Module 2: Clinical Features of Mantle Cell Lymphoma (MCL)

START

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Tutorial

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Glossary terms are identified by bold, yellow text.

Glossary terms are identified by bold, yellow text. Select the word to see the definition

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Clinical Connections encourage connections between the clinical content and the patient journey

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Module Overview

This module will provide you with an overview of the mantle cell lymphoma (MCL) signs and symptoms, progression and relapse MCL

- Learning Objectives
- Signs and Symptoms
- Progression of MCL
- Relapsed MCL
- Summary
- Progress Check

Upon completion of this module, you should be able to:

- List the signs and symptoms of MCL
- Discuss the progression of MCL

Clinical Features of MCL

Learning Objectives

This module will describe the clinical presentation, progression, and mechanisms of **relapse** of MCL.

Upon completion of this section, you should be able to:

SIGNS AND SYMPTOMS	• List the signs and symptoms of MCL
PROGRESSION	• Describe the progression of MCL
RELAPSE	• Explain the mechanisms of relapse of MCL

Clinical Features of MCL

Signs and Symptoms

MCL has a widespread, systemic nature. Therefore, patients may experience different symptoms resulting from involvement of multiple organs.[1]

B (general) symptoms:[2]

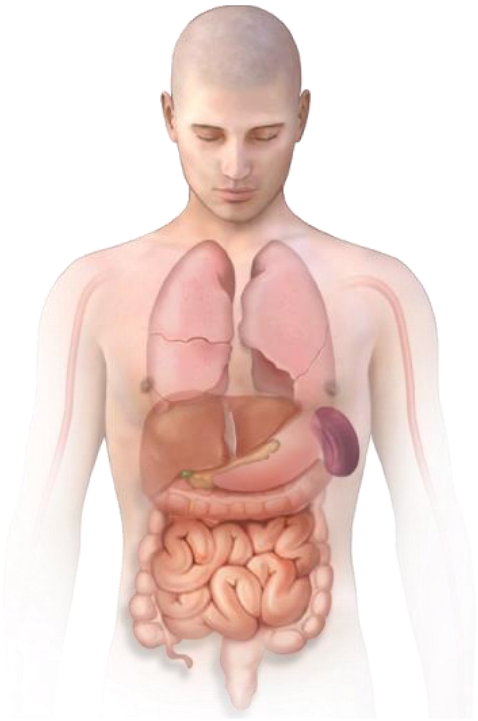
- Fever
- Unexpected weight loss
- Drenching night sweats

Enlargement of:[1]

- Tonsils
- Liver
- Spleen

Symptoms due to low blood cell counts:[2]

- Fatigue
- Easy bruising and frequent bleeding
- Frequent or severe infections



Symptoms due to GI complications:[2]

- Nausea
- Vomiting
- Indigestion
- Loss of appetite
- Abdominal pain

Symptoms due to pulmonary complications:[2]

- Chest pain or pressure
- Coughing or trouble breathing
- Bluish-red swelling in the head, arms, and upper chest
- Altered consciousness

Symptoms due to central nervous system (CNS) complications:[2]

- Double vision
- Facial numbness
- Trouble speaking

Clinical Features of MCL

Signs and Symptoms

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- Facial numbness
- Trouble speaking

Symptoms Due to Low Blood Cell Counts

Significant infiltration of the bone marrow by proliferating lymphoma cells can lead to low levels of certain blood cells in patients with MCL:[2]

- **Neutropenia** is defined as a **neutrophil** count below 1500/µL (a count below 500/µL is considered to be severe), and can lead to severe or frequent infections[3]
- **Anaemia** is defined as a haemoglobin level below 11.0 to 11.9 g/dL (women) or 11.0 to 12.9 g/dL (men) and is indicative of a low red blood cell count, which can lead to fatigue[4]
- **Thrombocytopenia** is defined as a platelet count below 150,000/µL, and can lead to easy bruising or bleeding[5]

Clinical Features of MCL

Signs and Symptoms

MCL has a widespread, systemic nature. Therefore, patients may experience different symptoms resulting from involvement of multiple organs.

