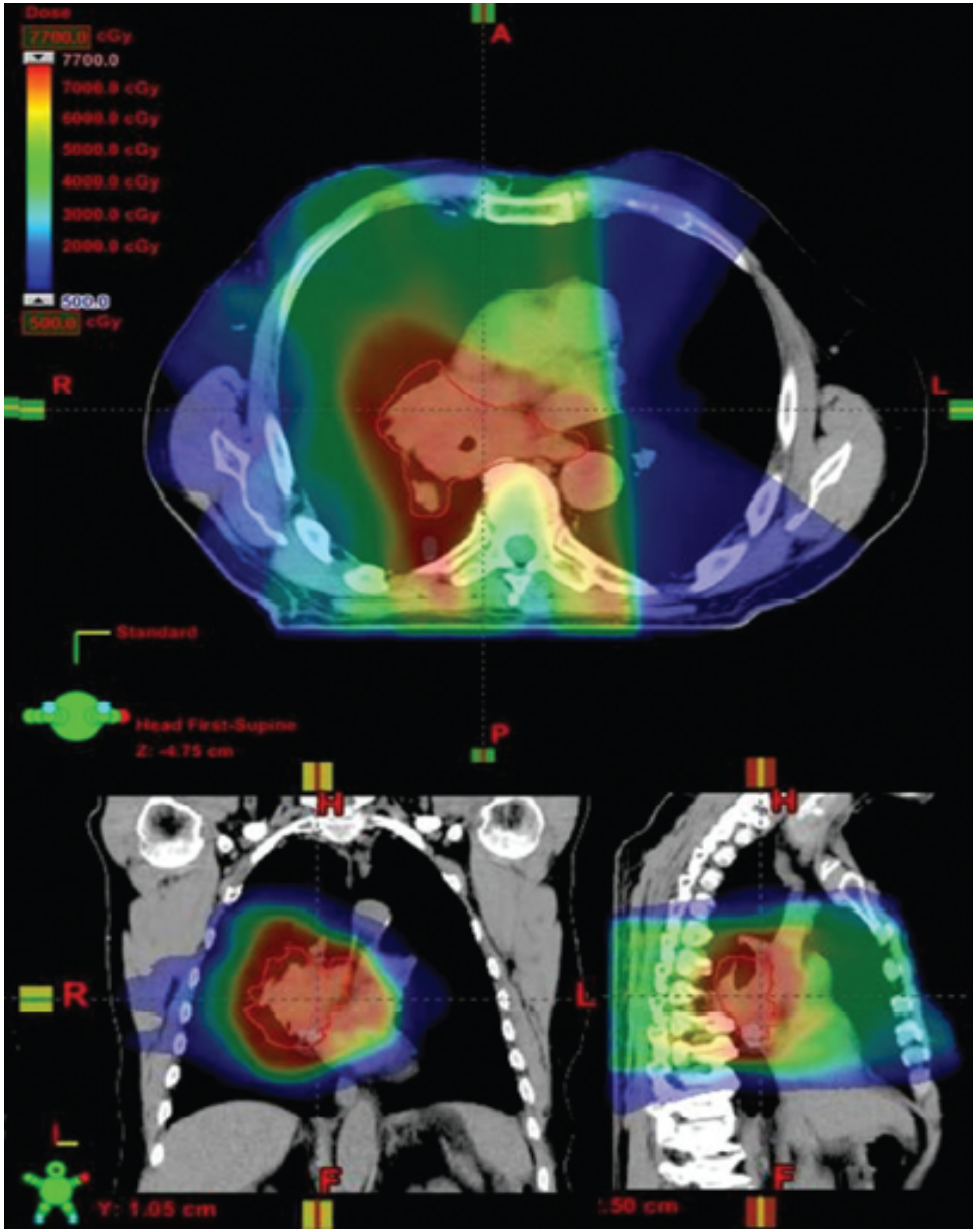
- Effective treatment modality for malignancy-related SVCS.
- Relative contraindications to RT :
  - previous RT in the same area (depending on detailed dose distribution)
  - certain connective tissue disorders (ie. scleroderma)
  - radioresistant tumor types ie. sarcoma
  - high tumor volume
  - individual potential for complications (ie. low circulatory or pulmonary reserves, immunocompromised, poor performance).



