Castleman disease
Pathology Toolkit

Enter
Pathology toolkit

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Exclusionary diseases

Diagnosis guidelines

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Castleman disease is an umbrella term for a group of rare lymphoproliferative disorders that share a spectrum of histological features.

- There are different clinical subtypes dependent on the localisation of the CD and the underlying aetiology:
  - Unicentric CD (UCD)
  - Multicentric CD (MCD)

Castleman disease is an umbrella term for a group of rare lymphoproliferative disorders that share a spectrum of histological features. There are different clinical subtypes dependent on the localisation of the CD and the underlying aetiology:

- **Unicentric CD (UCD)**: UCD is CD that is localised to a single lymph node station. It is usually asymptomatic and picked up incidentally. Symptoms can arise due to the location and size of the tumour or, occasionally, patients will experience mild systemic symptoms. The treatment for UCD is usually resection of the affected node, which is often curative.

- **Multicentric CD (MCD)**: 

Castleman disease is an umbrella term for a group of rare lymphoproliferative disorders that share a spectrum of histological features. There are different clinical subtypes dependent on the localisation of CD and the underlying aetiology:

- **Unicentric CD (UCD)**
- **Multicentric CD (MCD)**

Multicentric CD or MCD is CD that is found in multiple lymph node stations. Patients usually experience systemic inflammatory symptoms that can be episodic. Severe cytokine storms can cause life-threatening organ damage and even death. MCD is further subdivided by aetiology:

- **Human herpesvirus-8 associated MCD**
- **POEMS-associated MCD**
- **Idiopathic MCD**

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- Human herpesvirus-8 (HHV-8) MCD
- Idiopathic MCD

What is Castleman disease?

Castleman disease is an umbrella term for a group of rare lymphoproliferative disorders that share a spectrum of histological features. There are different clinical subtypes dependent on the localisation of CD and the underlying aetiology:

- **Unicentric CD (UCD)**
- **Multicentric CD (MCD)**
  - Multicentric CD or MCD is CD that is found in multiple lymph node stations. Patients usually experience systemic inflammatory symptoms that can be episodic. Severe cytokine storms can cause life-threatening organ damage and even death.
  - MCD is further subdivided by aetiology:
    - **POEMS syndrome (POEMS)**-associated MCD is where a monoclonal plasma cell disorder, called POEMS, is associated with MCD-like features.
    - **Human herpesvirus 8 (HHV-8)**-associated MCD
    - **Idiopathic MCD**

What is Castleman disease?

• Castleman disease is an umbrella term for a group of rare lymphoproliferative disorders that share a spectrum of histological features.  

• There are different clinical subtypes of CD and the underlying aetiology:
  - Unicentric CD (UCD)
  - Multicentric CD (MCD)
  - POEMS-associated MCD
  - Human herpesvirus-8 associated MCD
  - Idiopathic MCD

  Idiopathic MCD (iMCD) refers to MCD of unknown aetiology. It is separated into two types based on the symptoms experienced by the patient: iMCD TAFRO (thrombocytopenia, anasarca/ascites, reticulin fibrosis in the bone marrow, renal dysfunction, organomegaly) and iMCD-NOS (not otherwise specified). The former has a particularly severe disease course.  

The pathological aspect of diagnosing CD

Assess the tissue sample for signs of CD histopathology

Discern the clinical subtype of CD

Report to the clinician

What is Castleman disease?
Assess the tissue sample for signs of CD

Identification of CD-related histopathological signs is a required aspect of diagnosis for all clinical subtypes of CD.1


Discern the clinical subtype of CD

Report to the clinician
The pathological aspect of diagnosing CD

Identification of the clinical subtype of CD is necessary as the subtypes require different management.\(^1\)

Click to learn more about diagnosing this subtype.

- UCD
- HHV-8 MCD
- POEMS MCD
- iMCD

Assess the tissue sample for signs of CD histopathology

Report to the clinician

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Assess the tissue sample for signs of CD histopathology.

Identification of the clinical subtype of CD is necessary as the subtypes require different management.

Click to learn more about diagnosing this subtype.

UCD
POEMS MCD
HHV-8+ve MCD
iMCD

After a positive identification of CD features in the histopathology, a diagnosis of UCD can be reached from the clinical information. If the patient’s records show that only 1 lymph node station is affected, then the diagnosis is UCD.

The pathological aspect of diagnosing CD

Assess the tissue sample for signs of CD histopathology.

Assess the tissue sample for signs of CD histopathology.