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Sympto
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- Fatigue
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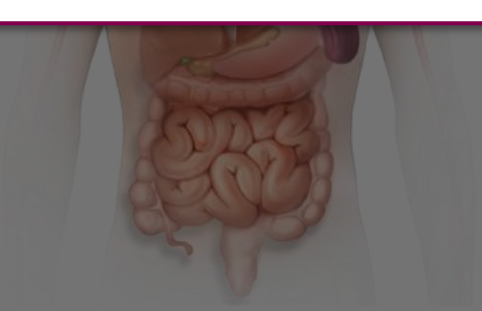

Symptoms due to Cl

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head, arms, and upper chest
- Altered consciousness

Symptoms due to central nervous system (CNS) complications:
- Double vision
- Facial numbness
- Trouble speaking

Symptoms Due to Pulmonary Complications

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Tumours that grow in the lymph nodes of the chest can constrict the windpipe, leading to coughing and difficulty breathing.[2]

Tumours in the chest can also press on and obstruct the **superior vena cava (SVC)**, the large vein that carries blood from the head and arms back to the heart. This can cause blood to back up in the veins, causing bluish-red swelling, trouble breathing, and altered consciousness (if it starts to affect the brain). This condition is known as **SVC syndrome** and must be treated immediately.[2]

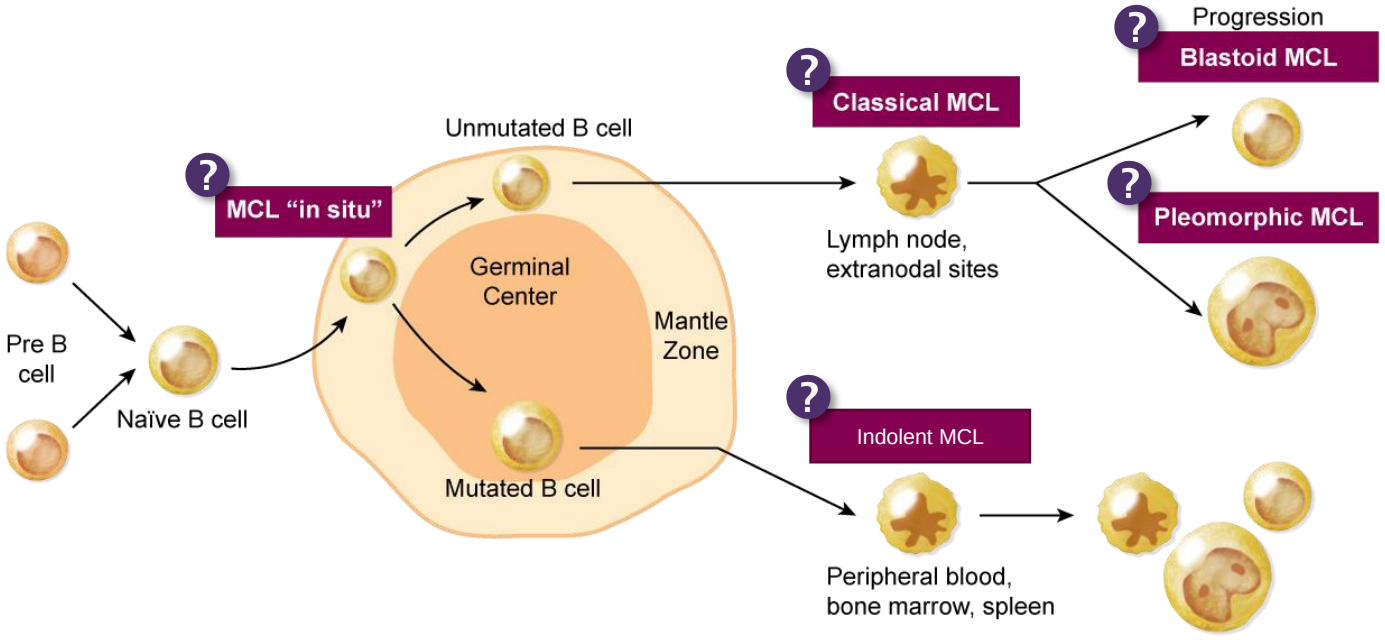
Clinical Features of MCL

Progression of MCL

The symptoms and severity of the disease can vary depending on which subtype of MCL patients have.[2,6]

As genetic mutations accumulate, MCL can progress, giving rise to 5 different subtypes:[6]

- Each subtype has a distinct median survival rate, localisation, disease course, and pathological characteristics.