MSVCS - radiotherapy

RT treatment plan:

- based on tumor histology and intent of treatment.
- RT fields based on CT simulation should:
  - encompass gross tumor volume and/or involved nodal regions
  - spare adjacent organs particularly lungs and esophagus.
- Field size may be altered during treatment course.
- Beam characteristics and doses vary widely.



MSVCS - radiotherapy

- Response rates vary across literature – a possible impact of ever improving RT techniques.
- Frequent situation: clinical improvement with lack of tumor shrinkage on imaging studies.
- Possible progression of radio-resistant tumors requiring alternative treatment.
- Occasionally, symptom worsening may be due to transient tumor swelling or thrombotic complication (remember about thromboprophylaxis!).
- Always remember about supportive care.

MSVCS - radiotherapy

- There is no evidence-based consensus on MSVCS treatment to date as good quality comparative studies are scarce.
- As per systematic review done by Rowell and Gleeson RT provided relief:
  - in ¾ of SVCS in SCLC and 2/3 of SVCS in NSCLC
  - time to clinical response ranges from 7-15 days, may be as short as 72 hours.
- The effectiveness of steroids and the optimal timing of stent insertion relative to radiotherapy or other treatment modalities remain an area of controversy.

MSVCS – radiotherapy?

The same systematic review (Rowell & Gleeson) concluded that stent insertion may provide relief in a higher proportion of patients and more rapidly (especially in high dynamics, life threatening SVCS) than chemotherapy and radiotherapy.

Rowell NP, Gleeson FV; Clin Oncol (R Coll Radiol). 2002;14(5):338.

Case 1 - aftermath

- The patient was diagnosed with NSCLC of upper right lobe
- Metastatic, non regional, lymph nodes on his neck provided HP verification
- As the patients condition was stable, he underwent palliative radiotherapy (5x4Gy) on tumor and involved mediastinal LN.
- Subsequent palliative chemotherapy was initiated.

MSVCS - radiotherapy

Questions?

Case 2

- 59 year old female, a dressmaker, living with husband and her disabled mother.
- Previous medical history:
  - obesity
  - hypertension, treated with single drug
  - mixed hyperlipidemia, treated with atorvastatin
  - mild depression, treated with citalopram

Case 2

- Four week history of mid- and lower back pain, radiating towards her buttocks, accompanied by leg stiffness.
- Rapid onset of symptoms while helping her mother to a bath.
- Pain intensity dependent on body position (worst while sitting, least while laying face down).

Case 2

- Diagnosed with ischialgia by her PCP and treated with 7-day course of ketoprofen 100mg bi-daily and tolperisone 50mg daily.
- With no improvement on mentioned therapy she was started on 14-day course of diclofenac 75mg bi-daily and group B vitamins, both in intramuscular injections as well as combined paracetamol 375mg +tramadole 37,5mg oral formulation bi-daily, with only transient improvement.
- No imaging studies were performed.

Case 2

- Finally, 6 weeks after onset, she woke up early in the morning to excruciating pain (NRS 10/10) accompanied by major weakness of both lower limbs, preventing her from getting up on her own.
- She was transported to local emergency department.
- On admission: Visibly suffering, pale, sweaty, HR 120/min, RR 160/90 mmHg.

Case 2

Started on morphine iv. until pain control was sufficient to continue with the examination.

- Spastic paraparesis of both lower limbs with prominent tendon reflexes
- Diminished perception of touch down from the level of under her breasts.
- Urgent MRI was ordered.

