Castleman disease Pathology Toolkit

Enter

Pathology toolkit

Castleman disease (CD) background information	The role of the pathologist in CD diagnosis	CD histopathology
Exclusionary diseases	Diagnosis guidelines	Case studies

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Pathology toolkit

Castleman disease (CD) background information

The role of the pathologist in CD diagnosis

Exclusionary diseases

Diagnosis guideline

Case study 1

Case study 2

Case study 3

Case study 4

Case study 5

Case study 6

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What is Castleman disease?

- Castleman disease is an umbrella term for a group of rare lymphoproliferative disorders that share a spectrum of histological features[1]

- There are different clinical subtypes dependent on the localisation of the CD and the underlying aetiology[1]:

Unicentric CD (UCD)

Multicentric CD (MCD)

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1. Fajgenbaum, D. et al. Blood 2017;129(12):1646–1657

What is Castleman disease?

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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.[1]

Multicentric CD (MCD)

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1. Fajgenbaum, D. et al. Blood 2017;129(12):1646–1657

What is Castleman disease?

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CD and the underlying aetiolog

Unicentric CD (UCD)

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.[1]
MCD is further subdivided by aetiology[1]:

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

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MCD is

Human herpesvirus-8 (HHV-8) MCD is associated with HHV-8 infection.[1]

POEMS-associated MCD

Idiopathic MCD

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1. Fajgenbaum, D. et al. Blood 2017;129(12):1646–1657

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Unicentric CD (UCD)

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Polyneuropathy, organomegaly, endocrinopathy, monoclonal gammopathy, skin changes (POEMS)-associated MCD is where a monoclonal plasma cell disorder, called POEMS, is associated with MCD-like features.[1]

Idiopathic MCD

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1. Fajgenbaum, D. et al. Blood 2017;129(12):1646–1657

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Unicentric CD (UCD)

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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 (thrombocytopaenia, 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.[1]

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1. Fajgenbaum, D. et al. Blood 2017;129(12):1646–1657

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

The pathological aspect of diagnosing CD

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

CD histopathology

Discern the clinical subtype of CD

Report to the clinician

1. Fajgenbaum, D. et al. Blood 2017;129(12):1646–1657

The pathological aspect of diagnosing CD

Assess the tissue sample for signs of CD histopathology

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

Report to the clinician

1. van Rhee, F. et al. Blood 2018;132(20):2115–2124

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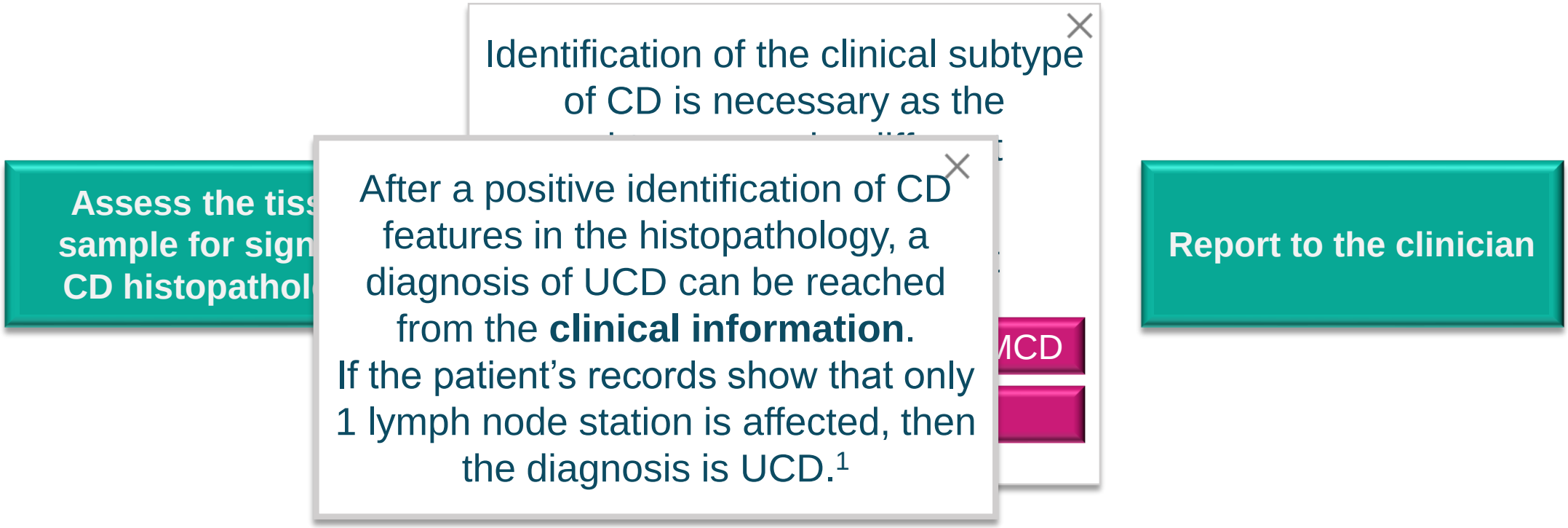
The pathological aspect of diagnosing CD



1. Fajgenbaum, D. et al. Blood 2017;129(12):1646–1657

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The pathological aspect of diagnosing CD

Assess the tissue sample for signs of CD histopathology

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After a positive identification of CD features in the histopathology, a diagnosis of **HHV-8 MCD** requires further **pathological** and **clinical** information.

If the patient's records show that multiple lymph node stations are affected, then a diagnosis of MCD can be made.

Latent anti-nuclear antigen (LANA) staining for HHV-8 infection can be used to diagnose HHV8+ve MCD.[1]

1. Fajgenbaum, D. et al. Blood 2017;129(12):1646–1657

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The pathological aspect of diagnosing CD

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After positive identification of CD features on histopathology, Polyneuropathy, organomegaly, endocrinopathy, monoclonal gammopathy, 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

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The pathological aspect of diagnosing CD

Assess the tissue sample for signs of CD histopathology

Identification of the clinical subtype of CD is necessary as the

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ort to the clinician

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]

Return to main menu to learn more about diagnostic criteria and exclusionary diseases

1. Fajgenbaum, D. et al. Blood 2017;129(12):1646–1657

The pathological aspect of diagnosing CD

Assess the tissue sample for signs of CD histopathology

Discern the clinical subtype of CD

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]

1. Fajgenbaum, D. et al. Blood 2017;129(12):1646–1657

CD histopathology

- 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.

Hypervascular subtype	Plasmacytic	Mixed

1. Fajgenbaum, D. et al. Blood 2017;129(12):1646–1657

Hypervascular

Hypervascular lymph nodes will show a combination of the following features[1]:

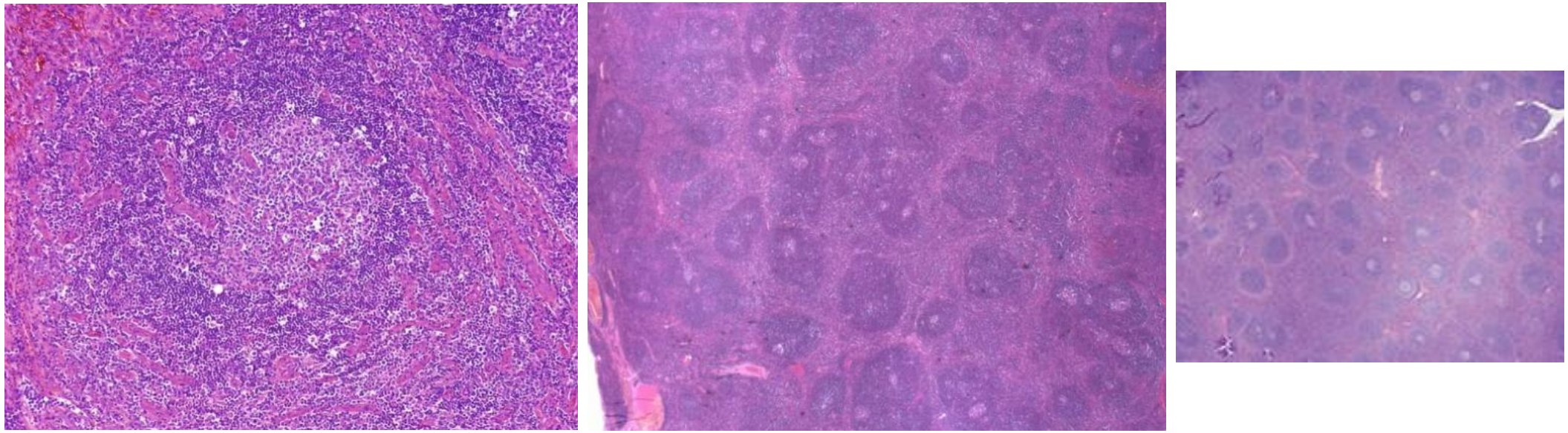
Hypervascularisation	Regressed germinal centers (GCs)	Prominent follicular dendritic cells (FDCs)	‘Onion skinning’
‘Lollipop sign’	Budding or twinning of follicles	FDC dysplasia	Sclerotic vessels

Click for more information

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.[1]

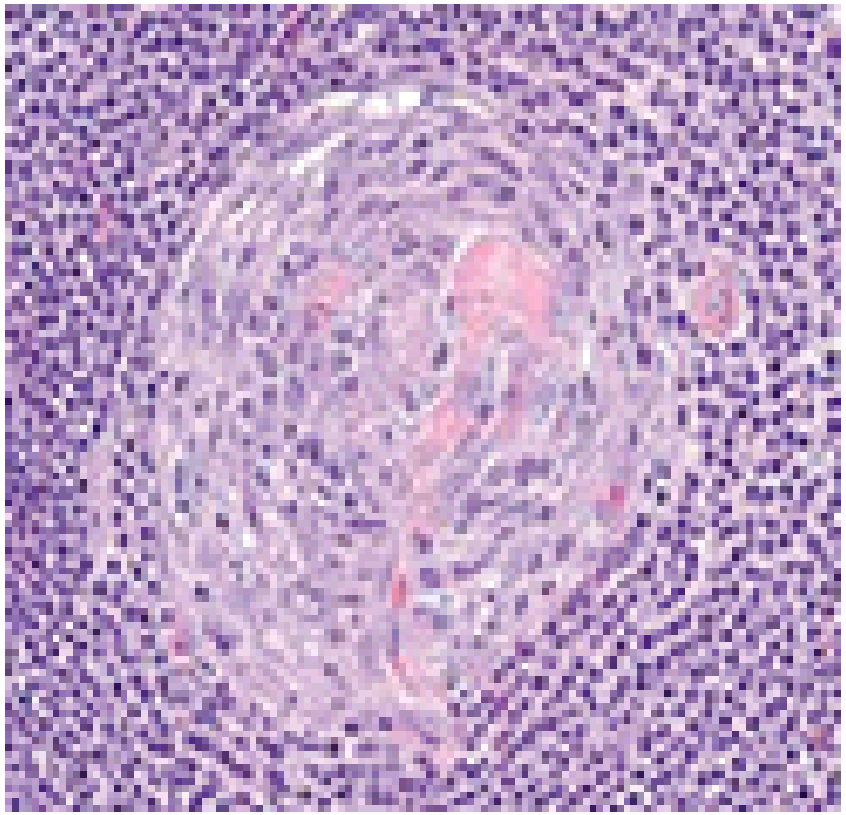
1. Fajgenbaum, D. et al. Blood 2017;129(12):1646–1657

Hypervascularisation



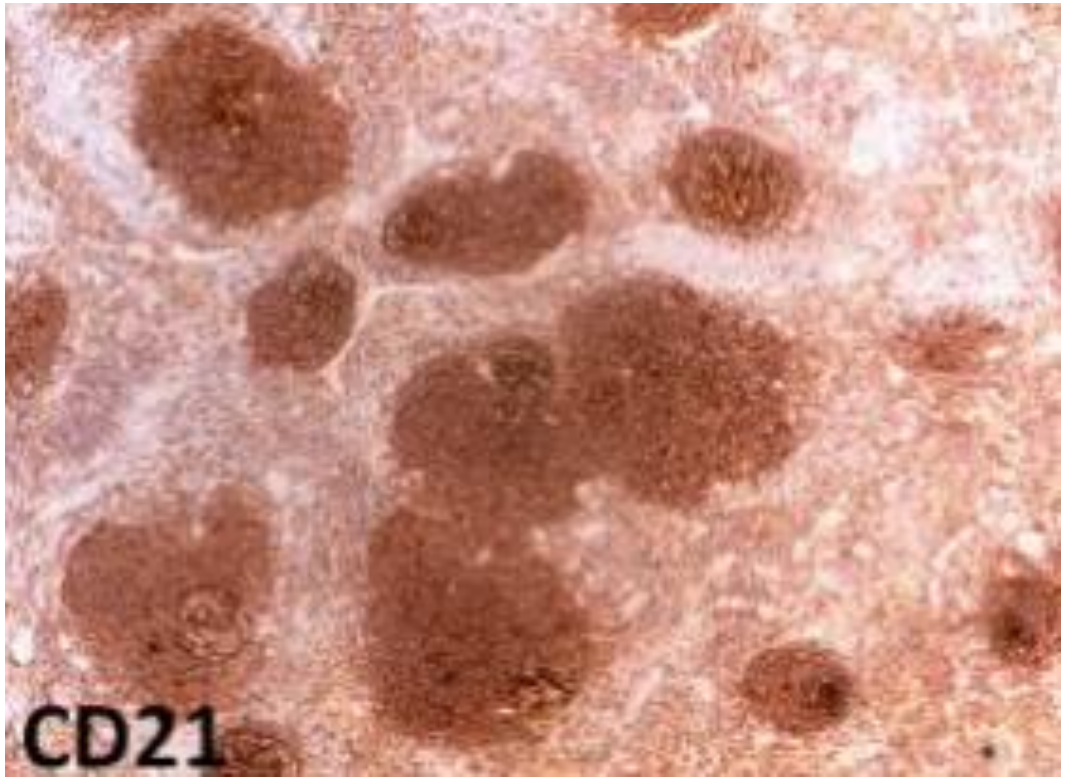
These images show high- and low-power views of hypervascularisation in CD

Regressed germinal centers



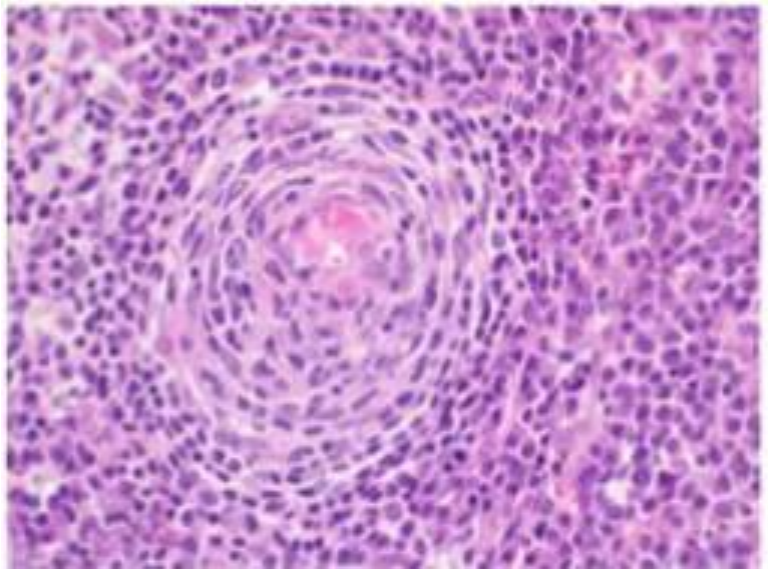
This image shows regressed germinal centers. The BCL2 and IgD stains highlight the regressed GCs.