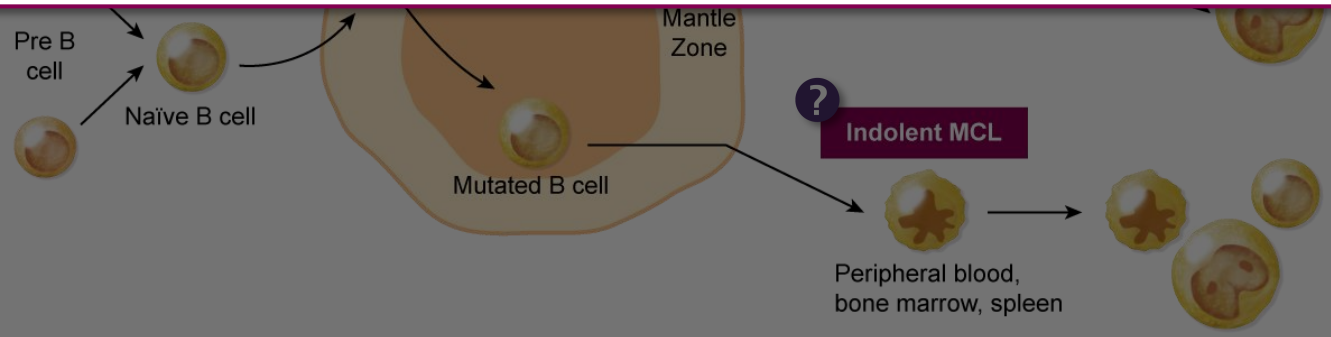


The symptoms and severity of the disease can vary depending on which subtype of MCL

MCL "in situ"

X

		MCL "in situ"
Median patient survival[7]	Long-term, even without treatment	• If MCL is in situ, (meaning "on site") cyclin D1–expressing B cells are restricted to the mantle zone of a peripheral lymphatic organ[6,8] • MCL "in situ":[6,7] – Is a rarely diagnosed early form of MCL – May be referred to as "in situ mantle cell neoplasia" to emphasize the low rate of progression
Localisation[9]	Restricted to mantle zone of peripheral lymphatic organs	
Disease course[6]	Indolent	

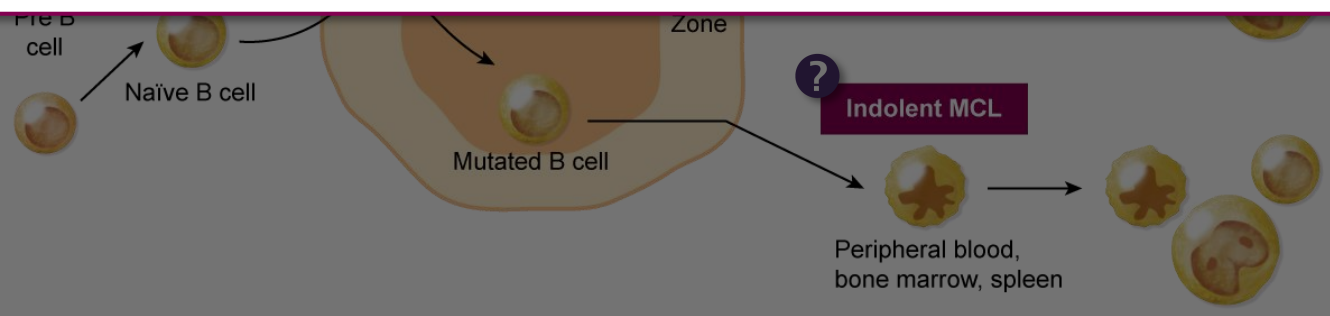


The symptoms and severity of the disease can vary depending on which subtype of MCL

Indolent MCL[9]