Case 2

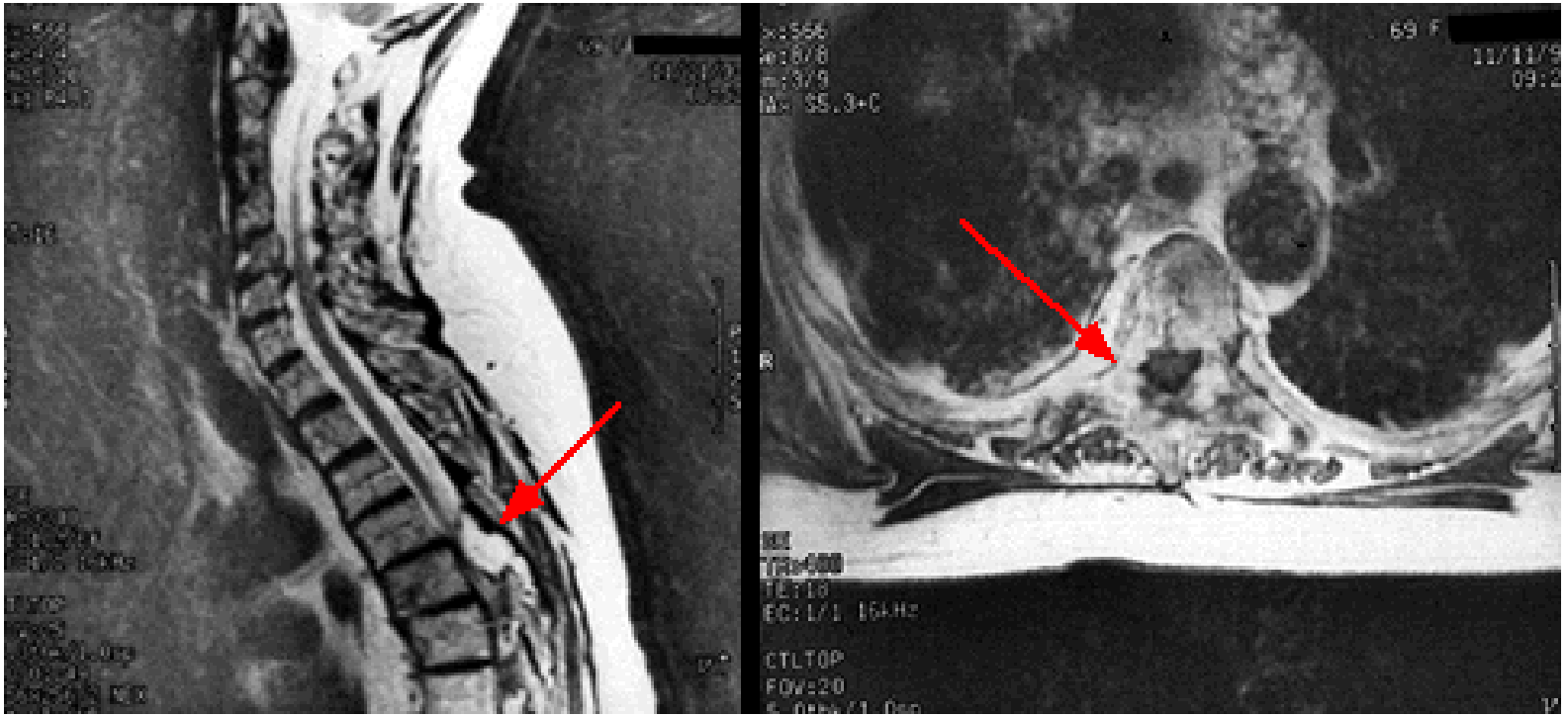
- While preparing the patient for the scan, a nurse found this:

