Late Complications after Therapy in Patient with Hodgkin's Disease

Speakers: Students of 4th Course
Monu
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Teacher Advisor: O. Babiy & N. Kumpan
The purpose of this report is to pay attention to the problem of late cardiac complications, which develop in remote (distant) period after combined therapy (beam and chemotherapy) of Hodgkin’s lymphoma on example of illustrative clinical case.
CUMULATIVE INCIDENCE OF CAUSE-SPECIFIC MORTALITY

Cumulative Incidence of Cause-Specific Mortality

- Second malignancy
- Cardiac
- Hodgkin lymphoma
- Other lymphoma
- Pulmonary infection

Years Since Treatment

Cumulative Incidence

OUR PATIENT

37 Yr Female
COMPLAINTS

• Dyspnea during exertion (especially when going uphill or upstairs), ordinary physical activity cause breathlessness
• Edema of ankles in the evening
• Face and eyelid puffiness in the morning
• Palpitations
• Tendency to low blood pressure (85/55 mmHg)
In 1993 Hodgkin's Lymphoma of mandibular, cervical, intrathoracic lymph nodes had been diagnosed.

The combination therapy had been carried out.

Chemotherapy: particular regimens and medicines patient currently do not remember.

Bilateral cervical, supra-, infraclavicular, axillar as well as mediastinal regions radiotherapy had been performed.

Since 1996 remission occurs, relapses did not observe.
HISTORY OF THE PRESENTING COMPLAINTS

- Since 2013 dyspnea and ankle swelling bother the patient
- She was surveyed in cardiologic center and for the first time was established diagnosis of
  "Mild pericardial effusion. Chronic congestive heart failure II FC NYHA"

It was prescribed:
SALT RESTRICTION in diet (< 3 g per day)
TORASEMIDE 5 mg in the morning and
IVABRADINE 7.5 bid

- Symptoms decreased (but not completely ceased), exercise tolerance slightly improved
During the last month dyspnea and exercise intolerance were exacerbated, even ordinary physical activity and walking ground level less then 500m led to breathlessness.

Also palpitations had developed.

Due to symptoms deterioration, patient had been referred to cardiologic department.
DRUG HISTORY

- TORASEMIDE 5 mg qd in the morning
- IVABRADINE 7.5 bid
EXAMINATION

VITAL SIGNS:

- Height of the patient – 160 cm
- Weight of the patient – 52 kg
- Temperature – 36.7°C
- Blood pressure – 80/60 mmHg
- Pulse – 110 bpm
- Respiratory rate – 30 pm

Hypotension and tachycardia occurs
EXAMINATION

- The general condition of the patient is satisfactory
- The consciousness is clear
- **Edema** is absent at the time of inspection
- All groups of **lymph nodes** are not palpable, in the axillar region to the right palpated dense scar tissue (painless, possibly post beam therapy)
- **Thyroid gland** is palpated, size is slightly increased, painless, has smooth surface, homogeneous structure, nodules are not detected
- **JVP** 4.7 cm above the sternal angle
EXAMINATION

RESPIRATORY & CARDIOVASCULAR SYSTEMS

- Lung auscultation: vesicular breath sound, additional sounds are not present
- Auscultation of the heart: $S_1$ and $S_2$ are soft, systolic murmur heard over mitral valve, pericardial friction rub along the left sternal border
Abdomen is soft and nontender, no rebound
Liver percussion: 13/12/9 cm
Liver is palpated 4 cm lower than right costal arch, nontender and soft, and has smooth surface
Spleen percussion: 10/15 cm
Spleen is palpated 6 cm lower than left costal arch, tenderless, and elastic consistency
The kidneys are not palpable
Urine, Stool are normal
INVESTIGATION METHODS