X

		Indolent MCL
Median patient survival	7–10 years	• Although MCL is often aggressive and associated with poor patient outcomes, MCL may more rarely present as an indolent disease • Indolent MCL: – Is a less aggressive form of MCL – Malignant cells are usually present in peripheral blood, bone marrow, and spleen – May be managed with a “watch and wait” treatment strategy
Localisation	Peripheral blood, spleen, and bone marrow	
Disease course	Indolent	

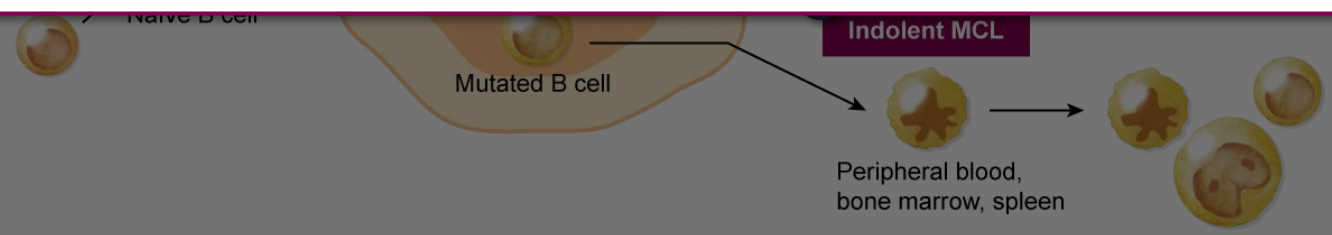


The symptoms and severity of the disease can vary depending on which subtype of MCL

Classical MCL

X

		Classical MCL
Median patient survival[9]	5–6 years	Classical MCL:[1,10] • Growth pattern typically corresponds to the progression of the disease: – Mantle-fashion: Malignant B cells replace the mantle zone – Nodular: Malignant B cells invade the peripheral lymphatic organ and appear as a solid tumour – Diffuse: Solid tumours have grown to the point of merging together • Symptomatic patients are promptly treated
Localisation[11]	Lymph nodes, extranodal sites (usually GI tract)	
Disease course[11]	Aggressive	



The symptoms and severity of the disease can vary depending on which subtype of MCL

Blastoid MCL

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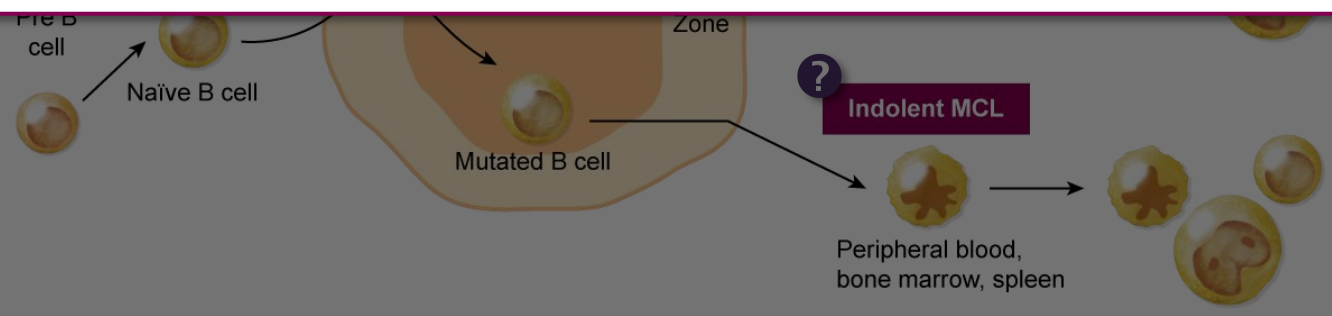
		Blastoid MCL
Median patient survival[12]	3–6 months	**Blastoid** MCL:[13] • Is an aggressive form of MCL with a poor prognosis • Can occur in younger patients • Is often associated with CNS involvement • Is characterised by larger cells resembling **lymphoblasts** that rapidly grow and divide
Localisation[13]	Wide spread, including lymph nodes, bone marrow, lungs, GI tract, liver, and CNS	
Disease course[13]	Aggressive	

