# Complications of Cancer Therapy: Part I

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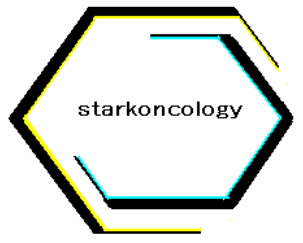


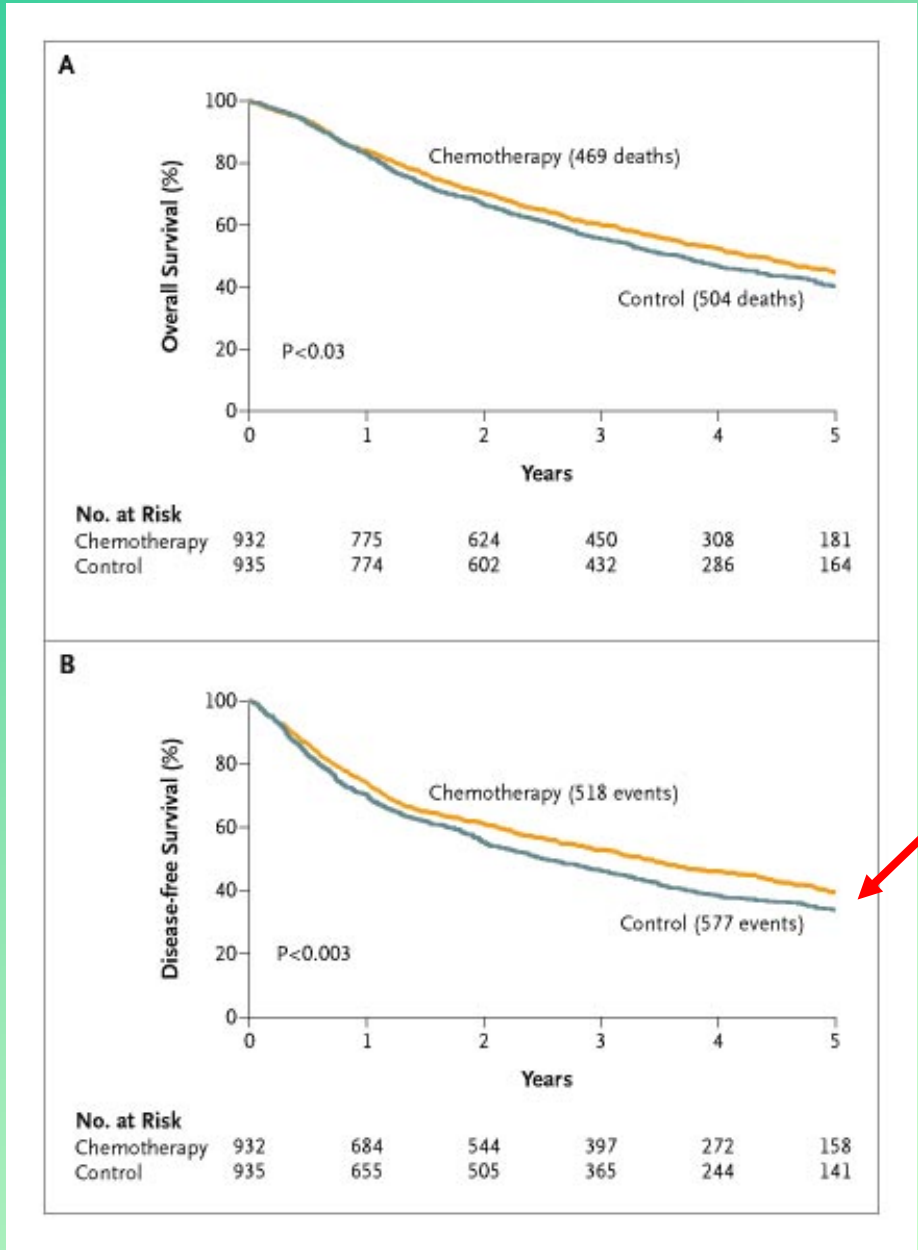
# Case Presentation

- 46 y.o. man developed cough
- Past smoking history
- Heavy prior alcohol use
- CXR done and abnormal…..
- CT done…..
- PET scan: nodule hot (SUV 8.1); rest of thorax negative for uptake
- Mild pulmonary hypertension (PA pressure 33)
- At surgery had two separate cancers…