1. Complete blood count
2. General urine test
3. Biochemical blood tests (ALT, AST levels, bilirubin levels, creatinine, BNP)
4. Thyroid function tests
5. ECG
6. 24 hour monitoring ECG
7. US of heart
8. Chest X-ray
9. CT scan of chest
10. US abdomen
11. US of thyroid gland
<table>
<thead>
<tr>
<th>Parameter</th>
<th>Value</th>
<th>Normal Range</th>
</tr>
</thead>
<tbody>
<tr>
<td>Complete blood count on the day of admission</td>
<td></td>
<td></td>
</tr>
<tr>
<td>ESR</td>
<td>10 mm/h</td>
<td></td>
</tr>
<tr>
<td>WBC (N 4.0-9.0 (10^9/L))</td>
<td>5.5 (10^9/L)</td>
<td>4.0-9.0 (10^9/L)</td>
</tr>
<tr>
<td>NE (N 1.7-7.7 (10^9/L); 47.0-72.0%)</td>
<td>2.9 (10^9/L)</td>
<td>1.7-7.7 (10^9/L); 47.0-72.0%</td>
</tr>
<tr>
<td>LY (N 0.4-4.4 (10^9/L); 19.0-37.0%)</td>
<td>2.0 (10^9/L)</td>
<td>0.4-4.4 (10^9/L); 19.0-37.0%</td>
</tr>
<tr>
<td>MO (N 0.0-0.8 (10^9/L); 3.0-11.0%)</td>
<td>0.5 (10^9/L)</td>
<td>0.0-0.8 (10^9/L); 3.0-11.0%</td>
</tr>
<tr>
<td>E (N 0.0-0.6 (10^9/L); 0.5-5.0%)</td>
<td>0.0 (10^9/L)</td>
<td>0.0-0.6 (10^9/L); 0.5-5.0%</td>
</tr>
<tr>
<td>BA (N 0.0-0.2 (10^9/L); 0.0-1.0%)</td>
<td>0.1 (10^9/L)</td>
<td>0.0-0.2 (10^9/L); 0.0-1.0%</td>
</tr>
<tr>
<td>PLT (N 180-320 (10^9/L))</td>
<td>245 (10^9/L)</td>
<td>180-320 (10^9/L)</td>
</tr>
<tr>
<td>RBC (N 3.9-5.0 (10^12/L))</td>
<td>4.28 (10^12/L)</td>
<td>3.9-5.0 (10^12/L)</td>
</tr>
<tr>
<td>Hb (N 120-160 g/L)</td>
<td>119 g/L</td>
<td>120-160 g/L</td>
</tr>
</tbody>
</table>

*All results falls under normal range*
**Urine analysis on the date of admission**

<table>
<thead>
<tr>
<th>Test</th>
<th>Result</th>
</tr>
</thead>
<tbody>
<tr>
<td>Colour</td>
<td>Light yellow</td>
</tr>
<tr>
<td>Specific gravity (N 1,001-1,040)</td>
<td>1,015</td>
</tr>
<tr>
<td>pH (N 5.0-7.0)</td>
<td>5.0</td>
</tr>
<tr>
<td>Protein (N absent)</td>
<td>Absent</td>
</tr>
<tr>
<td>Glucose (N absent)</td>
<td>Absent</td>
</tr>
<tr>
<td>Eritrocytes (N single)</td>
<td>0-1/HPF</td>
</tr>
<tr>
<td>Leucocytes (N 6-8 in field)</td>
<td>3-4/HPF</td>
</tr>
<tr>
<td>Transitional epithelium (N single)</td>
<td>0-1/HPF</td>
</tr>
<tr>
<td>Casts: hyliane, granular, etc. (N single)</td>
<td>Absent</td>
</tr>
<tr>
<td>Crystals (N absent)</td>
<td>Absent</td>
</tr>
</tbody>
</table>

*Urine analysis falls into normal range*
Biochemical blood profile on the date of admission

Plasma glucose (3.9 - 6.4 venous blood) - 4.4 mmol/L

<table>
<thead>
<tr>
<th>Test</th>
<th>Result</th>
</tr>
</thead>
<tbody>
<tr>
<td>Bilirubin Total (N 17-21 mkmol/L)</td>
<td>5.2 mkmol/L</td>
</tr>
<tr>
<td>AST (N &lt; 31 U/L)</td>
<td>16 U/L</td>
</tr>
<tr>
<td>ALT (N &lt; 31 U/L)</td>
<td>26 U/L</td>
</tr>
</tbody>
</table>