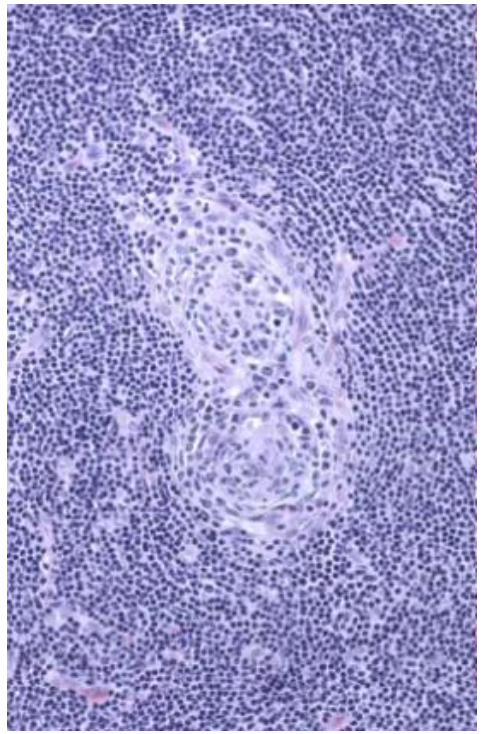
Prominent FDCs



This CD21 staining highlights extended FDC networks

Onion skinning

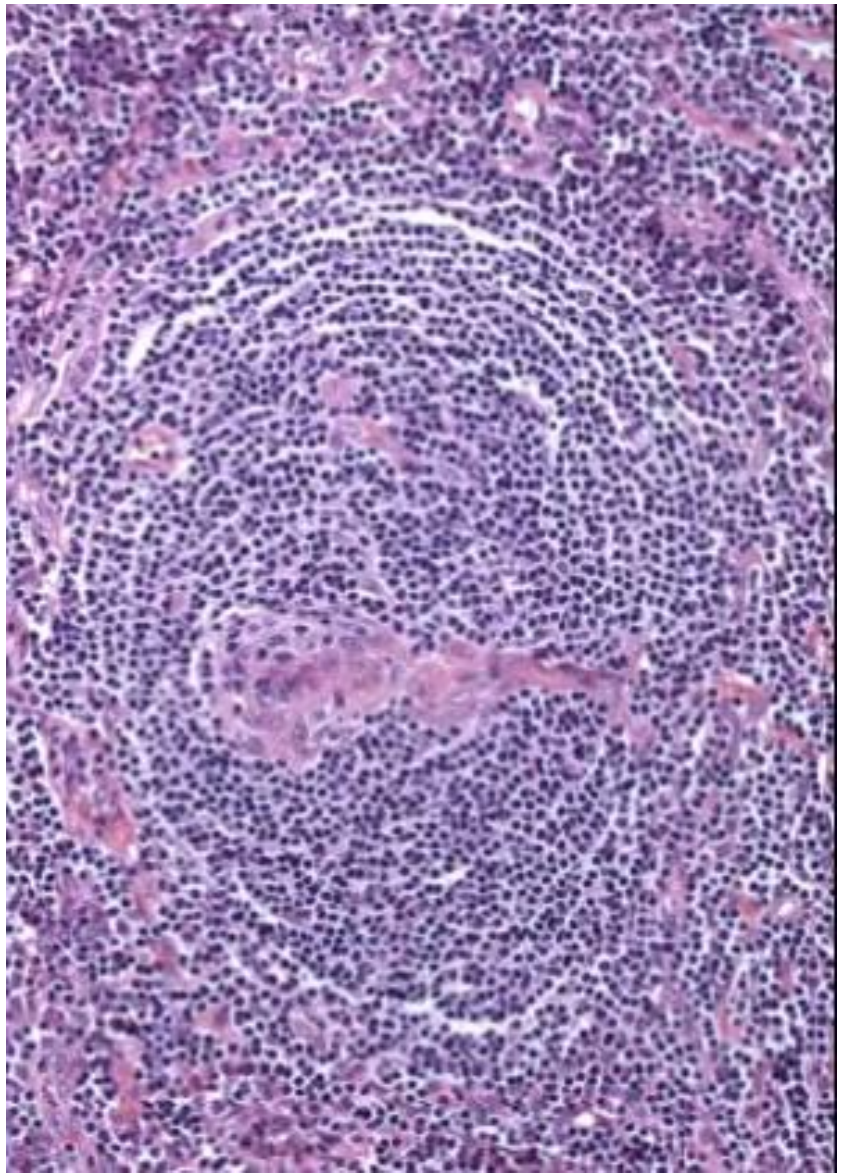




These images show '**onion skinning**' in the mantle zones. These are concentric rings of small lymphocytes around regressed GCs.

The image on the right shows **onion skinning** around a twinned GC.

Lollipop sign



Germinal centers showing the ‘lollipop sign’ of a radially penetrating vessel

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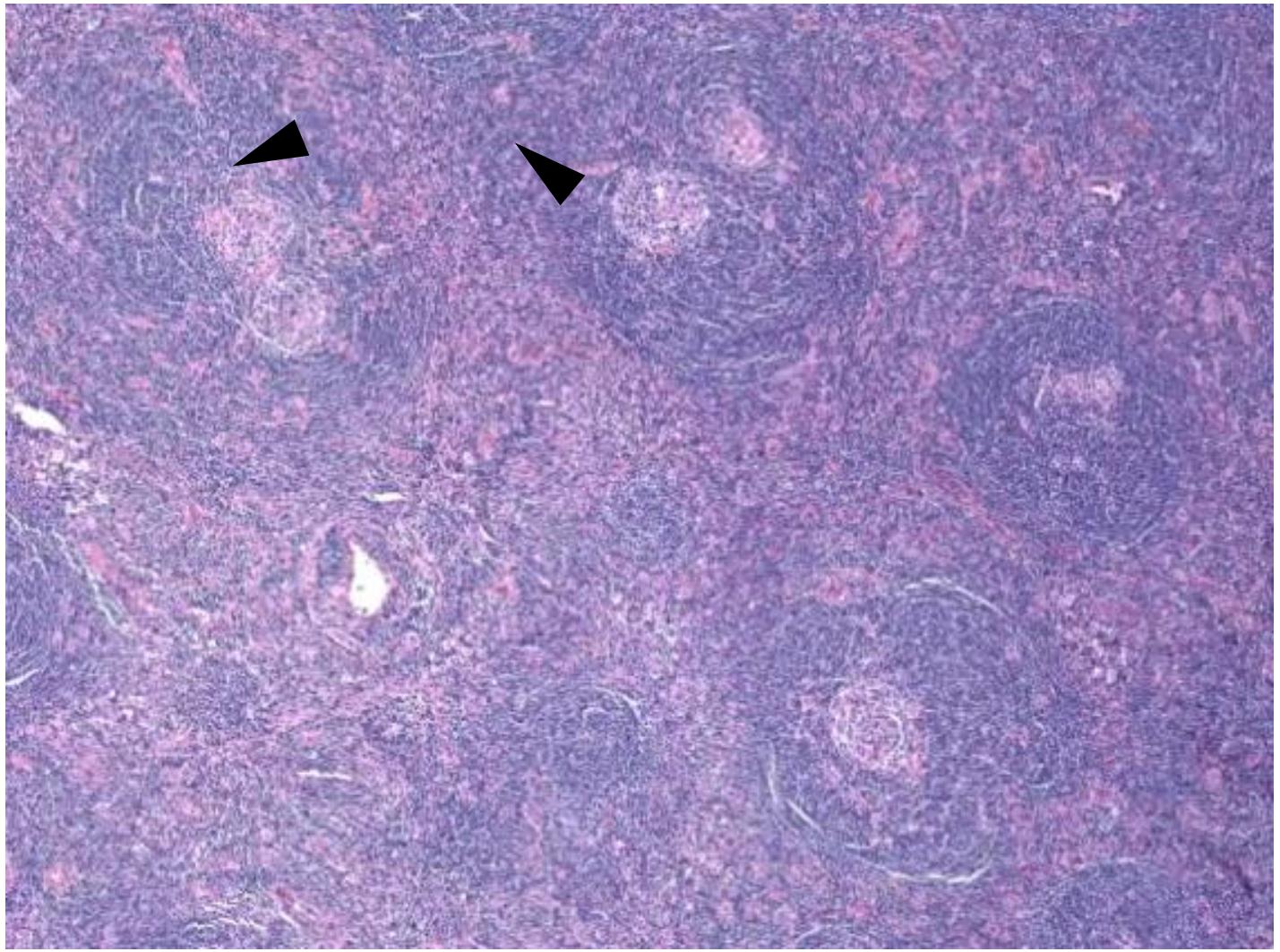
Budding or twinning of follicles



Examples of ‘budding’ or ‘twinning’ of follicles, where 2 or more GCs are located in a single follicle

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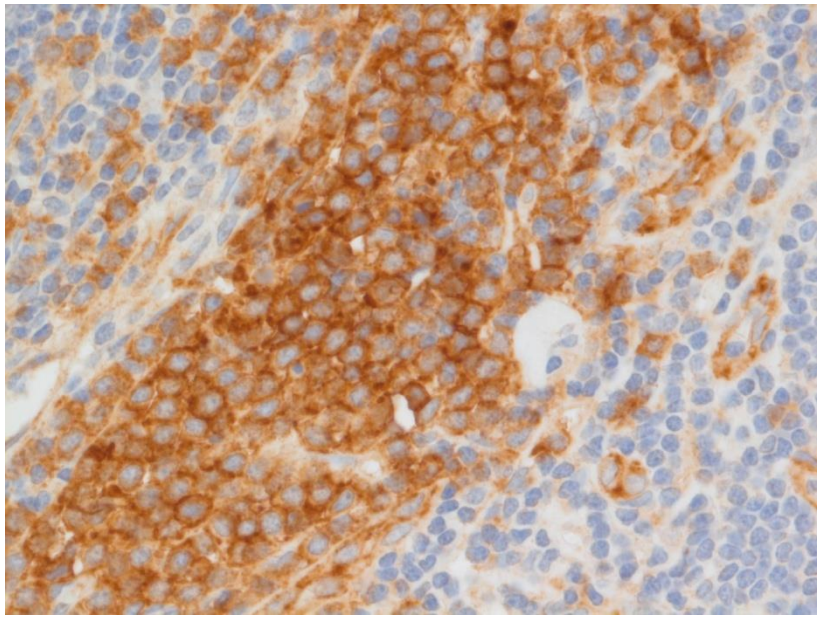
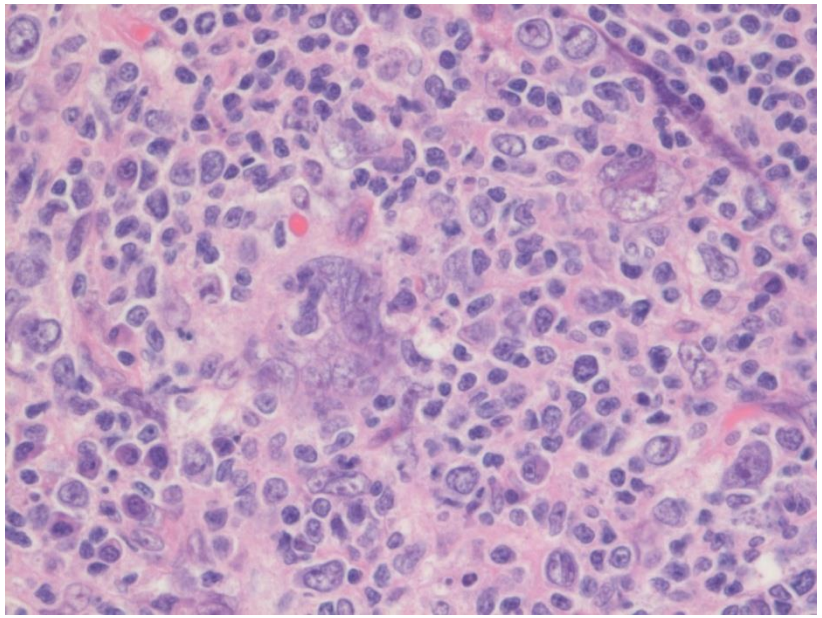
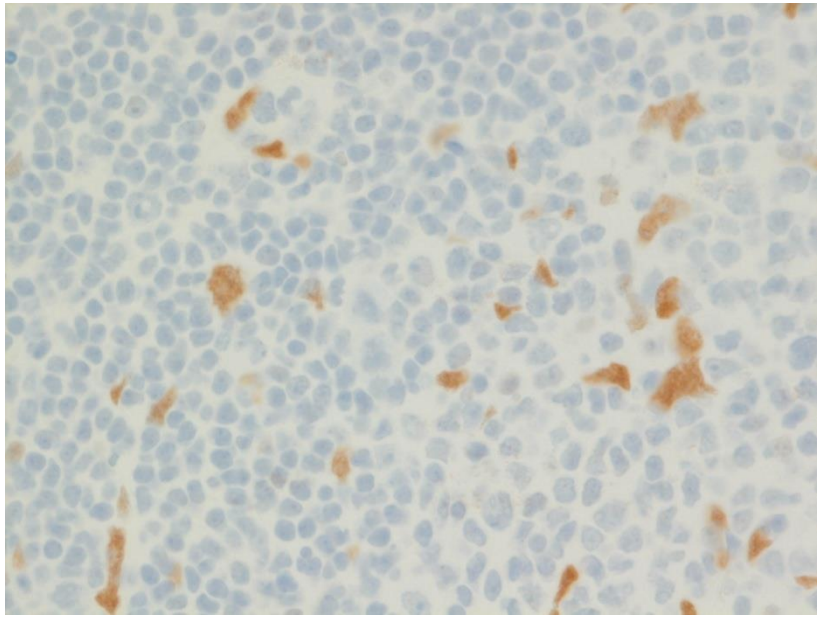
FDC dysplasia







Moderate ER staining ER in nuclei of FDCs.