Case 2

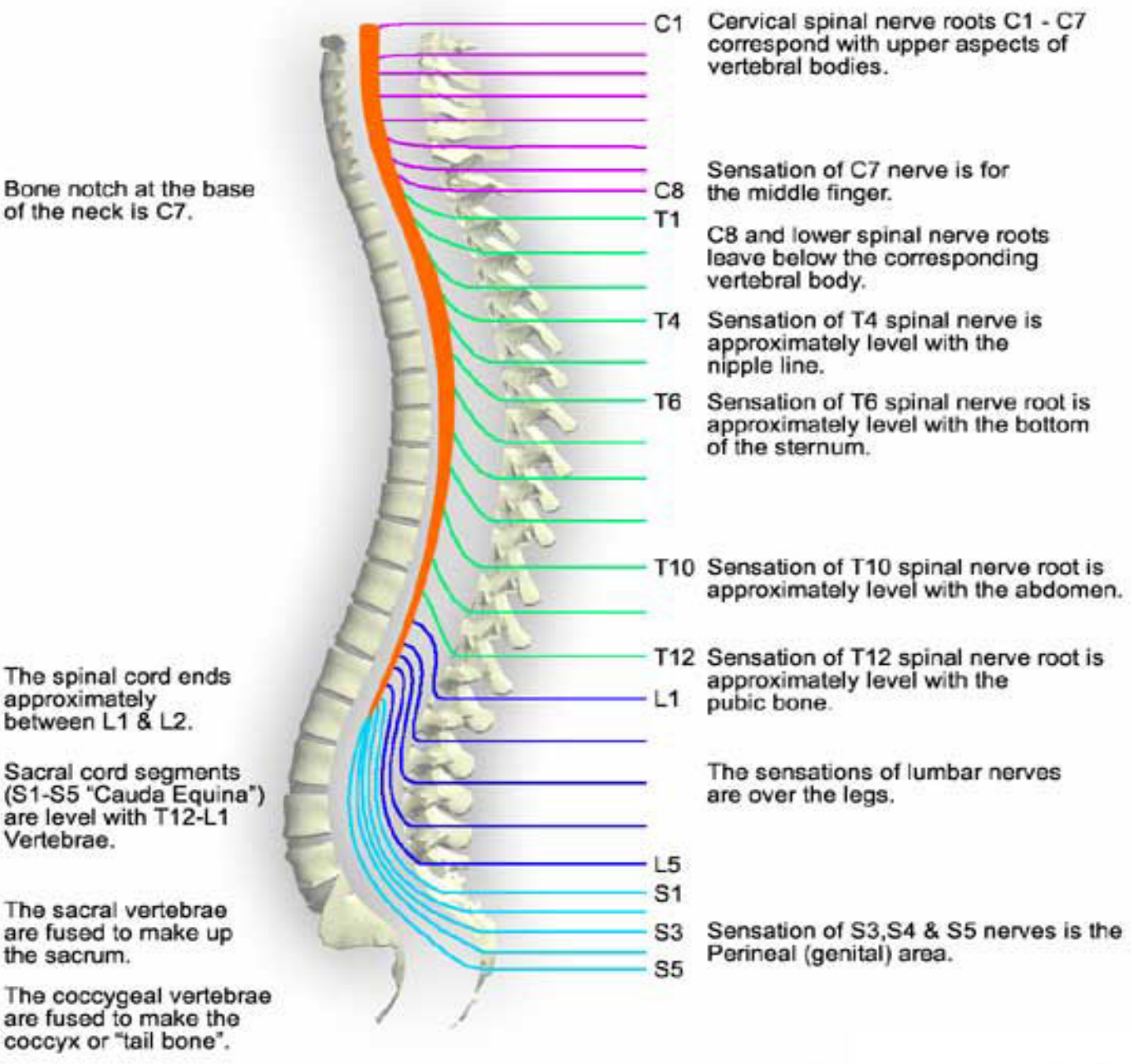
Diagnosis?

Malignant spinal cord compression.