Liver function tests fall in reference range
**CLINICAL DATA**

Biochemical blood profile on the date of admission

<p>| | |</p>
<table>
<thead>
<tr>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Creatinine</strong></td>
<td>97</td>
</tr>
<tr>
<td>(N 53-97 mkmol/L)</td>
<td>mkmol/L</td>
</tr>
<tr>
<td><strong>Serum Na</strong></td>
<td>137</td>
</tr>
<tr>
<td>(N 135-145 mmol/L)</td>
<td>mmol/L</td>
</tr>
<tr>
<td><strong>Serum K</strong></td>
<td>3.2</td>
</tr>
<tr>
<td>(N 3.5-5.1 mmol/L)</td>
<td>mmol/L</td>
</tr>
</tbody>
</table>

**eGFR** 60 ml/min/1.73m²

(The Cockcroft and Gault formula)

Kidney function: there is decrease in GFR, iatrogenic hypokalemia
CLINICAL DATA

Biochemical blood profile on the date of admission

<table>
<thead>
<tr>
<th>TSH</th>
<th>2.60 mkU/mL</th>
</tr>
</thead>
<tbody>
<tr>
<td>(N 0.25-5 mkU/mL)</td>
<td></td>
</tr>
</tbody>
</table>

Thyroid hormones falls into normal range
Biochemical blood profile on the date of admission

<table>
<thead>
<tr>
<th>Test</th>
<th>Result</th>
</tr>
</thead>
<tbody>
<tr>
<td>C-RP (N &lt; 6 mg/L)</td>
<td>&lt; 6 mg/L</td>
</tr>
<tr>
<td>Rheumatoid factor</td>
<td>&lt; 8 IU/mL</td>
</tr>
<tr>
<td>ASL-O (N &lt; 200 IU/mL)</td>
<td>&lt; 200 IU/mL</td>
</tr>
</tbody>
</table>

All results fall into normal range; ESR, C-RP results shows absence of inflammation; rheumatoid factor shows normal autoantibodies; ASL-O represents absence of streptococcal infection.
Sinus rhythm, 88 bpm, electrical alternans, vertical heart axis, complete RBBB, left ventricle overload, PR-segment depression in II, III, AVF, PR-segment elevation in AVR, ST-segment depression in I, II, III, AVF, V1-V6, ST-segment elevation in AVR, V1
Sinus rhythm, 88 bpm, electrical alternans, vertical heart axis, complete RBBB, left ventricle overload, PR-segment depression in II, III, AVF, PR-segment elevation in AVR, ST-segment depression in I, II, III, AVF, V1-V6, ST-segment elevation in AVR, V1
24 hour monitoring ECG

1) Sinus rhythm
2) Mean frequency 73 bpm (daytime 79 bpm, nighttime 63 bpm)
3) Min frequency 56 bpm
4) Max frequency 120 bpm
5) Single supraventricular premature beats (19 SPB)
6) Single ventricular premature beats (6 SPB)
7) Ischemic changes of ST-T were not observed

Significant abnormalities are not detected
CLINICAL DATA

Echocardiography

- Heart chambers: septal thickness 8 mm, LV posterior wall thickness 8 mm

Left ventricle

- EDD 40 mm  EDV 67 ml  Stroke volume 47 ml
- ESD 17 mm  ESV 20 ML

Right ventricle diameter 24 mm

- Aortic valve fibrosis and regurgitation I degree
- Mitral valve prolapse I degree
- Pericardial effusion:
  - posterior wall 3,5 mm
  - anterior wall 7 mm
  - apex 2,5 mm

- Collapse of inferior vena cava on inspiration more than 50%
- Heart contractility is preserved (EF 75%)

Mild pericardial effusion is present, myocardial contractility is preserved, aortic fibrosis and regurgitation I degree, mitral valve prolapse I degree
CLINICAL DATA

Echocardiography
CLINICAL DATA

Chest CT scan

- Signs of fibrosis of the lungs roots, likely beam therapy etiology
- Minimal upper mediastinal lymphadenopathy (paratracheal region); no reliable progression by comparison with 2008 year
- Cardiomegaly, mild hydropericardium (max fluid thickness 14 mm); occurrence of hydropericardium by comparison with 2008 year
- Diffuse changes in thyroid gland structure

Lung fibrosis and cardiomegaly with mild hydropericardium are detected
U.S of thyroid gland

- Thyroid gland is enlarged (goiter – 1st degree)
- Diffuse parenchyma changes: in both lobes occurs multiple cysts 2.5-4.0mm in diameter and hypoechogenic heterogenic inclusions with cystic component (right lobe 4.5*7.5mm in diameter and left lobe 9.5*7.5mm in diameter)