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

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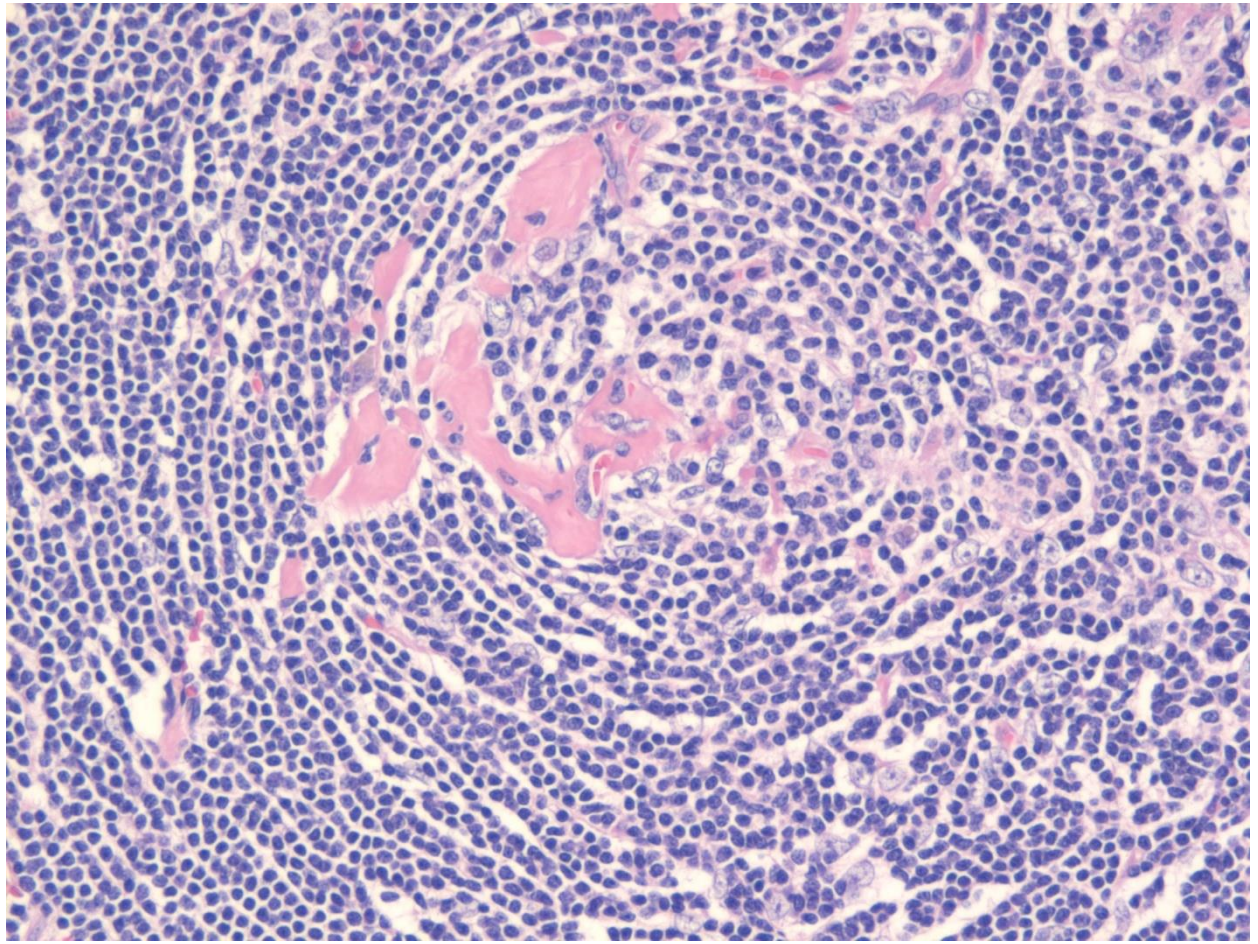
Sclerotic vessels



This images shows sclerotic vessels in hypervascular lymph nodes

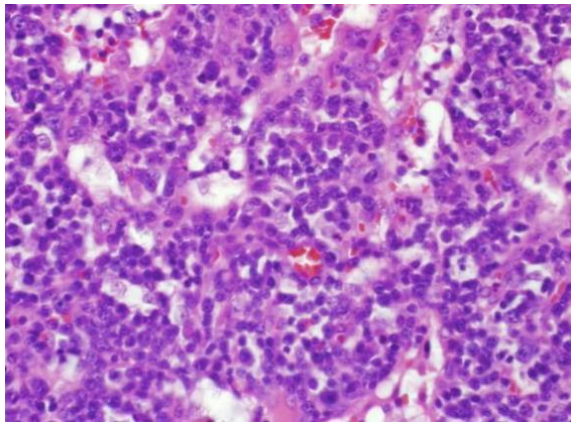
Plasmacytic histopathology

Plasmacytic lymph nodes will show a combination of the following features[1]:

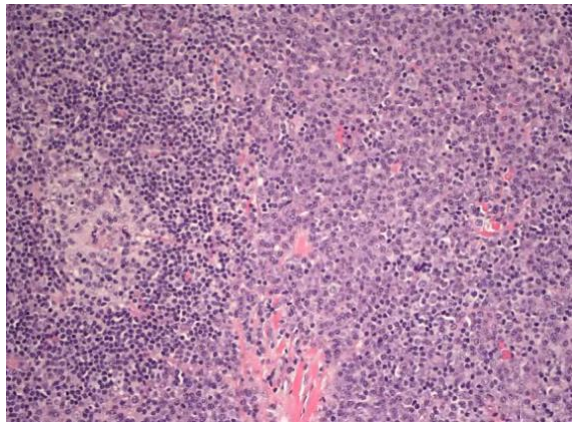
- Sheet-like plasmacytosis
- Increased numbers of follicles with hyperplastic GCs

1. Fajgenbaum, D. et al. Blood 2017;129(12):1646–1657

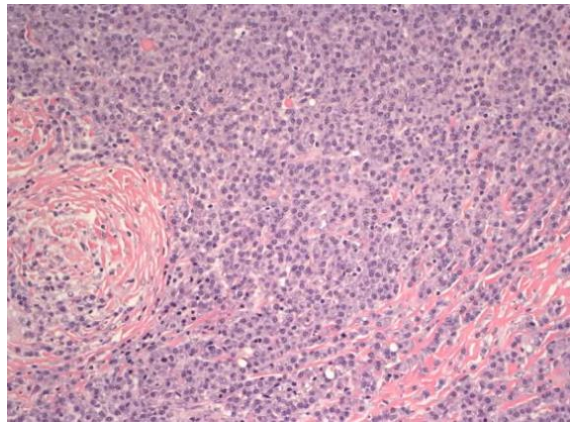
Plasmacytosis



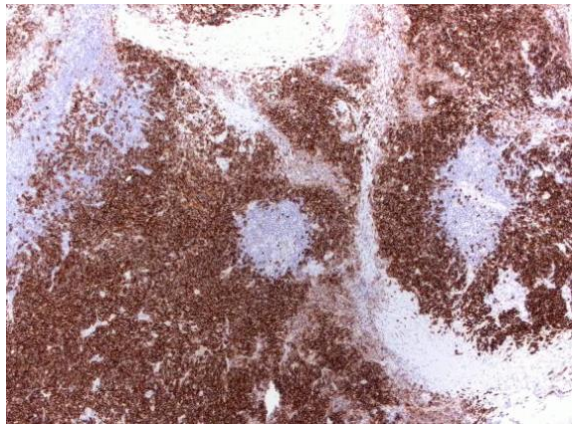
This image shows an infiltrate of plasma cells into the paracortical region



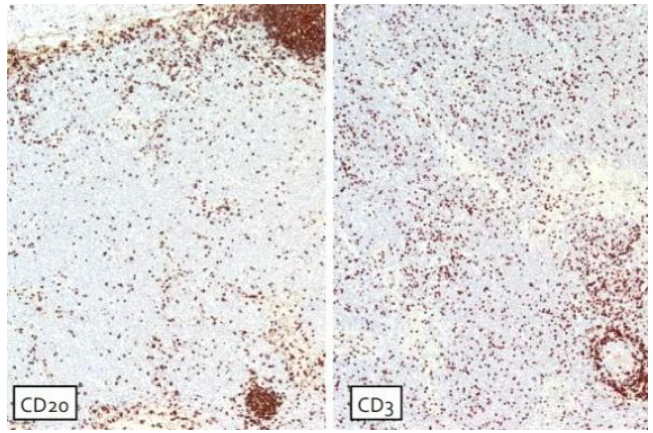
The right-hand side of this image shows a sheet of plasma cells in the interfollicular area



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

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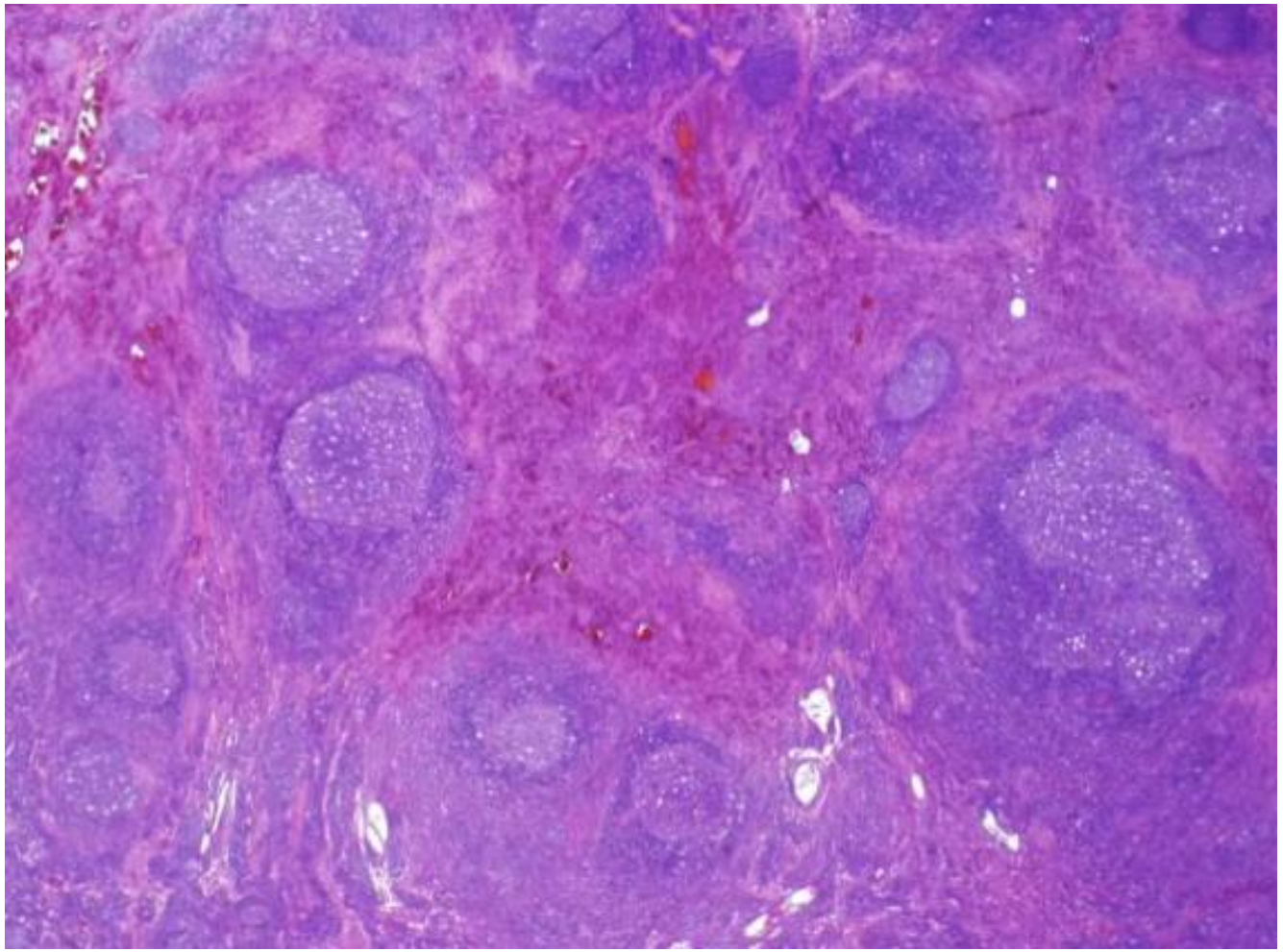
Increased numbers of follicles with hyperplastic GCs



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.