Identification of the clinical subtype of CD is necessary as the subtypes require different management. Click to learn more about diagnosing this subtype.

UCD
POEMS MCD
HHV-8+ve MCD
iMCD

After positive identification of CD features on histopathology, Polyneuropathy, Organomegaly, Endocrinopathy, Monoclonal gammapathy, Skin changes (POEMS)-associated MCD, a monoclonal plasma cell disorder, called POEMS can be confirmed using clinical features and histopathology of bone marrow biopsy demonstrating osteosclerosis and lambda-restricted plasmacytic cells.

Report to the clinician
Assess the tissue sample for signs of CD histopathology

Identification of the clinical subtype of CD is necessary as the subtypes require different management. Click to learn more about diagnosing this subtype.

Assess the tissue sample for signs of CD histopathology

After a positive identification of CD features in the histopathology, a diagnosis of iMCD requires further laboratory and clinical information, plus extensive exclusion of other diseases.¹

¹ Return to main menu to learn more about diagnostic criteria and exclusionary diseases
An excisional biopsy is often required for a correct diagnosis. You may need to request one from the clinician.¹

A bone marrow sample is often advised when iMCD is suspected, to evaluate for malignancy, POEMS and iMCD findings. It might need to be requested from the clinician.¹

There are several histopathological subtypes of CD, which are associated with different sets of features. All CD histopathological variants can show hypervascularisation.\(^1\)

- An **excisional biopsy** is required to see the full architecture. Core samples are thought to give insufficient detail for diagnosis.\(^1\)

- Different nodes from the same patient may show different histopathological variants.

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Hypervascular lymph nodes will show a combination of the following features:\endnote{1}:

- Hypervascularisation
- Regressed germinal centers (GCs)
- Prominent follicular dendritic cells (FDCs)
- ‘Onion skinning’
- ‘Lollipop sign’
- Budding or twinning of follicles
- FDC dysplasia
- Sclerotic vessels

The term ‘**hyaline vascular**’ is used to describe these features in UCD. The term ‘**hypervascular**’ is used for the same set of features in MCD, with the distinction made as MCD lesions with this spectrum of histology do not tend to display FDC dysplasia or sclerotic vessels.\endnote{1}

\begin{flushleft}
\textit{Click for more information}
\end{flushleft}

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These images show high- and low-power views of hypervascularisation in CD
This image shows regressed germinal centers. The BCL2 and IgD stains highlight the regressed GCs.
Prominent FDCs

This CD21 staining highlights extended FDC networks
Onion skinning

These images show ‘onion skinning’ in the mantle zones. These are concentric rings of small lymphocytes around regressed GCs.

The image on the right shows onion skinning around a twinned GC.
Germinal centers showing the ‘lollipop sign’ of a radially penetrating vessel
Examples of ‘budding’ or ‘twinning’ of follicles, where 2 or more GCs are located in a single follicle
FDC dysplasia

Moderate to strong epidermal growth factor receptor (EGFR) expression in dysplastic FDCs.

Moderate ER staining ER in nuclei of FDCs.
Sclerotic vessels

This images shows sclerotic vessels in hypervascular lymph nodes
Plasmacytic lymph nodes will show a combination of the following features$^1$:

- Sheet-like plasmacytosis
- Increased numbers of follicles with hyperplastic GCs

Plasmacytosis

This image shows an infiltrate of plasma cells into the paracortical region.

The right-hand side of this image shows a sheet of plasma cells in the interfollicular area.

Plasma cell infiltration into a sclerotic region of an extranodal tissue sample.

CD138 staining showing an infiltration of plasma cells in extralymphoid tissue.

CD20 and CD3 staining highlighting the reduced numbers of T cells in the interfollicular area due to plasma cell infiltration.
These low-power images show lymph node specimens with many large, hyperplastic GCs. Some of the GCs also contain tingible body macrophages, creating a ‘starry sky’ appearance.
‘Mixed’ histopathology is seen in specimens that show histology in between the plasmacytic and hypervascular variants. They tend to show\(^1\):

- Plasmacytosis and regressed follicles

Regressed GCs with plasmacytosis

This image shows regressed follicles with plasmacytosis and onion skinning
The international consensus diagnosis guidelines for iMCD were developed to aid clinicians and pathologists\(^1\)

iMCD is primarily a disease of exclusion

The guidelines were published in *Blood* in 2017\(^1\)

There are **TWO major criteria** that must be fulfilled according to the international consensus diagnosis guidelines.¹ One of these requires the expertise of a pathologist and the other of a clinician:

- **Pathologist:** The excisional lymph node biopsy specimen must show **histopathologic features** consistent with iMCD.¹ Regressed germinal centers or plasmacytosis of a certain severity are required to fulfil the criteria (click below to learn more).¹

- **Clinician:** **Multicentric lymphadenopathy** – enlarged lymph nodes (≥1cm in short-axis diameter) in ≥2 lymph node stations (e.g. neck and armpit)¹

To fulfil the minor diagnostic criteria, the patient must have at least two of the symptoms listed in the minor criteria, of which at least one must be a laboratory sign¹:

<table>
<thead>
<tr>
<th>Criterion</th>
<th>Threshold</th>
</tr>
</thead>
<tbody>
<tr>
<td>Laboratory*</td>
<td>**</td>
</tr>
<tr>
<td>Anaemia</td>
<td>Haemoglobin &lt;12.5 g/dL (males); &lt;11.5 g/dL (females)</td>
</tr>
<tr>
<td>Thrombocytopenia or thrombocytosis</td>
<td>Platelet count &lt;150 k/μL or &gt;400 k/μL</td>
</tr>
<tr>
<td>Hypoalbuminaemia</td>
<td>Albumin &lt;3.5 g/dL</td>
</tr>
<tr>
<td>Renal dysfunction or proteinuria</td>
<td>eGFR &lt;60 mL/min/1.73 m² or total protein 150 mg/24h or 10 mg/100 mL respectively</td>
</tr>
<tr>
<td>Polyclonal hypergammaglobulinaemia</td>
<td>Total gamma globulin or immunoglobulin G &gt;1700 mg/dL</td>
</tr>
</tbody>
</table>

*Laboratory cut-off thresholds are provided as guidance, but some variation between laboratories is acknowledged and local thresholds can be used

**CRP evaluation is mandatory and tracking is encouraged, but ESR is acceptable if CRP is not available

CRP = C-reactive protein; ESR = erythrocyte sedimentation rate

eGFR = estimated glomerular filtration rate

To fulfil the minor diagnostic criteria, the patient must have at least two of the symptoms listed in the minor criteria, of which at least one must be a laboratory sign:

<table>
<thead>
<tr>
<th>Criterion</th>
<th>Threshold</th>
</tr>
</thead>
<tbody>
<tr>
<td>Clinical</td>
<td></td>
</tr>
<tr>
<td>Constitutional symptoms</td>
<td>Night sweats, fever &gt;38°C, weight loss or fatigue (≥2 CTCAE lymphoma score for B-symptoms)</td>
</tr>
<tr>
<td>Fluid accumulation</td>
<td>Oedema, anasarca, ascites or pleural effusion</td>
</tr>
<tr>
<td>Eruptive cherry haemangiomatosis or violaceous papules</td>
<td></td>
</tr>
<tr>
<td>Enlarged spleen and/or liver</td>
<td></td>
</tr>
<tr>
<td>Lymphocytic interstitial pneumonitis</td>
<td></td>
</tr>
</tbody>
</table>

CTCAE = Common Terminology Criteria for Adverse Events

iMCD diagnosis guidelines: summary algorithm for assessment of lymph node with features of CD


*IMCD patients with TAFRO syndrome frequently demonstrate hypervascular or mixed pathology

The following diseases share symptoms with iMCD and must be excluded for an iMCD diagnosis:

<table>
<thead>
<tr>
<th>Disease type</th>
<th>Disease</th>
<th>Usually diagnosed by clinician or pathologist?</th>
<th>Link to guidelines</th>
</tr>
</thead>
<tbody>
<tr>
<td>Autoimmune</td>
<td>Rheumatoid arthritis</td>
<td>Clinician</td>
<td>ACR/EULAR 2010 guidelines</td>
</tr>
<tr>
<td>Autoimmune</td>
<td>Systemic lupus erythematosus</td>
<td>Clinician</td>
<td>SLICC 2012 guidelines</td>
</tr>
<tr>
<td>Autoimmune</td>
<td>Adult-onset Still’s disease</td>
<td>Clinician</td>
<td></td>
</tr>
<tr>
<td>Autoimmune</td>
<td>Autoimmune lymphoproliferative syndrome</td>
<td>Pathologist</td>
<td>NIH International Workshop guidelines</td>
</tr>
<tr>
<td>Autoimmune</td>
<td>Juvenile idiopathic arthritis</td>
<td>Clinician</td>
<td></td>
</tr>
<tr>
<td>Autoimmune</td>
<td>IgG4-related disease</td>
<td>Pathologist</td>
<td></td>
</tr>
<tr>
<td>Malignant/lymphoproliferative disorders</td>
<td>Lymphoma</td>
<td>Pathologist</td>
<td>IMWG 2014 guidelines</td>
</tr>
<tr>
<td>Malignant/lymphoproliferative disorders</td>
<td>Multiple myeloma</td>
<td>Pathologist</td>
<td></td>
</tr>
<tr>
<td>Malignant/lymphoproliferative disorders</td>
<td>Primary lymph node plasmacytoma</td>
<td>Pathologist</td>
<td></td>
</tr>
<tr>
<td>Malignant/lymphoproliferative disorders</td>
<td>FDC sarcoma</td>
<td>Pathologist</td>
<td></td>
</tr>
<tr>
<td>Malignant/lymphoproliferative disorders</td>
<td>POEMS</td>
<td>Clinician (unless bone marrow biopsy taken)</td>
<td>2019 diagnosis update</td>
</tr>
<tr>
<td>Infection-related disorders</td>
<td>HHV-8 infection</td>
<td>Pathologist</td>
<td></td>
</tr>
<tr>
<td>Infection-related disorders</td>
<td>Clinical Epstein-Barr virus (EBV)-lymphoproliferative disorders</td>
<td>Pathologist</td>
<td></td>
</tr>
<tr>
<td>Infection-related disorders</td>
<td>Inflammation and adenopathy caused by other uncontrolled infections</td>
<td>Clinician</td>
<td></td>
</tr>
</tbody>
</table>

Case study 1

Clinical history

- 37-year-old male
- Intravenous drug user
- Skin lesions and generalised lymphadenopathy
- Inguinal lymph node excision

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- Overall architecture is preserved
- Marked paracortical vascularity
- Hyperplastic follicles
Case study 1

Histopathology

- Hyperplastic reactive follicles with tingible body macrophages
- Well-defined mantle zones
- Paracortical expansion with haemorrhage
- Medullary sinuses obliterated (likely due to paracortical expansion)

- Vascular expansion in the follicles of small vessels with hyalinised walls
- The peri-follicular mantle zone has a frayed appearance with some clear cells

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Case study 1

Histopathology

- The medullary cords are preserved
- There is an infiltrate of plasma cells into the paracortical region
- Spindle cell proliferation forming slit-like spaces filled with red blood cells
- This feature raises suspicion of vascular neoplasm – sarcomas

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Histopathology

- Plasmablasts have prominent, centrally located single nuclei
- They appear mostly in HHV8-positive MCD, where they mostly express IgM
- Potential differential diagnoses include other plasmablastic conditions, especially types of lymphoma

HHV-8 immunohistochemistry shows HHV8-positive plasmablasts around a hyperplastic follicle
Case study 1

Histopathology

HHV-8 immunohistochemistry shows HHV8-positive spindle cells in the interfollicular region.

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Case study 1

**Histopathology**

Polytypic light chain expression in interfollicular plasma cells indicates that they are reactive

Lambda light chain restriction in plasmablasts around a germinal center

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## Conclusion

### Summary of pathology
- Plasmablasts are positive for HHV8-LANA and are lambda light-chain restricted. Interfollicular plasma cells are polytypic for kappa and lambda.
- Intrasinusoidal vascular/spindle cell proliferation is positive for HHV8-LANA
- IgG4 and EBV negative (not shown)
- Patient confirmed to be HHV-8 positive

### Differential diagnoses
- Non-specific lymphadenitis with polytypic plasmacytosis
- Autoimmune lymphadenitis
- Reactive follicular and paracortical hyperplasia
- Angioimmunoblastic T-cell lymphoma
- Follicular dendritic cell sarcoma
- iMCD

### Diagnosis
- HHV8-positive MCD, plasmacytic histopathological variant
- Kaposi sarcoma
Case study 2

**Clinical history**

- 20-year-old male with increasing cervical lymphadenopathy over the last 2 years, otherwise healthy
- Whole-body CT scan shows localised right-sided cervical lymphadenopathy, otherwise normal
- Bone marrow biopsy not performed
- Laboratory findings: normal peripheral blood counts and differential CRP, liver enzymes, LDH, β2-MG, total protein, electrolytes etc. in the normal range

- Excision of a cervical node 3.5 x 2.5cm
- Numerous follicles with expanded mantle zones
- Some regressed germinal centers
- Obliterated medullary sinuses