Goiter (1st degree) with diffuse nodular parenchyma changes is seen
U.S of Abdomen

- Liver: right lobe 11.5 cm, left lobe 5 cm; focal lesion of the 3rd segment of left lobe 10×12 mm in diameter
- Spleen: 4.5 cm/10 cm
- Left kidney: diminished in size (32×65 mm), lumbar displacement, diffuse hyperechogenicity of the parenchyma, thinning of the cortex, hypoechogenic inclusions (at least 2 inclusions) 6-14 mm in diameter
- Right kidney has normal size (56×103 mm)
- Urolithiasis of both kidneys (2-4 mm in diameter)

**Hemangioma of the left lobe of liver** is seen; **left kidney hypoplasia; urolithiasis**
CONSULTATION

Cardiac surgeon consultation

Diagnosis:

*Chronic effusive pericarditis, not compressive.*

*Chronic heart failure I-II FC*

At the moment patient does not require surgical treatment of pericarditis, but only conservative treatment
Diagnosis:

Diffuse goiter I degree, euthyroidism

Condition does not require any correction at the present time
CLINICAL SYNDROMES

- Pericardial effusion
- Heart failure
- Cardiosclerosis
- Pneumofibrosis
- Chronic kidney disease
- Hepatosplenomegaly
- Goiter
Clinical Syndromes Classification

Pericardial effusion

<table>
<thead>
<tr>
<th>Onset</th>
<th>Acute</th>
<th>Subacute</th>
<th>Chronic (&gt;3 months)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Size</td>
<td>Mild  &lt;10 mm</td>
<td>Moderate 10–20 mm</td>
<td>Large &gt;20 mm</td>
</tr>
<tr>
<td>Distribution</td>
<td>Circumferential</td>
<td>Loculated</td>
<td></td>
</tr>
<tr>
<td>Composition</td>
<td>Transudate</td>
<td>Exudate</td>
<td></td>
</tr>
</tbody>
</table>
Clinical Syndromes Classification

Grading the size of an effusion by echocardiography measurements

- Physiologic/trivial
  echo-free pericardial space < 5 mm ≈ 50-100 ml of fluid

- Small
  echo-free pericardial space 6-9 mm ≈ 100-250 ml of fluid

- Moderate
  echo-free pericardial space 10-19 mm ≈ 250-500 ml of fluid

- Large
  echo-free pericardial space >20 mm ≈ >500 ml of fluid
Pericardial effusion

According to the composition of the fluid:

- Serous
- Purulent
- Fibrinous
- Caseous
- Hemorrhagic
HEART FAILURE

Classification by time course

- Acute heart failure
- Chronic heart failure

Anatomical classification

- Left sided heart failure
- Right sided heart failure
- Total heart failure (Congestive HF)
## Heart Failure

The New York Heart Association (NYHA) Functional Classification

<table>
<thead>
<tr>
<th>Class</th>
<th>Symptoms</th>
</tr>
</thead>
<tbody>
<tr>
<td>I</td>
<td>No limitation of physical activity. Ordinary physical activity does not cause undue fatigue, palpitation, dyspnea (shortness of breath).</td>
</tr>
<tr>
<td>II</td>
<td>Slight limitation of physical activity. Comfortable at rest. Ordinary physical activity results in fatigue, palpitation, dyspnea (shortness of breath).</td>
</tr>
<tr>
<td>III</td>
<td>Marked limitation of physical activity. Comfortable at rest. Less than ordinary activity causes fatigue, palpitation, or dyspnea.</td>
</tr>
<tr>
<td>IV</td>
<td>Unable to carry on any physical activity without discomfort. Symptoms of heart failure at rest. If any physical activity is undertaken, discomfort increases.</td>
</tr>
</tbody>
</table>
## Heart Failure
### AHA/ACC Heart Failure Staging