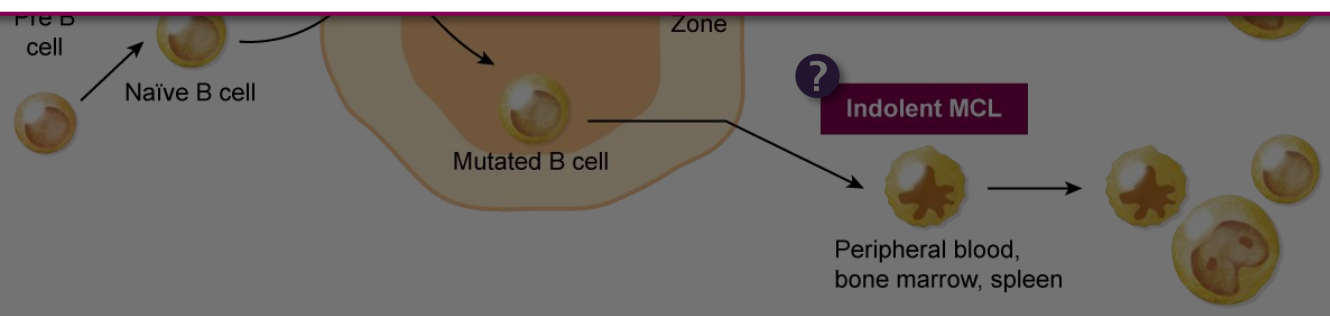


The symptoms and severity of the disease can vary depending on which subtype of MCL

Pleomorphic MCL

X

		Pleomorphic MCL
Median patient survival[12]	3.8–17 months	**Pleomorphic** MCL:[12,14,15] • Is a rare and aggressive form of MCL with a poor prognosis • Usually occurs in patients with a history of MCL • Is characterised by the presence of typically larger B cells with irregular contours that are highly variable in appearance
Localisation[14]	Wide spread, including lymph nodes, bone marrow, lungs, GI tract, liver, and CNS	
Disease course[14]	Aggressive	

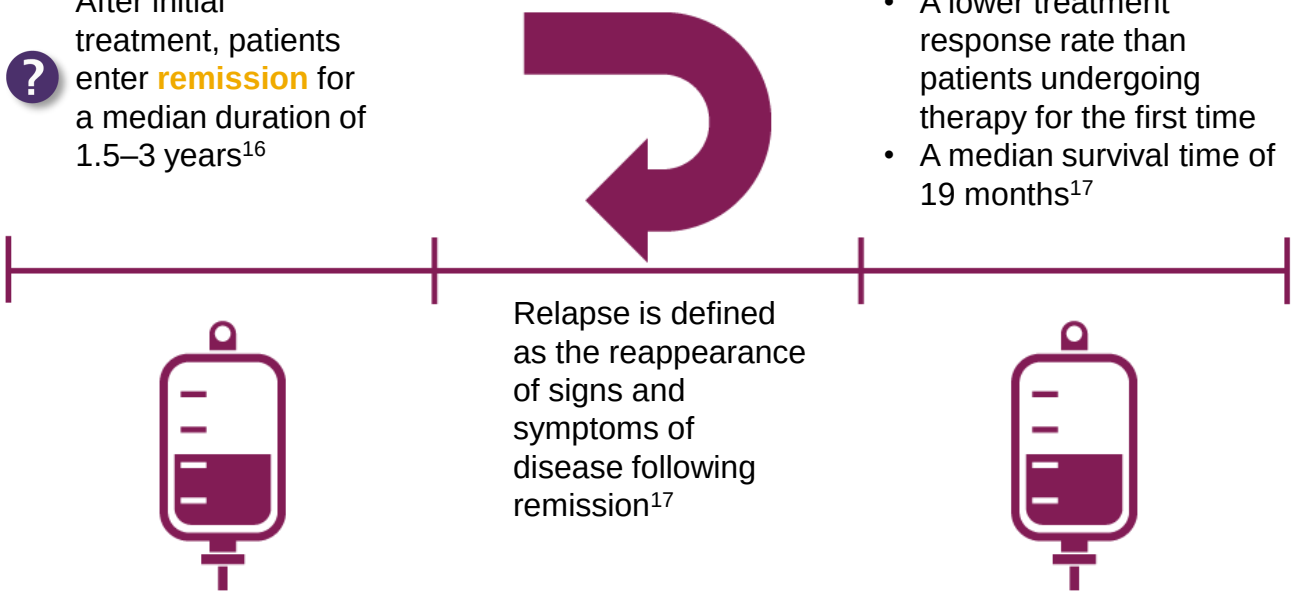


Although patients with MCL usually respond to initial treatment, they almost always relapse:[11]