MRI

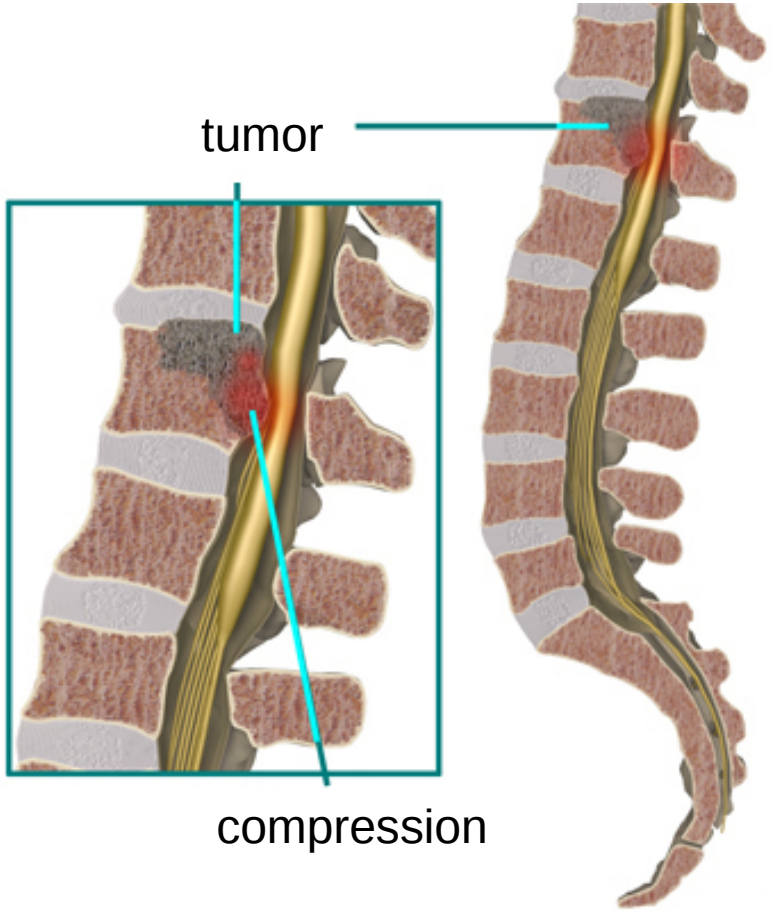


MSCC - overview



MSCC - overview

- Common complication of cancer
- Can cause pain and potentially irreversible loss of neurological function.
- Variable definitions denoting compression of either epidural sac or spinal cord itself.



MSCC - overview

- About 3-5% cancer patients regardless of histology
- Location:
  - Thoracic spine 60%
  - Lumbosacral spine 30%
  - Cervical spine 10%
- Typically multiple bone lesions present

MSCC - overview

MSCC - etiology

- Most common primary sites:
  - breast
  - lung
  - prostate
  - lymphoma
  - myeloma
- Possible with any neoplasm histology provided it's ability to spread in direct vicinity of spinal cord

MSCC - symptoms

- Pain – location and characteristics depending on compression extent and location.
- Motor dysfunction - muscle weakness – again corresponding to location
- Sphincter dysfunction
- Sensory loss – often not obvious
- Ataxia – often not obvious

MSCC - symptoms

Pain:

- various severity, may initially be mild
- duration of more than 1 - 2 weeks
- often may feel like a 'band' around the trunk (typical for Th spine)
- can radiate over the lower back towards lower limbs (typical for L-S spine)

MSCC - symptoms

Motor dysfunction:

- weakness tends to be symmetrical
- severity greatest with C and Th mets
- C and Th level typically hyper-reflexive below the lesion and demonstrate Babiński sign (extensor plantar reflex).

MSCC - symptoms

Sensory dysfunction:

- present in majority of cases although less commonly reported than motor symptoms
- numbness and paresthesias ('pins and needles' or 'ants marching')
- sensory level
- ataxia – feeling unsteady, instable gait
- sexual dysfunction

MSCC - symptoms

Sphincter dysfunction:

- Problems with miction may include:
  - urinary incontinence
  - urine retention and/or hesitancy
- Constipation or problems controlling bowels

MSCC - management

Early detection

- The most important prognostic factor for regaining ambulation after treatment of an MSCC is pretreatment neurologic status.
- Another important prognostic factor is time from symptoms onset to spinal cord decompression
- Currently median time from symptoms onset to diagnosis is about 2 months.

MSCC - management

Multimodality treatment

Goals:

- Pain control
- Complications avoidance
- Neurologic function preservation/improvement

MSCC - management

Treatment options:

- High dose glicocorticosteroids
- Analgesia
- Surgery – decompression & stabilization
- Radiotherapy
- Chemotherapy
- Hormone therapy

MSCC - management

- Glicocorticosteroids:
  - decrease tissue edema
  - suppress inflammation in affected area
  - decrease pain severity
  - neuroprotection?