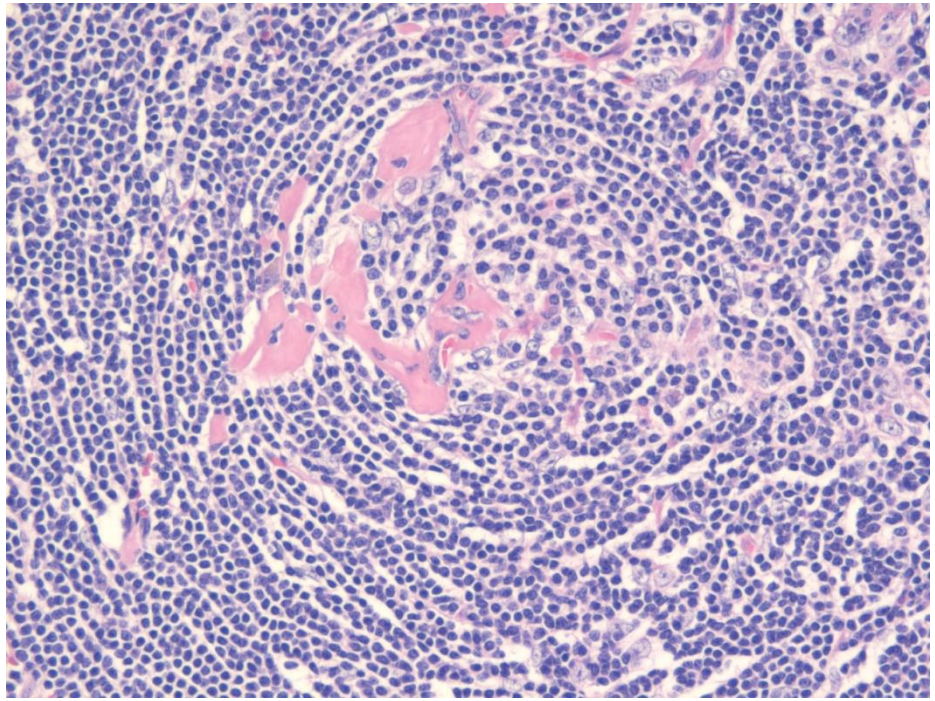
Mixed histopathology

‘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

1. Fajgenbaum, D. et al. Blood 2017;129(12):1646–1657

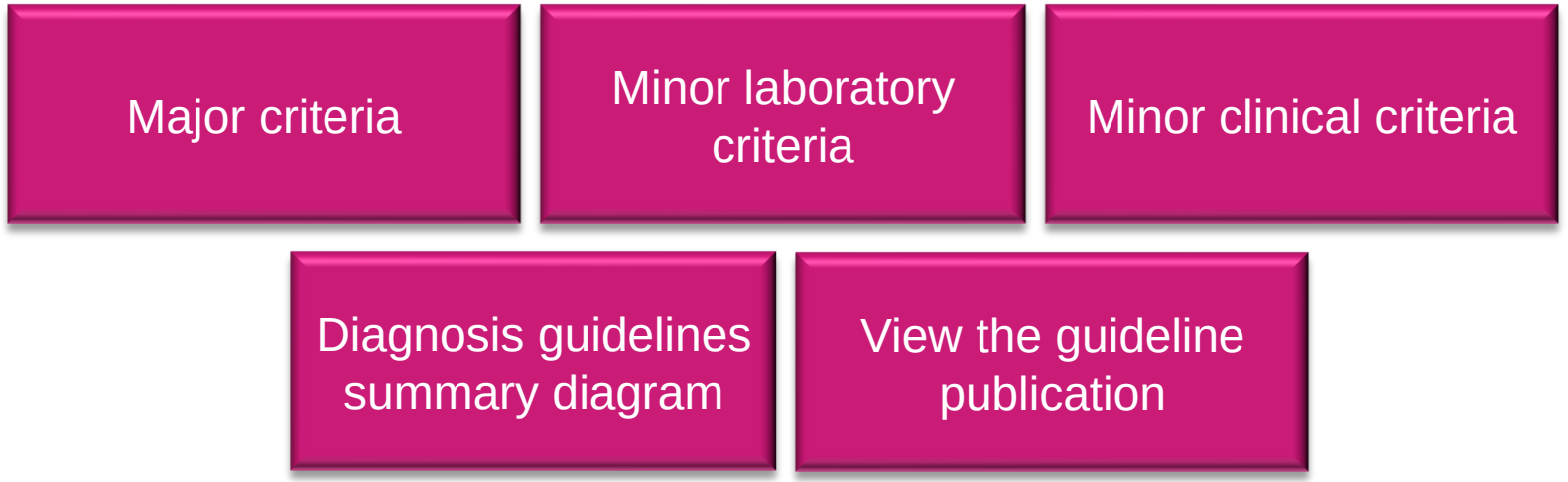
Regressed GCs with plasmacytosis



This image shows regressed follicles with plasmacytosis and onion skinning

iMCD diagnosis guidelines

- 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]



1. Fajgenbaum, D. et al. Blood 2017;129(12):1646–1657

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iMCD diagnosis – the major criteria

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 the minor laboratory and clinical criteria

1. Fajgenbaum, D. et al. Blood 2017;129(12):1646–1657

iMCD diagnosis – the minor laboratory criteria

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[1]:

Criterion		Threshold
Laboratory*	Elevated CRP or ESR	>10 mg/L or >15 mm/h respectively**
	Anaemia	Haemoglobin <12.5 g/dL (males); <11.5 g/dL (females)
	Thrombocytopaenia *or* thrombocytosis	Platelet count <150 k/μL *or* >400 k/μL
	Hypoalbuminaemia	Albumin <3.5 g/dL
	Renal dysfunction *or* proteinuria	eGFR <60 mL/min/1.73m^2 *or* total protein 150mg/24h or 10mg/100mL respectively
	Polyclonal hypergammaglobulinaemia	Total gamma globulin or immunoglobulin G >1700 mg/dL

*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

1. Fajgenbaum, D. et al. Blood 2017;129(12):1646–1657

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iMCD diagnosis – the minor clinical criteria

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[1]:

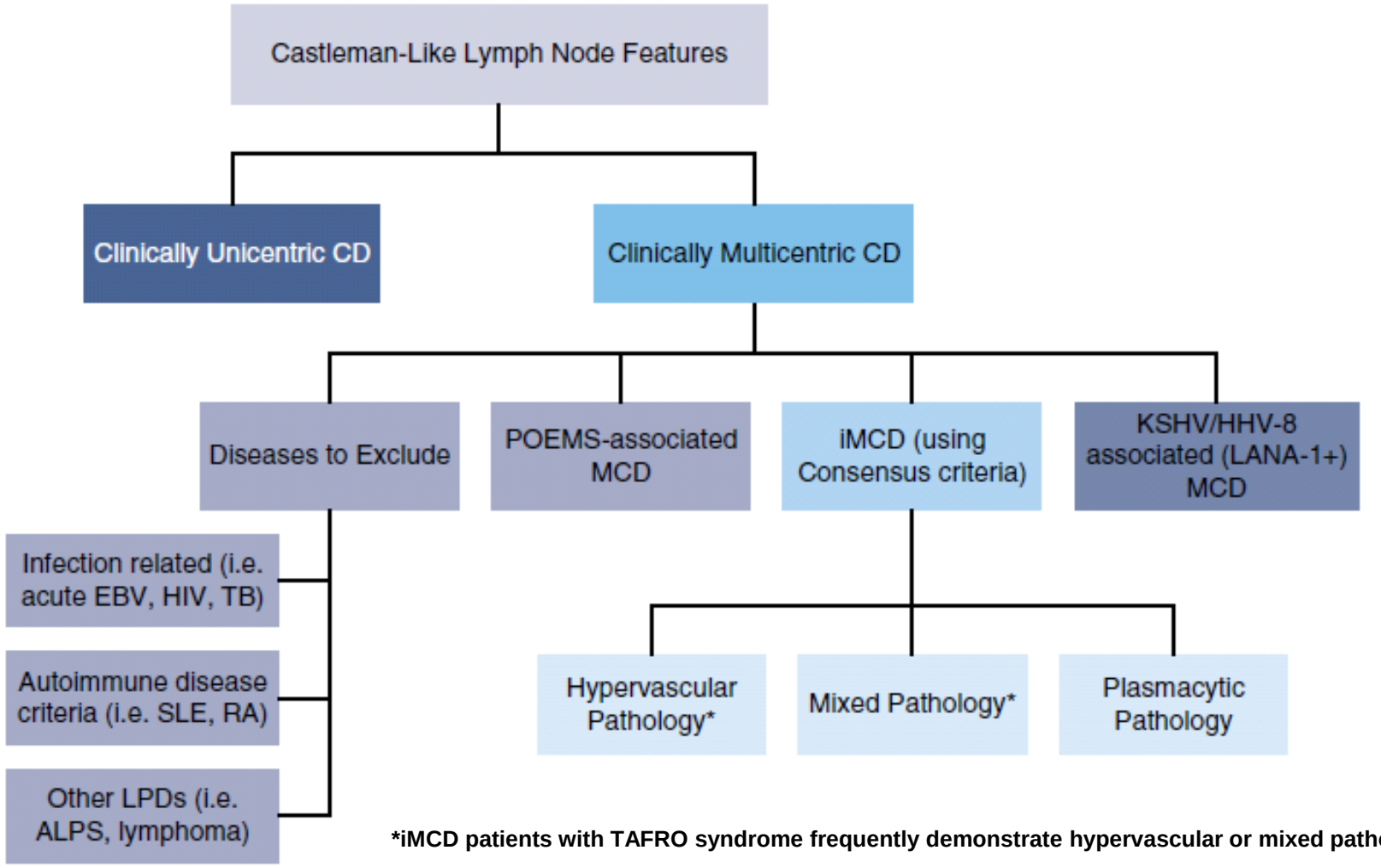
Criterion		Threshold
Clinical	Constitutional symptoms	Night sweats, fever >38°C, weight loss or fatigue (≥2 CTCAE lymphoma score for B-symptoms)
	Fluid accumulation	Oedema, anasarca, ascites or pleural effusion
	Eruptive cherry haemangiomatosis or violaceous papules	
	Enlarged spleen and/or liver	
	Lymphocytic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

CTCAE = Common Terminology Criteria for Adverse Events

To the diagnosis guideline overview

1. Fajgenbaum, D. et al. Blood 2017;129(12):1646–1657

iMCD diagnosis guidelines: summary algorithm for assessment of lymph node with features of CD[1]



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

Diagram taken from Fajgenbaum, D. et al. Blood 2017;129(12):1646–1657

To exclusionary diseases

1. Fajgenbaum, D. et al. Blood 2017;129(12):1646–1657

iMCD diagnosis – exclusionary diseases

The following diseases share symptoms with iMCD and must be excluded for an iMCD diagnosis[1]:

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

To case studies

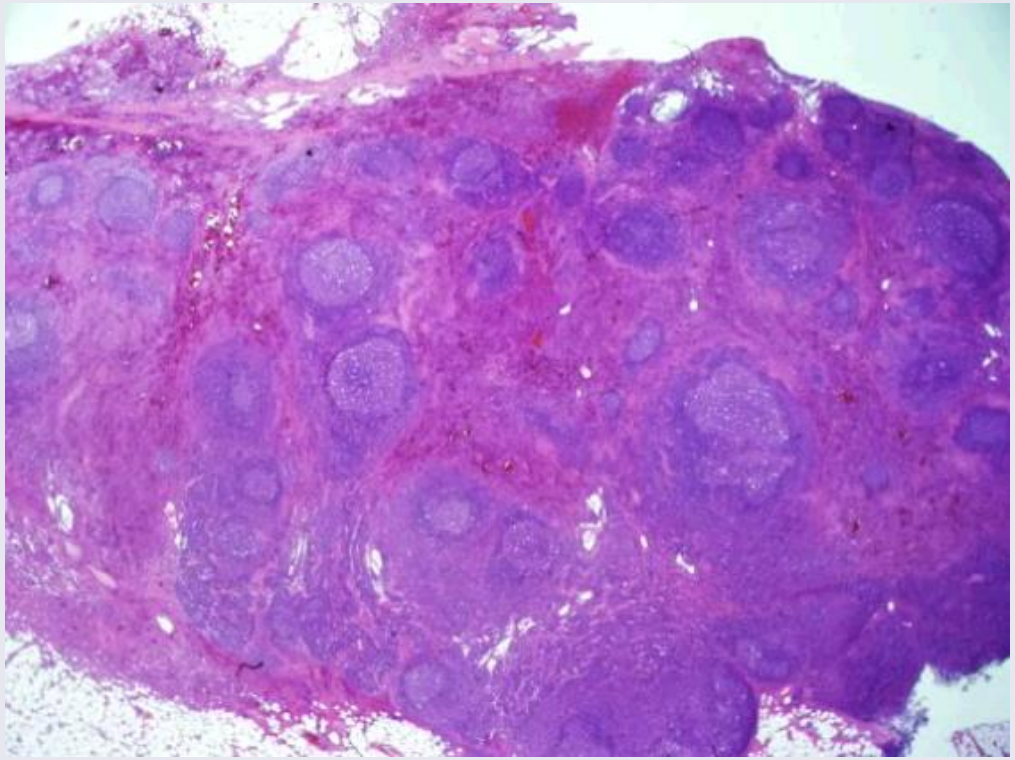
1. Fajgenbaum, D. et al. Blood 2017;129(12):1646–1657

