Gastrointestinal Lymphoma

- classification
- aetiology and pathogenesis
- diagnosis and staging
- therapy
- specifics of intestinal lymphoma
<table>
<thead>
<tr>
<th>B-cell-lymphoma</th>
<th>T-cell-lymphoma</th>
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<tbody>
<tr>
<td>marginalzone-B-cell-lymphoma of MALT-type</td>
<td>enteropathy-associated T-cell-lymphoma (EATCL)</td>
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<tr>
<td>follicular lymphoma (grade I-III)</td>
<td>peripheral T-cell-lymphoma (previously: non-EATCL)</td>
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<td>mantle cell lymphoma</td>
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<td>(lymphomatous polyposis)</td>
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<tr>
<td>diffuse large B-cell-lymphoma</td>
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<tr>
<td>with/without MALT components</td>
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<td>Burkitt-lymphoma</td>
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<td>immunodeficiency associated lymphoma</td>
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Helicobacter pylori and MALT-lymphoma

aetiopathogenetic role of Hp for MALT-lymphoma

molecular biological findings

epidemiological data

animal studies

morphological data
Helicobacter pylori and gastric MALT lymphoma

Hp induces acquisition of lymphoid tissue in the gastric mucosa: **Condition** for the development of gastric MALT lymphoma

Hp represents an antigenic stimulus for the lymphoma growth: **Progression** of gastric MALT lymphoma
Pathogenesis of intestinal lymphoma

- Antigen dependent proliferation of early stages of IPSID
- Lymphoma may regress after elimination of the proliferative stimulus
Pathogenesis of intestinal lymphoma

antigen → overstimulation of intestinal immune system → morphology:
lymphoplasmacellular infiltrate

chronic infection ← antibiotic therapy
Risik factors for intestinal lymphoma

• immune deficiency syndroms

• immunsuppression
  post transplantation
  immunsuppressive therapy *
  prior chemo- or radiotherapy
  AIDS

• malabsorption syndromes
  sprue

• inflammatory bowel disease *

* not proven
Sprue and intestinal T-cell-lymphoma

- lymphoma risk is increased up to 40 times
- dependent on the type of sprue?:
  - classical sprue
  - oligosymptomatic sprue
  - asymptomatic sprue
  - potential sprue
    not known!
- lymphoma incidence drops down along with the duration of gluten-free diet
Gastrointestinal Lymphoma

**histology** (low grade – high grade) and **stage** (I1, I2, II-IV) are the decisive prognostic factors and therapeutic determinants

Cogliatti et al., Gastroenterology 1991
Radaszkiewicz et al., Gastroenterology 1992
How can we reliably diagnose gastric lymphoma?

- Clinical symptoms are unspecific
- The endoscopic appearance of gastric lymphoma varies widely
- Up to 20% reveal low and high grade components
- Diagnosis of gastric lymphoma is an incidental finding in most cases

Kolve M, Fischbach W, Greiner A, Gastrointest Endosc 1999
ENDOSCOPIC-BIOOPTIC TECHNIQUE

Gastric mapping

- 10 biopsies from suspicious areas in formalin (and native) for histological (molecular) work-up.
- 4 biopsies from unsuspicious areas in antrum und corpus (each quadrant) as well as 2 biopsies from fundus.
- 1 biopsy from corpus and antrum resp for urease test.

In special case use of giant forcep or snare.
Diagnostic aspects in intestinal lymphoma

- intestinal lymphoma was diagnosed by explorative laparoscopy or laparotomy until recently

- new diagnostic procedures are available nowadays:
  - capsule endoscopy
  - double / single balloon enteroscopy
Capsule endoscopy in gastrointestinal lymphomas

patients:

n = 27 with known gastrointestinal lymphoma

results:

n = 7 with intestinal lymphoma: all revealed pathological findings on CE: ulcerations, nodes, plaques, villous atrophy

n = 20 with gastric lymphoma:
5 had abnormal findings on CE: intestinal manifestation?
capsule endoscopy
same patient on EGD: follicular lymphoma, grade I
duodenum, ileum, colon

same endoscopic aspect
capsule endoscopy

follicular lymphoma of the ileum
capsule endoscopy
same patient on EGD:
MALT lymphoma
capsule endoscopy