<table>
<thead>
<tr>
<th>Class</th>
<th>Objective Assessment</th>
</tr>
</thead>
<tbody>
<tr>
<td>A</td>
<td>No objective evidence of cardiovascular disease. No symptoms and no limitation in ordinary physical activity.</td>
</tr>
<tr>
<td>C</td>
<td>Objective evidence of moderately severe cardiovascular disease. Marked limitation in activity due to symptoms, even during less-than-ordinary activity. Comfortable only at rest.</td>
</tr>
<tr>
<td>D</td>
<td>Objective evidence of severe cardiovascular disease. Severe limitations. Experiences symptoms even while at rest.</td>
</tr>
</tbody>
</table>
Clinical Syndromes Classification

Heart Failure

Table 3.1  Definition of heart failure with preserved (HFpEF), mid-range (HFmrEF) and reduced ejection fraction (HFrEF)

<table>
<thead>
<tr>
<th>Type of HF</th>
<th>HFrEF</th>
<th>HFmrEF</th>
<th>HFpEF</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Symptoms ± Signs&lt;sup&gt;a&lt;/sup&gt;</td>
<td>Symptoms ± Signs&lt;sup&gt;a&lt;/sup&gt;</td>
<td>Symptoms ± Signs&lt;sup&gt;a&lt;/sup&gt;</td>
</tr>
<tr>
<td>2</td>
<td>LVEF &lt;40%</td>
<td>LVEF 40–49%</td>
<td>LVEF ≥50%</td>
</tr>
<tr>
<td>3</td>
<td>_</td>
<td>1. Elevated levels of natriuretic peptides&lt;sup&gt;b&lt;/sup&gt;; 2. At least one additional criterion: a. relevant structural heart disease (LVH and/or LAE), b. diastolic dysfunction (for details see Section 4.3.2).</td>
<td>1. Elevated levels of natriuretic peptides&lt;sup&gt;b&lt;/sup&gt;; 2. At least one additional criterion: a. relevant structural heart disease (LVH and/or LAE), b. diastolic dysfunction (for details see Section 4.3.2).</td>
</tr>
</tbody>
</table>

BNP = B-type natriuretic peptide; HF = heart failure; HFmrEF = heart failure with mid-range ejection fraction; HFpEF = heart failure with preserved ejection fraction; HFrEF = heart failure with reduced ejection fraction; LAE = left atrial enlargement; LVEF = left ventricular ejection fraction; LVH = left ventricular hypertrophy; NT-proBNP = N-terminal pro-B type natriuretic peptide.

<sup>a</sup>Signs may not be present in the early stages of HF (especially in HFpEF) and in patients treated with diuretics.

<sup>b</sup>BNP > 35 pg/ml and/or NT-proBNP > 125 pg/mL.
Cardiosclerosis

- Following myocarditis
- Atherosclerotic
- Postinfarction

- Focal
- Diffuse
Clinical Syndromes Classification

**Interstitial Lung Diseases**

- ILD of Known Cause or Association
  - Medications
  - Radiation
  - Connective Tissue Disease
  - Vasculitis & DAH
  - Hypersensitivity Pneumonitis
  - Pneumoconioses

- Idiopathic Interstitial Pneumonias

- Sarcoidosis & Other Granulomatous Diseases

- Other
  - LAM
  - Pulmonary LCH
  - Eosinophilic Pneumonias
  - Alveolar Proteinosis
  - Genetic Syndromes

Adapted from: ATS/ERS Guidelines for IIP. AJRCM. 2002;165:277-304.
# Clinical Syndromes Classification

## Types of Drug Induced Renal Injury in Patients with Oncologic Disease

<table>
<thead>
<tr>
<th>Clinical Syndromes</th>
<th>Causes</th>
</tr>
</thead>
<tbody>
<tr>
<td>Acute tubular necrosis, Interstitial nephritis</td>
<td>Cisplatin, carboplatin, methotrexate, mitomycin-C, cyclosporine, ifosfamide, zoledronate, gemcitabine, interferons, urea derivatives, antibiotics, radiopaque substances</td>
</tr>
<tr>
<td>Glomeruli</td>
<td>Interferons, VEGF inhibitors, adriamycin, mitomycin-C, methotrexate, gemcitabine, urea derivatives, pamidronate</td>
</tr>
<tr>
<td>Renal vascular lesions</td>
<td>VEGF inhibitors, mitomycin-C, gemcitabine, cisplatin, bleomycin</td>
</tr>
</tbody>
</table>
## Clinical Syndromes Classification