Case study 1

Click here to view a video of pathologists speaking through this case study

Clinical history

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



- Overall architecture is preserved
- Marked paracortical vascularity
- Hyperplastic follicles

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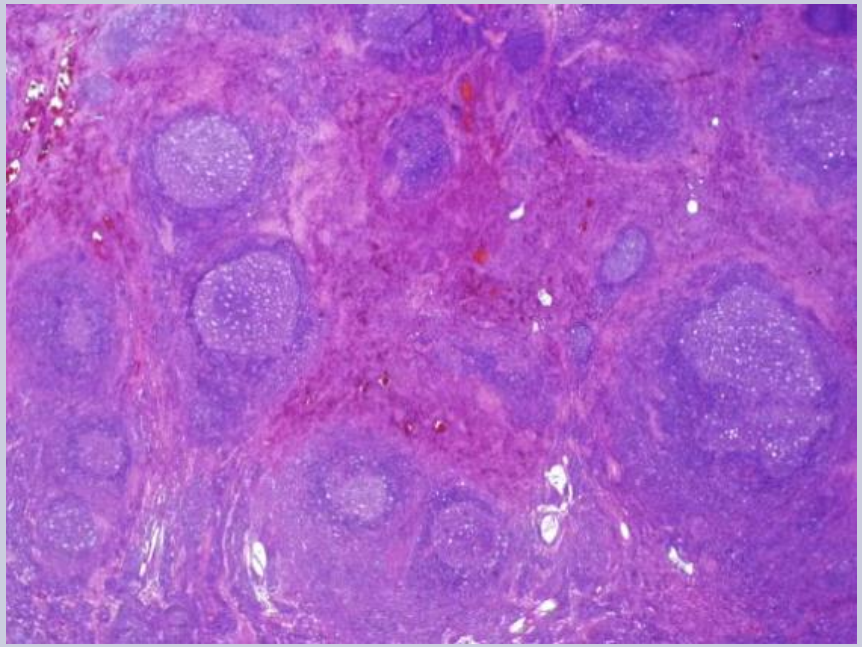
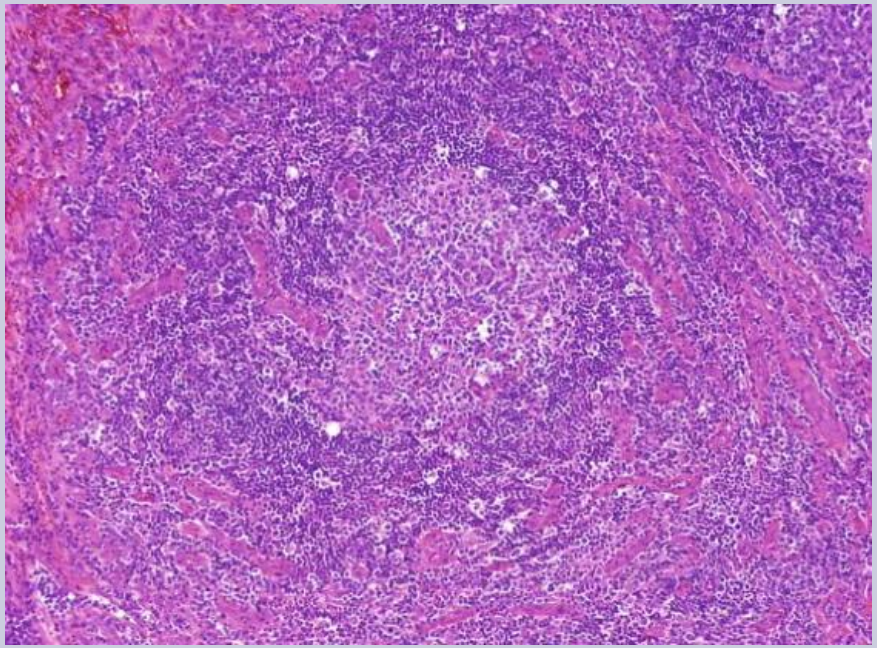
Case study 1

Click here to view a video of pathologists speaking through this case study

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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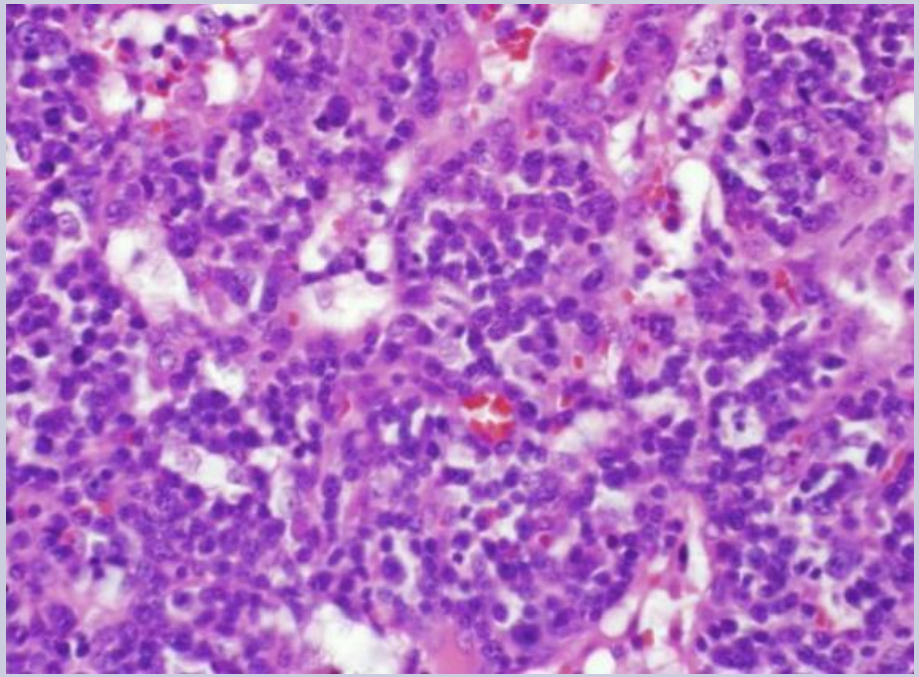
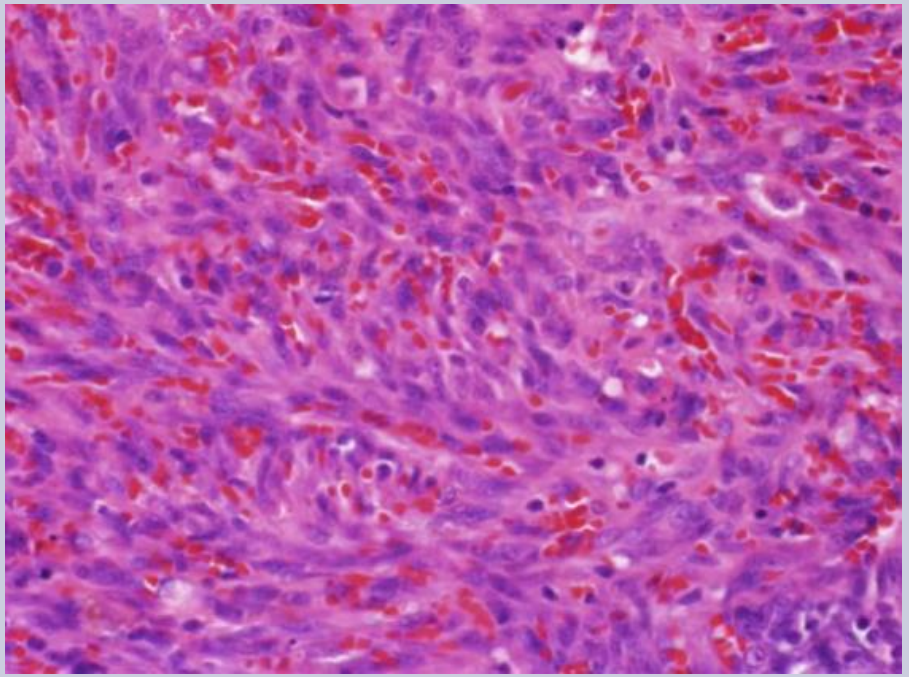
Case study 1

Click here to view a video of pathologists speaking through this case study

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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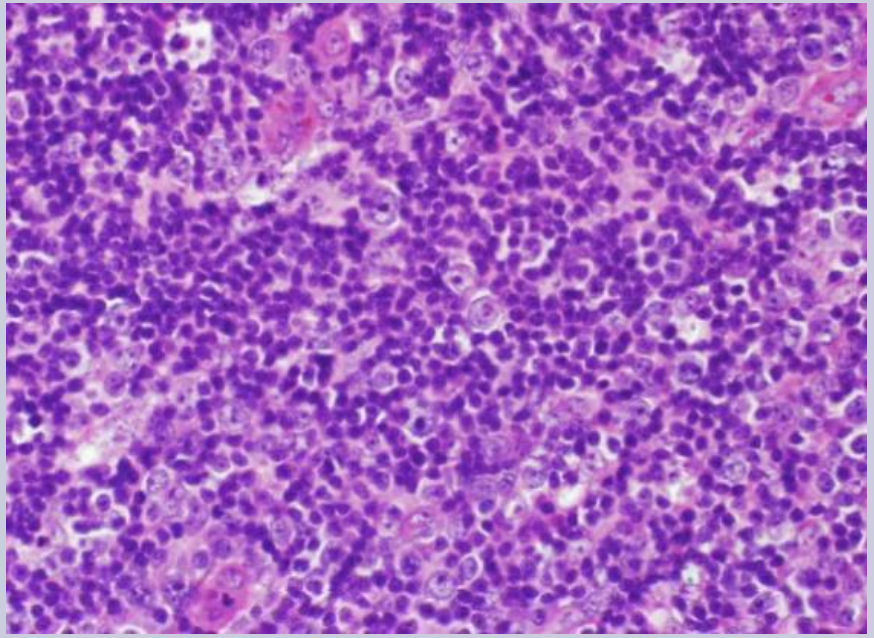
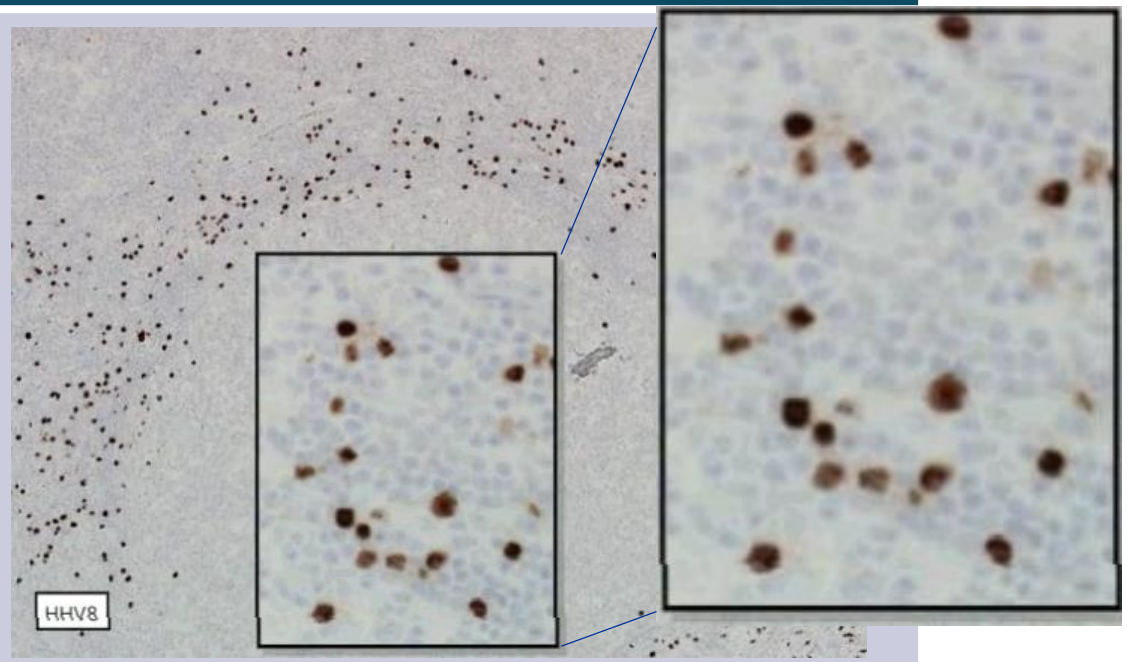
Case study 1