# Case Presentation, cont.

- 2.5 cm squamous-cell carcinoma with visceral pleural involvement
- 1.8 cm adenocarcinoma without pleural involvement
- All nodes negative
- Staged up as $T_2N_0$ or Stage IB
- By current criteria was offered adjuvant chemotherapy to improve outcome

# Overall Survival (Panel A) and Disease-free Survival (Panel B)




**Highly significant difference for sample size**

starkoncology

Adjuvant Chemo Data

The International Adjuvant Lung Cancer Trial Collaborative Group, N Engl J Med 2004;350:351-360

# Case Presentation, cont.

- Received first cycle of taxol and carboplatin, followed the next day by an injection of Pegfilgrastim (“Neulasta”).
- Two days later presented to ED with severe abdominal pain
- CT obtained….

# Case Presentation, cont.

- Taken to OR for splenectomy
- Pathology….
- Recovered uneventfully and went on to receive the rest of his chemotherapy, including Neulasta
- Is now recovered from both operations and chemotherapy and is resuming normal quality of life

# Complications of Cancer Therapy

- New series for these conferences
  - Designed to illustrate to medical community complexities and pitfalls of contemporary cancer treatment and introduce examples
- Modern treatments are complex and often become available before extensive clinical trials are complete because of the pressure on the FDA for early approval