After initial treatment, patients enter **remission** for a median duration of 1.5–3 years[16]

Patients who relapse have:

- A lower treatment response rate than patients undergoing therapy for the first time
- A median survival time of 19 months[17]



Relapse is defined as the reappearance of signs and symptoms of disease following remission[17]

Minimal residual disease (MRD) may play an important role in relapse[18]

Although patients with MCL usually respond to initial treatment, they often relapse:

Remission X

Remission in MCL is evaluated using the malignant lymphoma response evaluation criteria, which defines remission in patients as:[19]

- Complete disappearance of all detectable clinical evidence of disease and disease-related symptoms present before therapy
- Significant reduction in size or absence of any detectable mass on imaging studies
- Reduced spleen and/or liver size, if enlarged before treatment
- Absence of lymphoma in the bone marrow, if involved before treatment

symptoms of
disease following
remission

Minimal residual disease (MRD) may play an important role in relapse

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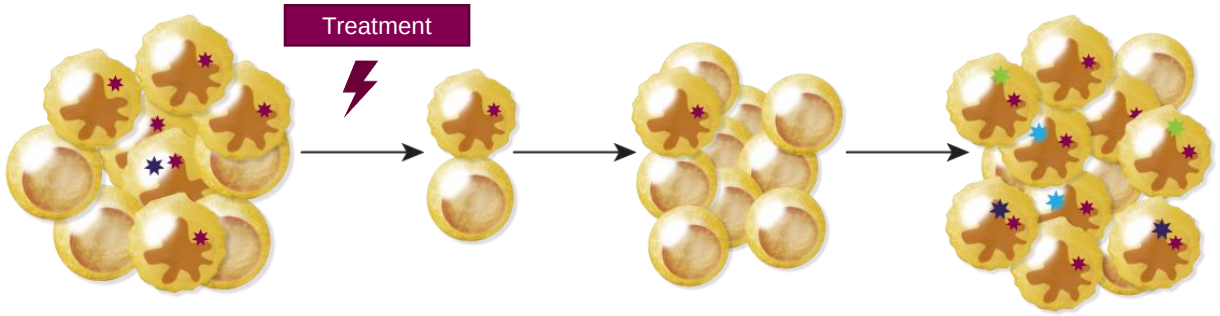
Minimal Residual Disease

X

MRD is a condition in which an undetectable, trace amount of malignant cells remain after treatment:[20]

- MRD positivity is typically defined as ≥ 10^{-4} (1 in 10,000) MCL cells[21]

These malignant cells can proliferate and result in disease relapse.[2,21]



The presence of MRD can be tested using highly sensitive DNA- and RNA-based molecular techniques; however, MRD-guided treatment strategies are not yet recommended in clinical routines.[18]

Clinical Features of MCL

Summary

SIGNS AND SYMPTOMS

- MCL has a widespread, systemic nature. Therefore, patients may experience different symptoms resulting from the involvement of multiple organs:
  - Blood
  - Liver
  - Spleen
  - GI tract
  - Tonsils
  - CNS
  - Lungs

PROGRESSION

- As genetic mutations accumulate, MCL can progress into 5 subtypes:
  - MCL “in situ”
  - Leukaemic non-nodal MCL
  - Classical MCL
  - Blastoid MCL
  - Pleomorphic MCL

RELAPSE

- Relapse is defined as the appearance of signs and symptoms of disease following remission
- Patients who relapse have a lower treatment response rate than patients undergoing initial therapy:
  - Relapsed patients have a median survival time of 19 months