- Dosing is controversial:
  - dexamethasone 96mg a day – best evidence, high adverse effects rate
  - 16mg a day was found non inferior in single small trial
  - Equivalent or even higher methylprednisolone often used

MSCC - management

Analgesia:

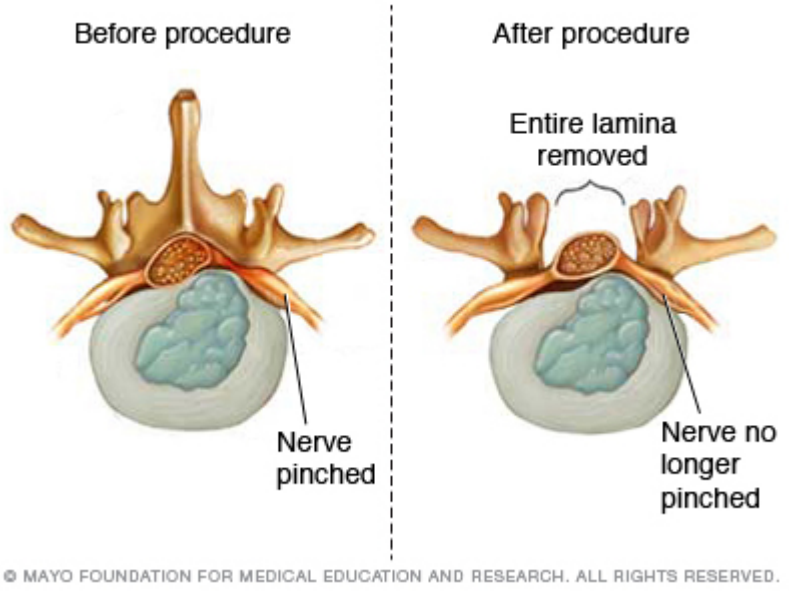
- usually opiates are required
- glicocorticosteroids
- dosing individual
- Remember about neuropathic component of nocyception in this setting – coanalgesics.

MSCC - management

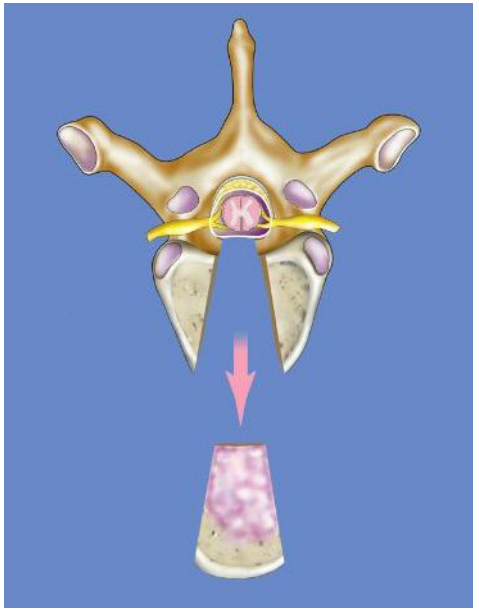
Surgery:

- decompression
- stabilization
- reconstruction

laminectomy



corporectomy



- Should be considered in all medically feasible patients, but qualification must be very careful.
- <u>Modern techniques superior to RT alone</u>

MSCC - management

Radiotherapy:

- pain control
- tumor suppression
- various doses for various tasks
- target margin size is controversial
- Remained a standard of care for many years until the advent of current neurosurgical techniques.
- According to most recent data best results when administered after surgery.

MSCC - management

Post-surgical radiotherapy:

- Consider in all feasible patients
- Choose target volume and dosing regimen individually – consider more aggressive treatment plan in patient with higher life expectancy

MSCC - management

Single modality radiotherapy:

- Patients not feasible for surgery or surgery not available
- Recurrence after treatment – as salvage therapy.

Systemic therapy (chemotherapy, hormone treatment):

- maintenance after local therapy (surgery and/or RT)
- single modality for patients not feasible for local therapy

Prognosis

- Median survival with MSCC is 6 months
- Ambulatory patients with radiosensitive or chemosensitive tumors have the best prognosis and are most likely to remain mobile

Case 2 - aftermath

- The patient was diagnosed with luminal A, disseminated breast cancer.
- She underwent laminectomy of involved vertebrae with simultaneous spine stabilization and subsequent radiotherapy.
- As she did not regain ambulation and recovered slowly, she was started on palliative hormonal treatment (not feasible for more aggressive options).
- 8 months later - died of complication resulting from immobility

MSCC

Questions?

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Thank You

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