MALT lymphoma?
Double-Balloon-Enteroscopy

60 - 70 cm proximal of the valvula
Diffuse large B-cell-lymphoma
New diagnostic procedures for the mid gut

- **capsule endoscopy:**
  easy, high acceptance, less time consuming (physician) but no histology

- **double balloon enteroscopy:**
  cumbersome (patient), time consuming (physician) but histology available
Diagnostic strategy in suspected intestinal lymphoma

patient with symptoms or findings suspicious for or patient at risk for primary intestinal lymphoma

capsule endoscopy

pathological or suspicious findings

double / single balloon enteroscopy
Staging of gastrointestinal lymphoma

When gi lymphoma is diagnosed and confirmed by a reference pathology

- a staging procedure including
  - abdominal and cervical ultrasound
  - abdominal and thoracic CT scan
  - bone marrow puncture
  - ileocolonoscopy
  - endoscopic ultrasound (EUS)

- is necessary!
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Therapeutic strategies in gastric lymphoma

**MALT**

- **Stage I 1/2**
  - Hp eradication
  - (Hp-: eradication ?)
  - if no response or relapse:
  - RTx (surgery)
  - mh residuals:
  - watch-and-wait

- **Stage II 1/2**
  - RTx (surgery)
  - (Hp eradication)

- **Stage III / IV**
  - R-CTx

**DLBCL**

- R-CTx + RTx
  - (surgery + CTx)
  - (Hp eradication)

R-CTx + RTx
  - (surgery + CTx)

R-CTx ± RTx
Long-term outcome after Helicobacter pylori eradication therapy

**Conclusions**

The majority of patients have a favourable long-term outcome.

Hp eradication offers a real chance of cure

Fischbach W. et al., Gut 2004
Wündisch Th. et al. J Clin Oncol 2005
Most patients with minimal histological residuals of MALT lymphoma after successful eradication of Hp reveal a favourable course of disease without any oncological treatment.

A watch-and-wait strategy appears to be safe and may become the approach of choice

(Fischbach W et al., Lancet 2002 and Gut 2007)
Therapeutic options in gastric lymphoma

- surgery
- radiotherapy
- chemotherapy
- combined treatment
- H. pylori eradication

Aim: cure of disease!
Treatment of intestinal lymphoma

- No generally accepted standard (except DLBCL: R-CHOP)

- T-cell lymphoma (EATCL; Non-EATCL): Budesonid, prednisone, basiliximab, CHOP, Campath, Fludarabin, HD-BEAM + stem cell tx
Intestinal Lymphoma: patient’s outcome

Intestinal Non-Hodgkin’s Lymphoma: A Multicenter Prospective Clinical Study
Daum S et al., J Clin Oncol 2003

B-cell-lymphoma: comparable to gastric lymphoma

T-cell-lymphoma: much worse than gastric lymphoma
Current therapeutic strategies in intestinal T-cell lymphoma

Sprue like T-cell-lymphoma

Definition:
- symptomatic sprue refractory to gluten-free diet
- loss of antigen expression of intraepithelial lymphocytes or
- clonal expression of intestinal T-cells:
  - „early EATCL“ (no overt lymphoma)
Sprue like T-cell-lymphoma

Steroids
systemic - topic

follow-up

regression

staging

no regression

Anti-IL-2-receptor Mab
Basiliximab

regression

staging

no regression

individual therapy

no response

CHOP 14

no response
Current therapeutic strategies in intestinal T-cell lymphoma

T-cell-lymphoma

Definition:

overt (endoscopy, imaging) lymphoma
Intestinal T-cell-lymphoma

> 65 y., WHO > 1

CHOP-14

> 65 y., WHO < 1

< 65 y., WHO < 1

CHOP-21

staging after 3 cycles

CHOP-14 6x

no

response

Campath

HD-BEAM

stem cell tx.

no

response

Fludarabin + Campath

response

no
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Specifics of intestinal lymphoma

• are rare
• have a worse prognosis (compared to gastric lymphoma)
• can be better diagnosed nowadays: capsule endoscopy, DBE
• no therapeutic standard up to now: except R-CHOP for DLBCL
• need for future studies