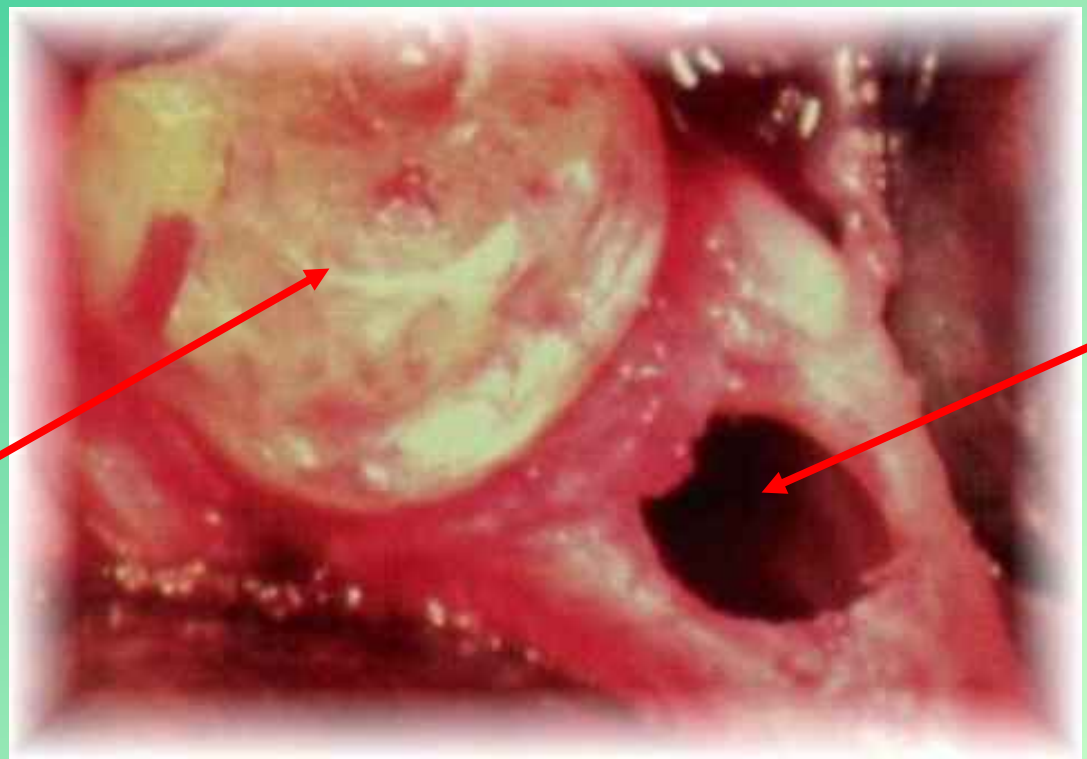
# Complications, continued

- Most complications can be anticipated and prevented or ameliorated; examples:
  - Neutropenia
  - Thrombocytopenia
  - Cardiac Toxicity
  - Neurotoxicity
  - Allergy from foreign macromolecules
  - Hypercoagulability from drugs in addition to diseases themselves

# Complications, continued

- Some complications can be anticipated but not prevented; examples:
  - Alopecia
  - Sterility
  - Pulmonary fibrosis
  - Mandibular osteonecrosis…

# Mandibular Osteonecrosis



**Site of recent tooth extraction**

**Hole in adjacent mandible**

**Subject of next conference on complications….**

# New Generation of Complications

- New targeted therapies have unusual but predictable complications:
  - Gleevec – soft tissue toxicity
  - Iressa and Tarceva – skin toxicity

# Tarceva Skin Rash

# New Generation of Complications

- New targeted therapies have unusual but predictable complications:
  - Gleevec – soft tissue toxicity
  - Iressa and Tarceva – skin toxicity
  - Monoclonal antibodies (Herceptin, Rituxan) – varying degrees of allergy; can be severe

# Hematopoietic Stimulators or "Growth Factors"

- Original use in helping patients recover more quickly from allo- or auto-bone-marrow or stem-cell transplant
- Now widely used in reversing anemia in cancer, renal failure and AIDS patients
- Also widely used to prevent severe neutropenia in patients receiving chemotherapy who are at risk

# Neutrophil Stimulators

- Use of white-cell growth factors now widely accepted in:
  - The elderly at risk for sepsis
  - Patients being treated aggressively with chemo for cure
  - Patients who have already had a bout of neutropenia +/- sepsis from prior chemo given without white-cell support
- Bone pain is thought to be only usual toxicity (plus expense to the health-care system)

# Splenic Rupture Following White-Cell Support

- Pathophysiology: splenic swelling following administration of G-CSF and GM-CSF reported in transplant literature
- Reported in several patients acting as stem-cell donors for allogeneic bone-marrow transplant
  - Such patients receive a five-day course of G-CSF typically before their stem-cells are harvested; rupture occurred 1-2 days after course is complete

# Splenic Rupture: literature review, continued

- Incidence is probably 1:1000 in bone-marrow transplant donors
- Also reported in patients with underlying bone-marrow disorders (acute leukemia, myelodysplastic syndrome) in whom the spleen was enlarged and/or diseased prior to starting treatment; rupture occurred after starting white-cell support
- Spontaneous rupture can also occur in patients with splenomegaly from hematologic malignancy
- Ours is the first known case of a patient with a solid tumor getting white-cell support

# Back to Our Case

- Rupture occurred two days after Neulasta shot – presumably before maximal splenic swelling occurred
- Role of prior alcoholism speculative
  - No obvious signs of cirrhosis or portal hypertension seen at surgery but focus of surgeon was to do operation under difficult circumstances

# What next?

- Case reported to Amgen
- Now splenic rupture is in black-box warning in package insert
- Incidence so low as to make it impractical to withhold these agents in the average patient
- Even in “high-risk” patient risk is still very low
- These agents have greatly improved cancer care for hundreds of thousands of patients

# Complications of Cancer Therapy: Tentative Conclusions

- Recall words of heart surgeon during my medical-school years:
  - "You do big operations, you get big complications"
- Same can be said for contemporary cancer therapy, with narrow therapeutic windows
- Stay tuned in coming months for other examples
- Other members of staff encouraged to contribute unusual cases….