Clinical Features of MCL

Progress Check

1. Which of the following are classified as B (general) symptoms?

A) Chest pain or pressure, coughing, and trouble breathing

B) Double vision, facial numbness, and trouble speaking

C) Fever, unexpected weight loss, and drenching night sweats

D) Frequent bruising and bleeding, fatigue, and infection

Clinical Features of MCL

Progress Check

1. Which of the following are classified as B (general) symptoms?

A) Chest pain or pressure, coughing, and trouble breathing

B) Double vision, facial numbness, and trouble speaking

C) Fever, unexpected weight loss, and drenching night sweats

D) Frequent bruising and bleeding, fatigue, and infection

C) Fever, unexpected weight loss, and drenching night sweats are B (general) symptoms.

2. Which of the following forms of MCL can occur in younger patients and is often associated with CNS involvement?

A) Blastoid MCL

B) Classical MCL

C) Pleomorphic MCL

D) MCL “in situ”

2. Which of the following forms of MCL can occur in younger patients and is often associated with CNS involvement?

A) Blastoid MCL

B) Classical MCL

C) Pleomorphic MCL

D) MCL “in situ”

A) Blastoid MCL can occur in younger patients and is often associated with CNS involvement.

3. Which of the following forms of MCL is generally restricted to the mantle zone of a peripheral lymphatic organ?

A) Blastoid MCL

B) Classical MCL

C) Pleomorphic MCL

D) MCL “in situ”

3. Which of the following forms of MCL is generally restricted to the mantle zone of a peripheral lymphatic organ?

A) Blastoid MCL

B) Classical MCL

C) Pleomorphic MCL

D) MCL “in situ”

D) MCL “in situ” is generally restricted to the mantle zone of a peripheral lymphatic organ.

4. Which of the following statements about MCL relapse is correct?

A) Patients with MCL usually respond to initial treatment, but often relapse after a median of 1.5 to 3 years

B) Patients with MCL usually do not respond to initial treatment

C) Patients with relapsed MCL have a longer median survival time than those that have never achieved complete remission

D) Patients with relapsed MCL typically respond better to treatment than those undergoing therapy for the first time

4. Which of the following statements about MCL relapse is correct?

A) Patients with MCL usually respond to initial treatment, but often relapse after a median of 1.5 to 3 years

B) Patients with MCL usually do not respond to initial treatment

C) Patients with relapsed MCL have a longer median survival time than those that have never achieved complete remission

D) Patients with relapsed MCL typically respond better to treatment than those undergoing therapy for the first time

A) Patients with MCL usually relapse after a median remission duration of 1.5 to 3 years, after which they become less responsive to treatment and have a shorter median survival time than patients entering treatment for the first time.

Glossary

Select the definition to return.

Anaemia

Low red blood cell count.[1]

B (general) symptom

A general symptom, such as fever, drenching night sweats, and unexpected weight loss.[2]

Blastoid

Pertaining to the process of budding by cells or tissue. Blastoid MCL is an aggressive form of the disease that can develop from classical MCL. It is characterised by the presence of large cells resembling lymphoblasts.[6,13,22]

Lymphoblast

An immature lymphoid cell that develops into a lymphocyte, or an activated lymphocyte that undergoes a transformation after activation by antigen.[23,24]

Minimal residual disease (MRD)

The remaining fraction of largely undetectable cancerous cells after a patient has entered remission.[20]

Neutropenia

Reduction in the number of neutrophils in the blood.[3]

Neutrophil

A white blood cell that localises to infected or inflamed tissues to engulf particles.[25]

Pleomorphic

Consisting of a heterogeneous population of cells. Pleomorphic MCL is a rare and aggressive form of the disease that can develop from classical MCL. It is characterised by the presence of atypical, large B cells.[12,14,15,26]

Relapse

The recurrence of symptoms or disease after apparent recovery.[8]

Remission

A reduction in or disappearance of the signs and symptoms of cancer.[27]

Superior vena cava (SVC)

The major vein receiving blood from other veins superior to the diaphragm.[28]

Superior vena cava (SVC) syndrome

A complex of symptoms caused by compression of the superior vena cava.[24]

Thrombocytopenia

Low platelet count.[1]

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