### Chronic Kidney Disease


<table>
<thead>
<tr>
<th>Stage</th>
<th>Description</th>
<th>GFR (mL/min/1.73 m²) Action</th>
<th>Plan</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Kidney damage with normal or elevated GFR</td>
<td>≥90</td>
<td>Diagnosis, treatment of underlying condition and comorbidities, cardiovascular disease risk reduction</td>
</tr>
<tr>
<td>2</td>
<td>Kidney damage with mildly decreased GFR</td>
<td>60-89</td>
<td>Estimating progression</td>
</tr>
<tr>
<td>3</td>
<td>Moderately decreased GFR</td>
<td>30-59</td>
<td>Evaluating and treating complications</td>
</tr>
<tr>
<td>4</td>
<td>Severely decreased GFR</td>
<td>15-29</td>
<td>Preparation for renal replacement therapy</td>
</tr>
<tr>
<td>5</td>
<td>Kidney failure (ESRD)</td>
<td>&lt;15 (or dialysis, transplantation)</td>
<td>Replacement therapy (dialysis or transplantation)</td>
</tr>
</tbody>
</table>

ESRD, end-stage renal disease; GFR, glomerular filtration rate.

Causes of Hepatomegaly with Splenomegaly

- **Chronic liver disease** with portal hypertension: any cause of liver disease

- **Hematological disease**: Myeloproliferative disease, Leukemia, Lymphoma, Sickle cell anemia, Thalassemia, etc.

- **Infections**: Acute viral hepatitis, CMV/EBV, Malaria, Leishmaniasis, etc.

- **Infiltration**: Amyloidosis, Sarcoidosis

- **Miscellaneous**: Drug abuse, Acromegaly, SLE, Multiple sulfatase deficiency, Osteopetrosis
WHO goiter classification

**Grade 0** – no goiter presence is found (the thyroid impalpable and invisible)

**Grade 1** – neck thickening is present in result of enlarged thyroid, palpable, however, not visible in normal position of the neck; the thickened mass moves upwards during swallowing. Grade 1 includes also nodular goiter if thyroid enlargement remains invisible

**Grade 2** – neck swelling, visible when neck is in normal position, corresponding to enlarged thyroid- found in palpation
Goiter classification according to thyroid function

- Non-toxic goiter
- Toxic goiter
- Hypothyroid goiter
Goiter classification according to the thyroid structure

- Diffuse
- Nodular
**FINAL DIAGNOSIS**

**Main disease**
Hodgkin's Lymphoma, remission

**Complications**

Late Hodgkin's lymphoma therapy complications:
- Chronic mild pericardial effusion,
- Diffuse cardiosclerosis following aseptic myocarditis,
- Aortic valve sclerosis,
- Sinus tachycardia, right bundle branch block
- Chronic congestive heart failure with preserved EF (75%), II FC NYHA,
- Hypoplasia? (Druid induced atrophy?) of the left kidney,
- CKD II stage,
- Hepatomegaly with splenomegaly,
- Diffuse nodular non-toxic goiter
Heart Failure

- Diet: salt restriction, rich in potassium
- Rate control: IVABRADINE 7.5 mg bid
- Diuresis control: TORACEMIDE 5 mg qod
- Hypokalemia: POTASSIUM CHLORIDE 600 mg bid (under control of serum potassium)
- ACE-inhibitors: RAMIPRIL 1.25 mg qd
MANAGEMENT

Pericardial Effusion

- NSAIDs
  Aspirin 500 mg qd

Gastroprotection

Pantoprazole 40 mg qd
OUTCOME

- Despite of therapy, pericardial effusion persist by control echocardiography data
  posterior echo-free 3 mm
  anterior echo-free 6 mm
  apex echo-free 3.5 mm
- Symptoms ceased insignificantly, physical tolerance slightly increased, but lower extremities edema and morning eyelid puffiness are observed
CONCLUSION

- Patients who have been treated for Hodgkin's disease, despite being cured of their malignancy, may develop iatrogenic complications that lead to premature mortality.
- The frequency of long-term complications in patients treated for Hodgkin's disease makes continued follow-up an important part of their care.
- This follow-up should include efforts to prevent morbidity and mortality by early diagnosis and attention to risk factors.
- Future treatment regimens for Hodgkin's disease should be designed attempting to minimize these complications.
thank you