Click here to view a video of pathologists speaking through this case study

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

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Case study 1

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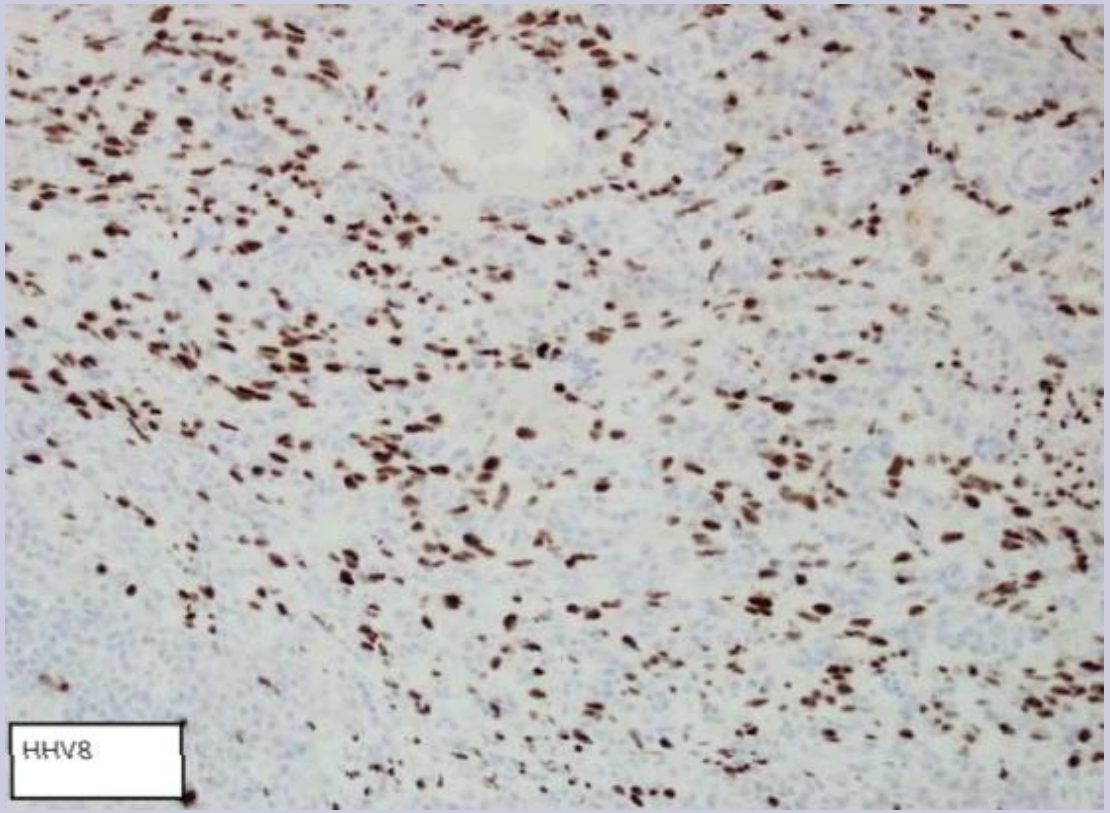
Histopathology



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

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Case study 1

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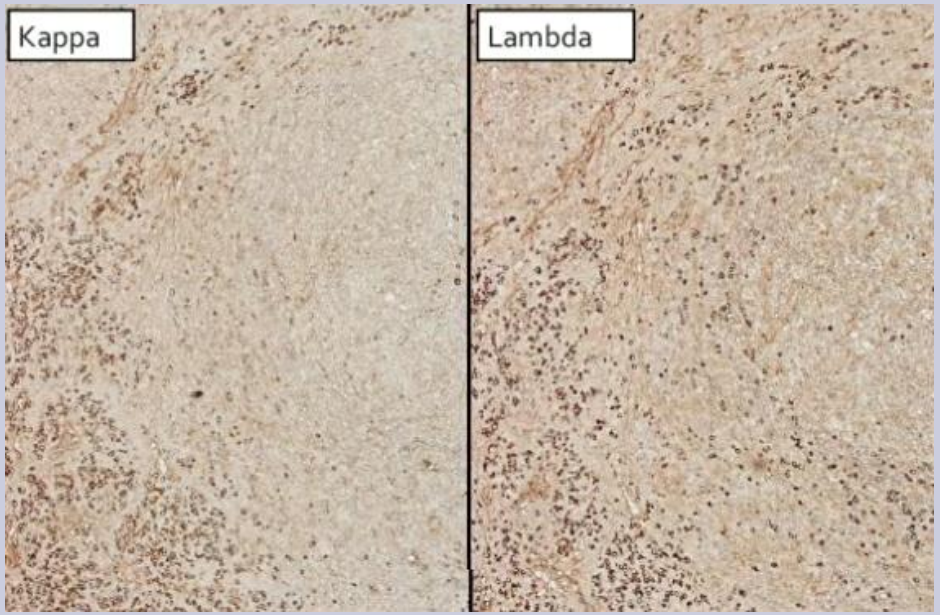
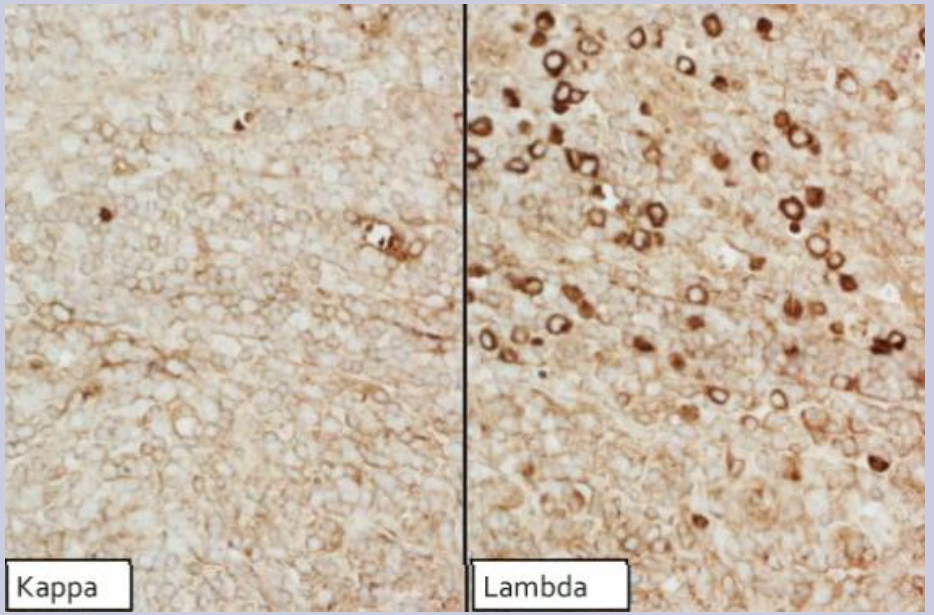
Histopathology



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



Lambda light chain restriction in plasmablasts around a germinal center

Case study 1

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

Return to case study menu

Case study 2

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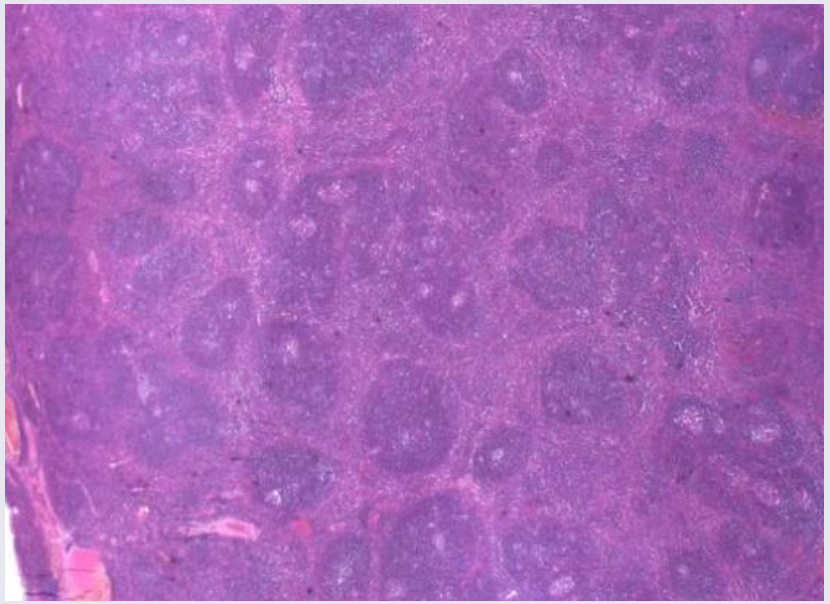
Clinical history

- 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, β_2-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

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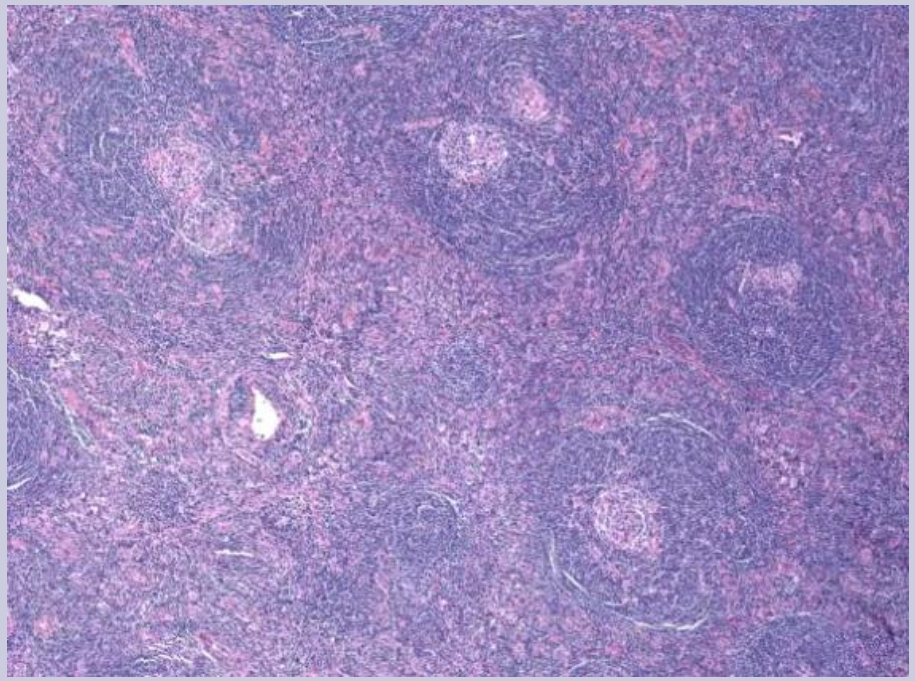
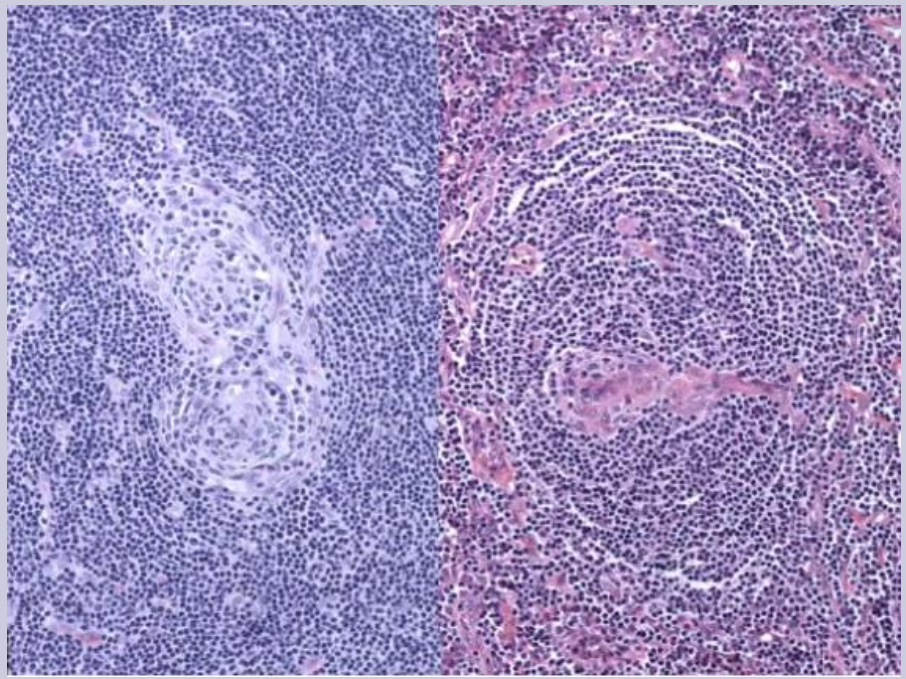
Histopathology



- Expanded mantle zones with concentrically arranged lymphocytes giving an ‘onion skin’ appearance
- Regressed germinal centers with some ‘budding’ or ‘twinning’ of follicles



- Twinned follicle with onion skinning
- Radiating vessel penetrating a germinal center – also known as the ‘lollipop sign’