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### Case study 2

<table>
<thead>
<tr>
<th>Histopathology</th>
</tr>
</thead>
<tbody>
<tr>
<td>- Expanded mantle zones with concentrically arranged lymphocytes giving an ‘onion skin’ appearance</td>
</tr>
<tr>
<td>- Regressed germinal centers with some ‘budding’ or ‘twinning’ of follicles</td>
</tr>
<tr>
<td>- Twinned follicle with onion skinning</td>
</tr>
<tr>
<td>- Radiating vessel penetrating a germinal center – also known as the ‘lollipop sign’</td>
</tr>
</tbody>
</table>

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Case study 2

**Histopathology**

- Physiological distribution of CD20+ B cells and CD3+ T cells
- There are very few CD3+ cells in nodules in germinal centers due to the regression

- Concentrically arranged and condensed CD23 FDCs, with CD10+ germinal center cells
- Mantle cells are IgD+ and BCL2+

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There are clusters of CD123+ plasmacytoid cells in the interfollicular areas.
### Conclusion

| Summary of pathology | • Regressed germinal centers with ‘onion skinning’
|                      | • Interfollicular proliferation of lymphocytes, numerous vessels with focal sclerosis and few plasma cells
|                      | • Medullary sinuses obliterated, no residual normal T-zones
|                      | • HHV-8 (LANA) and EBV (EBER) in situ hybridisation negative (not shown)
|                      | • No clonal B- or T- cell receptor rearrangements by PCR |

| Differential diagnoses | • Reactive lymph node with regressed germinal centers
|                        | • iMCD
|                        | • HHV-8 MCD |

| Diagnosis | • UCD, hyaline vascular histopathological variant |
Case study 3

Clinical history

- 20-year-old female
- 2005, 2006, 2007: recurrent Bell’s palsy for 2 months with spontaneous resolution; 2013: chest pain, increasing in intensity over weeks.
- Severe microcytic anaemia (Hb 63 g/L), ESR: 128, CRP: 111 mg/L, IgG: 40.1 g/L (elevated), IgA: 5.35g/L (elevated), IgM: 1.48 g/L, IgG4: 1.77 g/L (elevated).
- Imaging showed a large mass at the anterior aortic root causing aortic compression and pulmonary artery compression. Some mediastinal lymphadenopathy.
- Mini-thoracotomy with biopsy of mass.

- Soft tissue mass
- Follicles with regressive features with well-defined, not extended mantle zones
- Interfollicular diffuse plasma cell infiltrate
- Focal sclerotic bands

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### Histopathology

- Regressed germinal center without expansion of the mantle zone
- The right-hand side shows sheet of plasma cells in the interfollicular region
- Plasma cell infiltration into sclerotic tissue

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Histopathology

CD138 staining showing infiltrating plasma cells surrounding lymphoid tissue

Extensive expression of kappa light chain compared with lambda in the sheet-like plasma cells (ratio 5:1)
**Case study 3**

**Histopathology**

- IgG expression in sheet of plasma cells
- This pattern raises suspicion of CD or plasmacytoma

Slightly elevated IgG4 expression in the sheet-like plasma cells

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### Case study 3

#### Conclusion

| Summary of pathology | • CD20+ B cells confined to the follicles with interspersed CD3+ T cells (not shown)  
|                      | • Plasma cell immunophenotype: CD138+, kappa/lambda: 5/1, IgG+, IgG4+ (5–10%), IgA- (not shown), IgM- (not shown)  
|                      | • HHV-8 and EBV negative (not shown) |
| Differential diagnoses | • Non-specific lymphadenitis with polytypic plasmacytosis  
|                        | • Autoimmune lymphadenitis  
|                        |   • Lupus lymphadenitis  
|                        |   • Rheumatoid arthritis  
|                        | • Plasmacytoma  
|                        | • UCD |

| Diagnosis | • CD, plasma cell variant favoured  
|           | • Likely multicentric disease requiring clinical confirmation |
Clinical history

- 48-year-old male
- 2004: peripheral oedema, progressive shortness of breath, peripheral neuropathy
- CT scans: splenomegaly and enlarged lymph nodes in peri-aortic, mesenteric, bilateral axillary and inguinal regions
- Serology: IgA/lambda paraprotein
- Imaging: lytic/sclerotic lesions in the vertebra, sacrum and iliac bones
- Bone marrow: a small population of IgA/lambda plasma cells

Axillary lymph node biopsy
- Overall architecture is preserved
- Numerous follicles with regressive features and well-defined mantle zones
### Case study 4