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Case study 2

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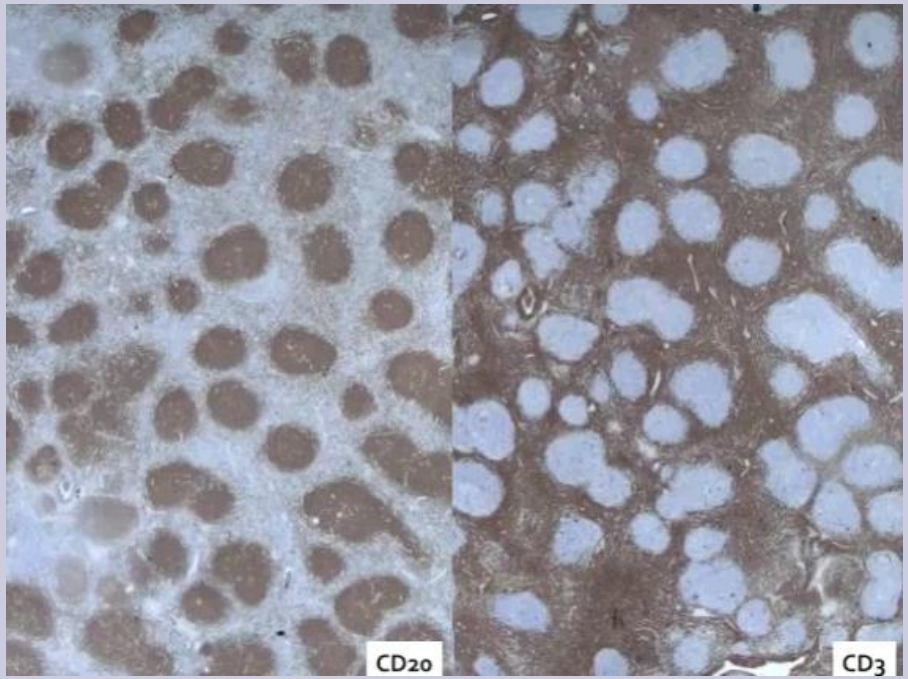
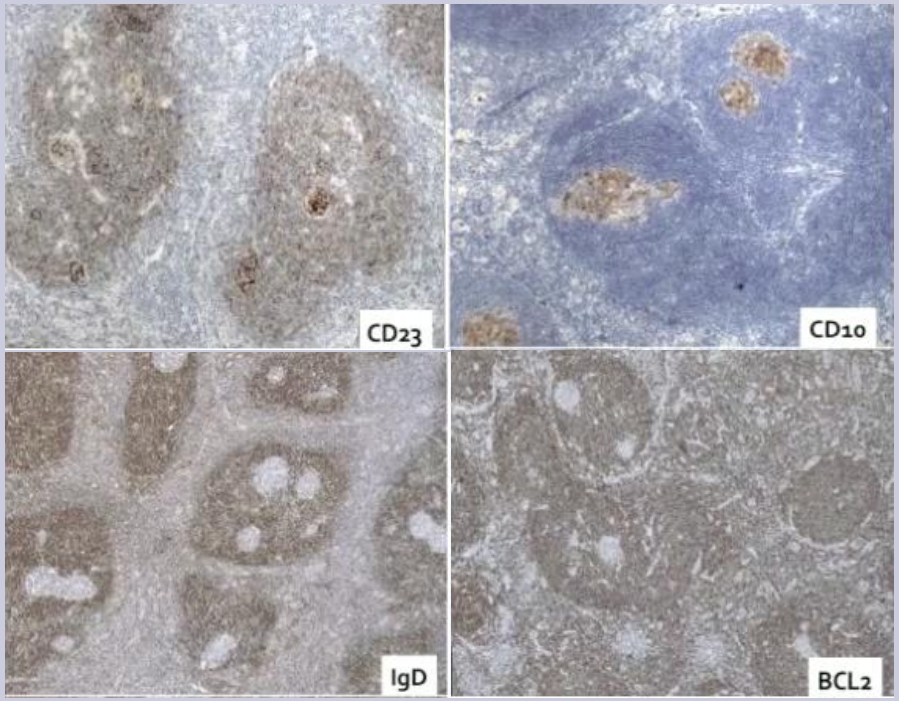
Histopathology



- 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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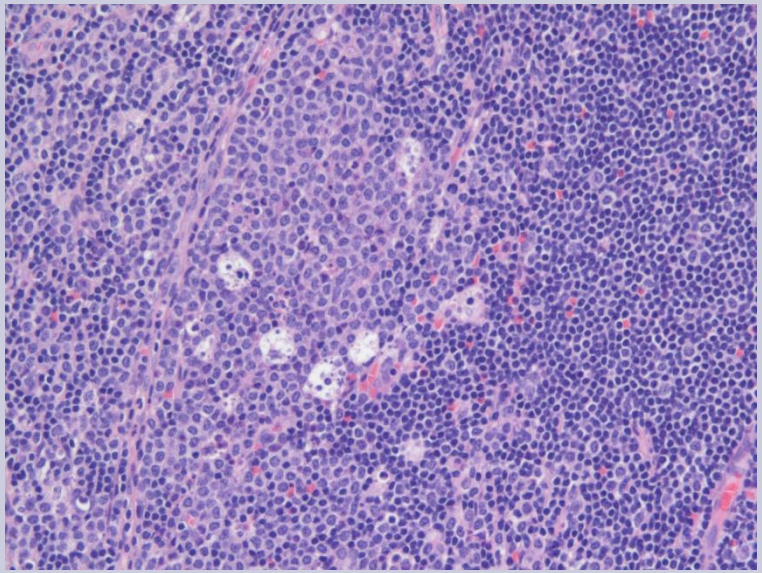
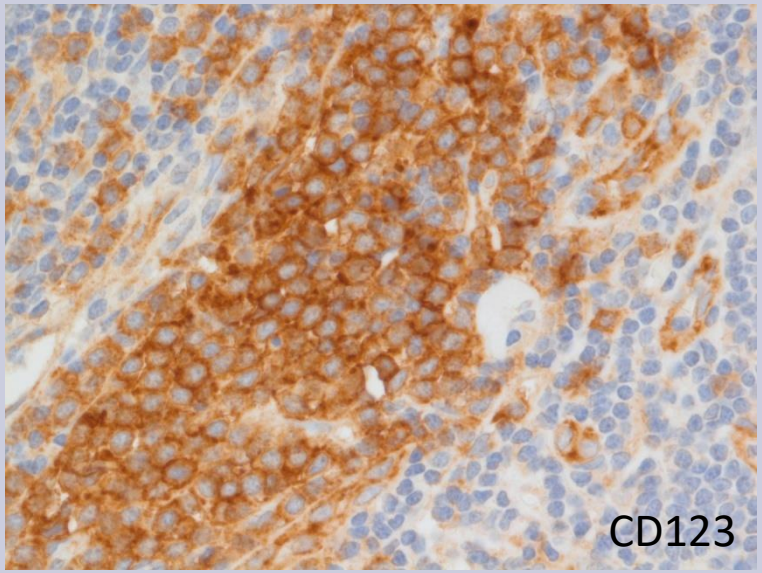
Case study 2

Histopathology





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

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Case study 2

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

Return to case study menu

Case study 3

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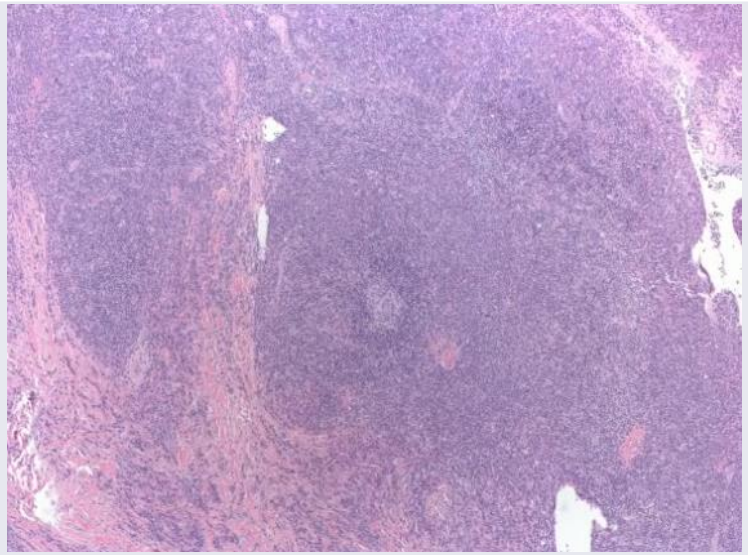
Clinical history

- 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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Case study 3

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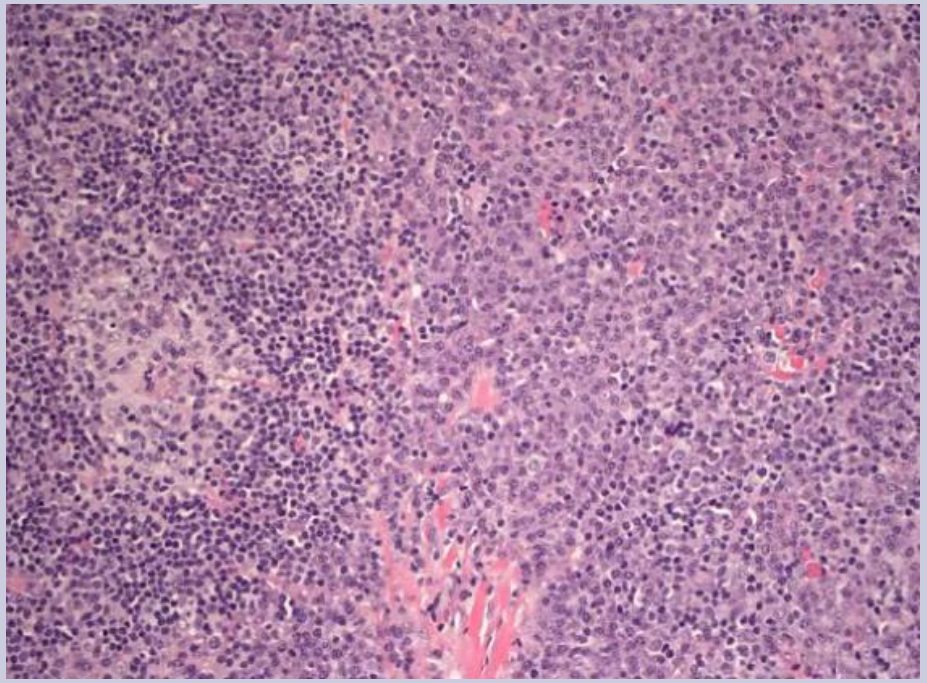
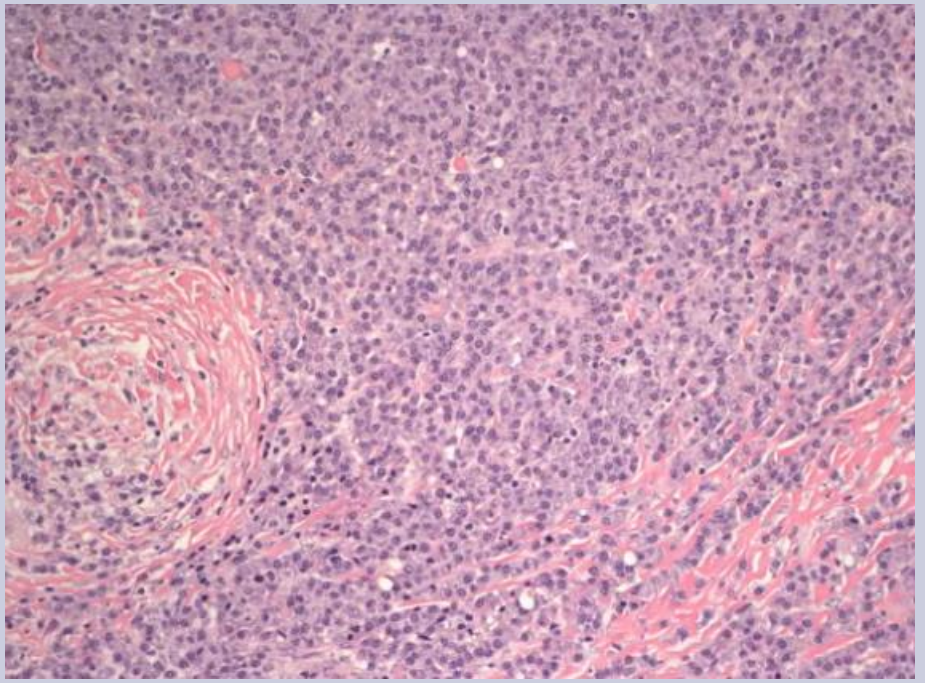
Histopathology



- 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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Case study 3

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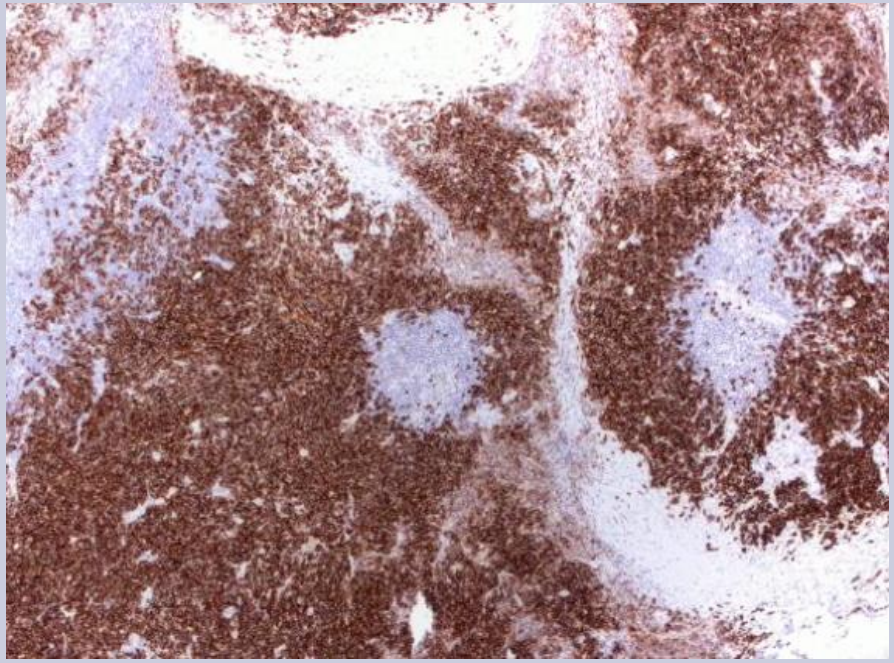
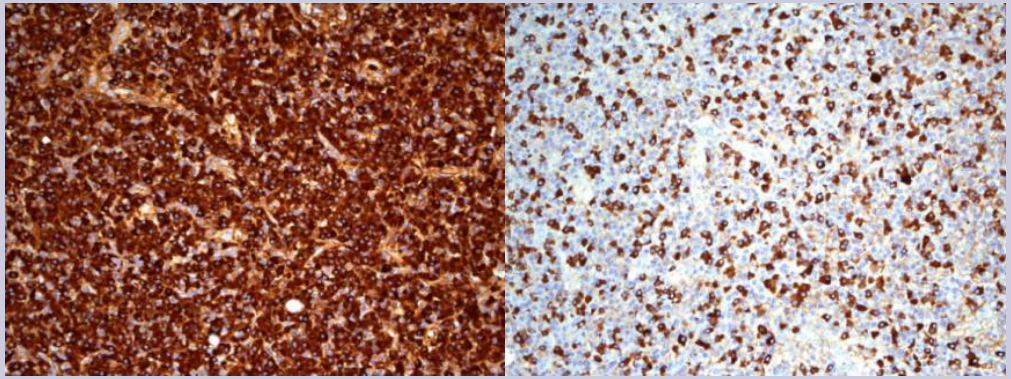
Histopathology