#### Histopathology

| • Numerous follicles with regressive features and well-defined mantle zones | There is an excess of plasma cells expressing IgA/lambda |
| • Interfollicular plasma cell infiltrate in a background of fine sclerosis | |

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### Conclusion

<table>
<thead>
<tr>
<th>Summary of pathology</th>
</tr>
</thead>
<tbody>
<tr>
<td>• Physiological distribution of CD20+ B cells and CD3+ T cells (not shown)</td>
</tr>
<tr>
<td>• An excess of plasma cells expressing IgA/lambda</td>
</tr>
<tr>
<td>• HHV-8 and EBV negative (not shown)</td>
</tr>
<tr>
<td>• Bone marrow had a small population of IgA/lambda plasma cells (not shown)</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Differential diagnoses</th>
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</thead>
<tbody>
<tr>
<td>• Reactive lymph node with plasmacytosis</td>
</tr>
<tr>
<td>• Autoimmune lymphadenitis</td>
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<td>• IgG4-related disease</td>
</tr>
<tr>
<td>• Lupus lymphadenitis</td>
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<tr>
<td>• Rheumatoid arthritis</td>
</tr>
<tr>
<td>• UCD, HHV-8 MCD, iMCD</td>
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</table>

<table>
<thead>
<tr>
<th>Diagnosis</th>
</tr>
</thead>
<tbody>
<tr>
<td>• POEMS-associated MCD, plasmacytic variant</td>
</tr>
</tbody>
</table>
## Clinical history

- 58-year-old male
- 2001: proteinuria, night sweats
- CT scans: hepatosplenomegaly, abdominal lymphadenopathy
- Serology: IgG 179g/L (elevated), IgA 7.86g/L (elevated), IgM 1.61g/dL (normal)

- Overall architecture is preserved
- Numerous follicles with regressive features and well-defined mantle zones. Some primary follicles, some big germinal centers with extended mantle zones.
- Interfollicular plasma cell aggregates
- Medullary sinuses open
- Some sclerosis
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Case study 5

Histopathology

Regressed germinal centers with ‘onion skinning’

There are some plasma cell aggregates in the interfollicular regions
Case study 5

Histopathology

- CD21 stain showing extended FDC networks
- Polytypic interfollicular plasma cells, with a slight kappa excess, as expected in reactive plasma cells

- CD138 shows plasmacytosis in the bone marrow
- These cells are polytypic (not shown)
## Conclusion

### Summary of pathology
- Physiological distribution of CD20+ B cells and CD3+ T cells (not shown)
- An excess of plasma cells expressing IgG (not shown)
- Polytypic interfollicular plasma cell expansion
- HHV-8 and EBV negative (not shown)

### Differential diagnoses
- Reactive lymph node with plasmacytosis

### Diagnosis
- iMCD, plasma cell variant
Case study 6

Clinical history

- 54-year-old male
- Abdominal discomfort, no systemic symptoms
- Abdominal mass on physical examination
- Imaging: 6cm mass located in the mesentery, well circumscribed, heterogeneous with cystic areas

- Three distinct components
  - Peripheral hyalinising sclerosis
  - Inner layer of lymphoid tissue reminiscent of CDHV with dysplastic FDCs
  - Central area of high-grade sarcoma
### Histopathology

| B-cell follicles are based on CD21+ FDC meshworks | Sarcoma region |

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Case study 6

<table>
<thead>
<tr>
<th>Histopathology</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Clusterin</strong></td>
</tr>
<tr>
<td><strong>CXCL13</strong></td>
</tr>
<tr>
<td><strong>Fascin</strong></td>
</tr>
<tr>
<td><strong>Podoplanin</strong></td>
</tr>
</tbody>
</table>

- The sarcoma is positive for clusterin, podoplanin, CXCL13 and fascin
- The sarcoma is negative for S100, CD21, SMA, desmin, CD117, ALK (not shown)

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### Conclusion

#### Summary of pathology
- Peripheral hyalinising sclerosis with an inner layer of lymphoid tissue with dysplastic FDCs, and central area of high-grade sarcoma
- The lymphoid component is composed of organised CD20+ B cells and CD3+ T cell areas (not shown)
- HHV-8 and EBV negative (not shown)

#### Differential diagnoses
- Gastrointestinal stromal tumour
- High-grade sarcoma, not otherwise specified
- Synovial sarcoma
- Follicular dendritic cell sarcoma

#### Diagnosis
- UCD, hyaline-vascular variant
- Follicular dendritic cell sarcoma