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)

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Case study 3

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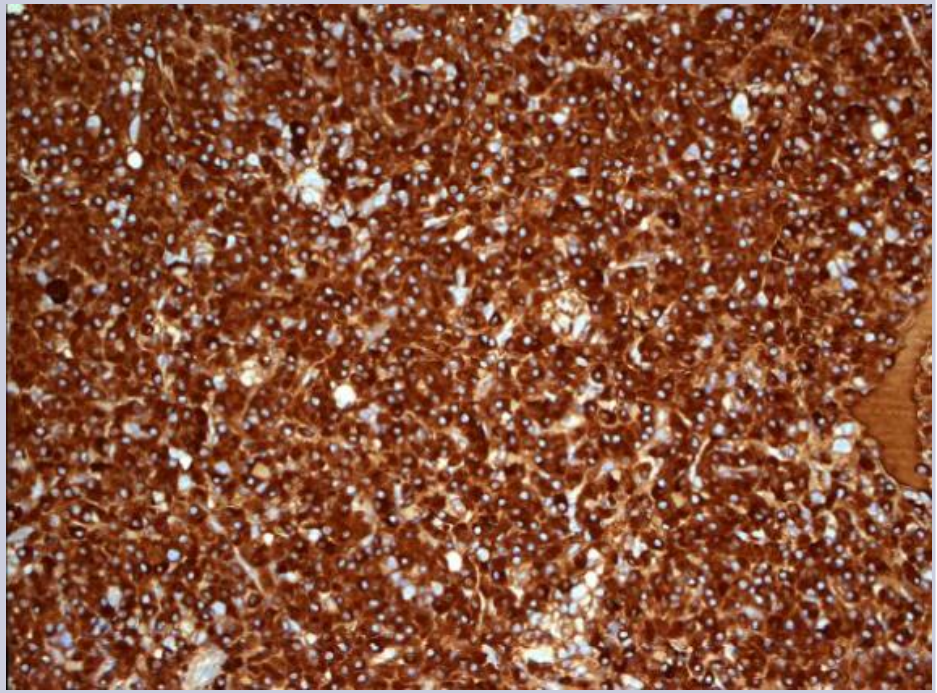
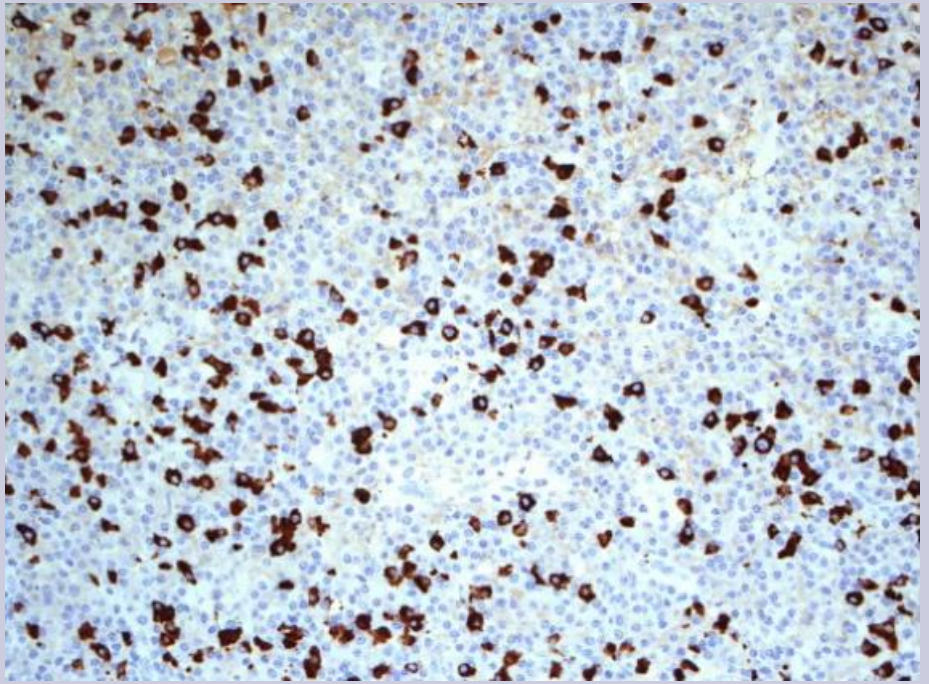
Histopathology



- 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

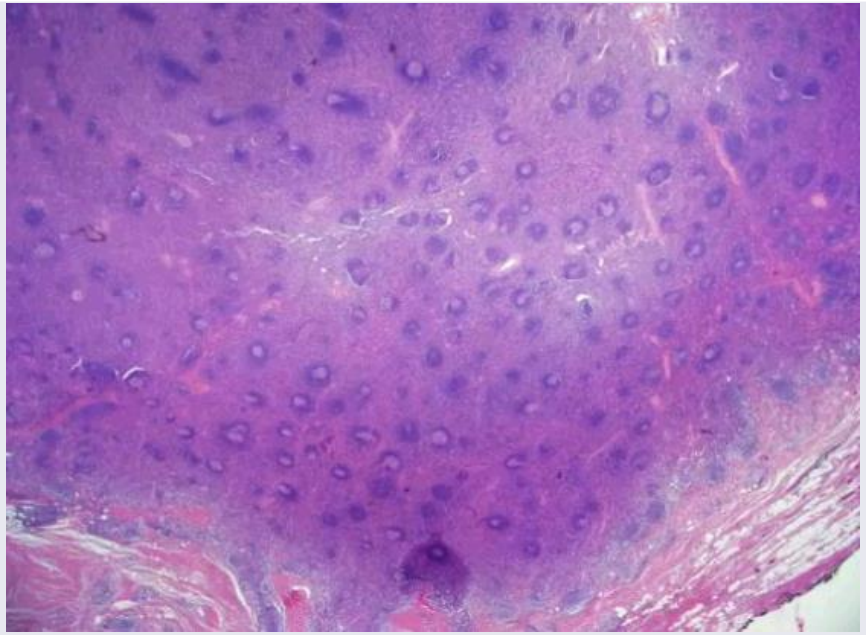
Return to case study menu

Case study 4

Click here to view a video of pathologists speaking through this case study

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

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Case study 4

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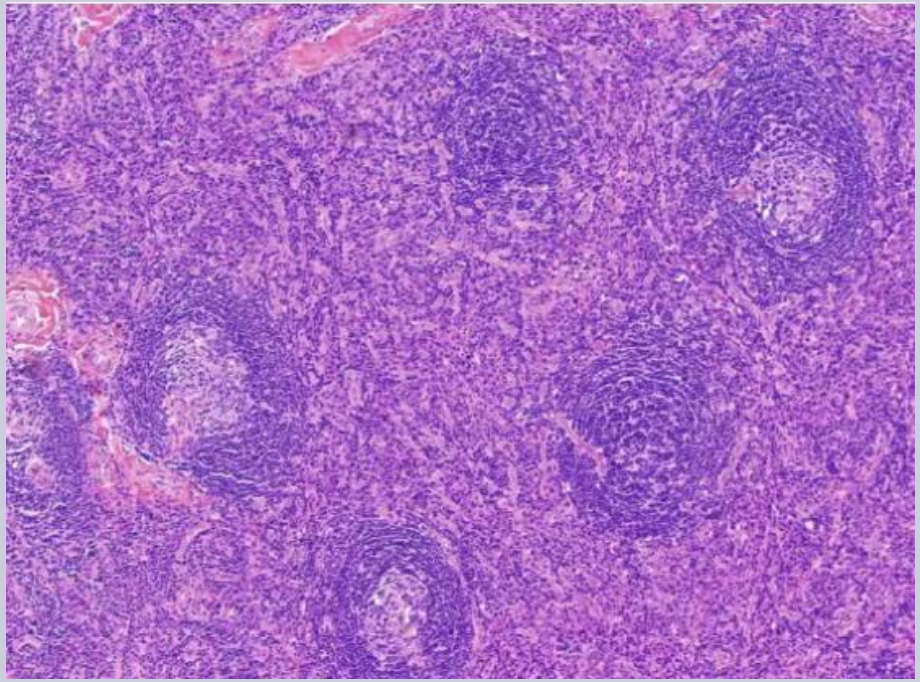
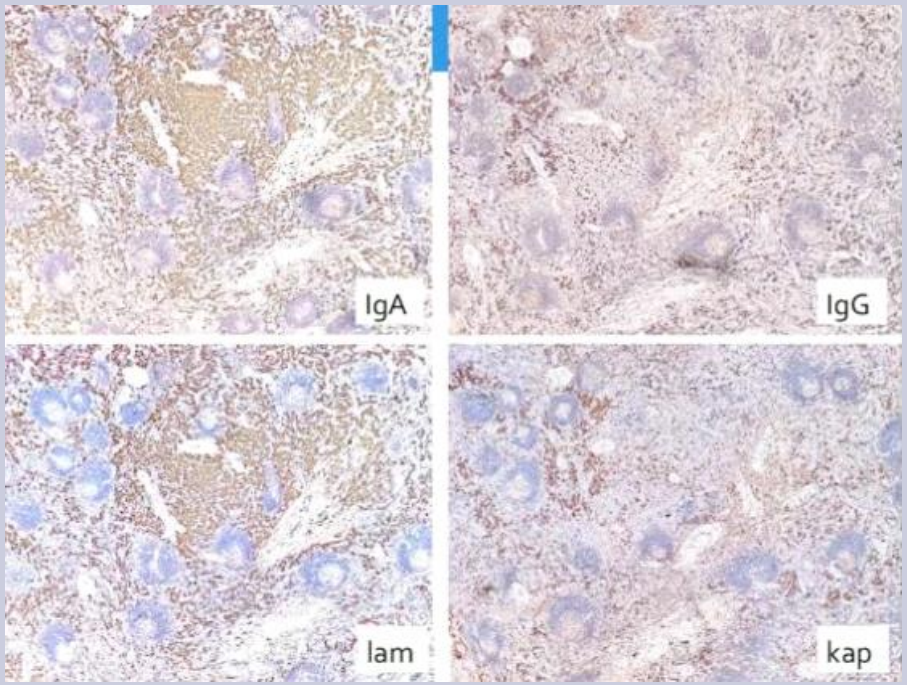
Histopathology



- Numerous follicles with regressive features and well-defined mantle zones
- Interfollicular plasma cell infiltrate in a background of fine sclerosis



There is an excess of plasma cells expressing IgA/lambda

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Case study 4

Conclusion	
Summary of pathology	• Physiological distribution of CD20+ B cells and CD3+ T cells (not shown) • An excess of plasma cells expressing IgA/lambda • HHV-8 and EBV negative (not shown) • Bone marrow had a small population of IgA/lambda plasma cells (not shown)

Differential diagnoses	• Reactive lymph node with plasmacytosis
	• Autoimmune lymphadenitis
	  • IgG4-related disease
	  • Lupus lymphadenitis
	  • Rheumatoid arthritis
	• UCD, HHV-8 MCD, iMCD

Diagnosis	• POEMS-associated MCD, plasmacytic variant

Return to case study menu

Case study 5

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)

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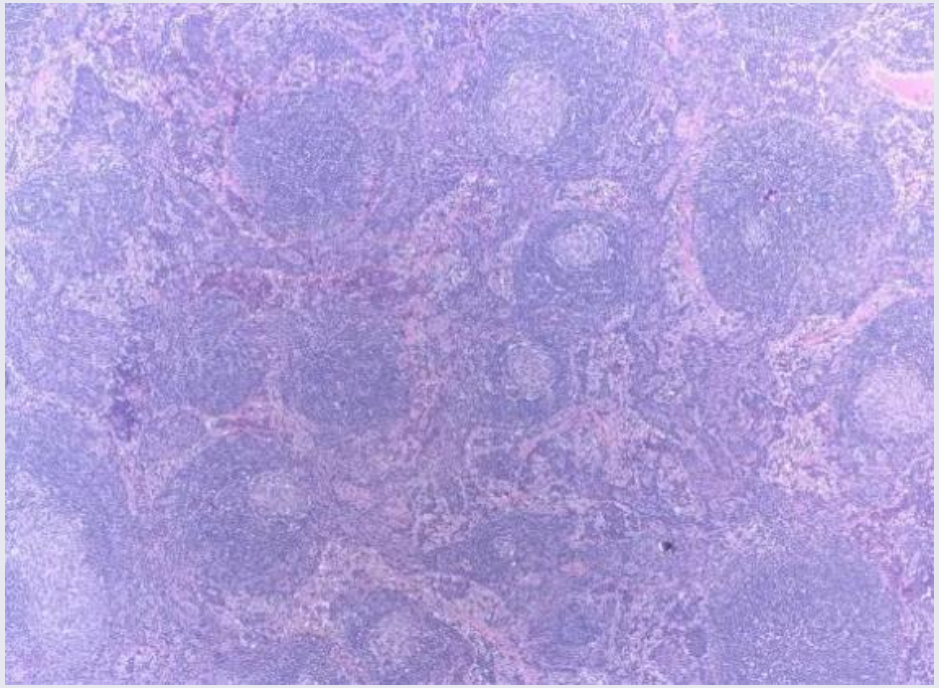

- Overall architecture is preserved
- Numerous follicles with regressive features and well-defined mantle zones. Some primary follicles, some big germinal centers with extended mantle zones.
- Interfollicular plasma cell aggregates
- Medullary sinuses open
- Some sclerosis

Case study 5

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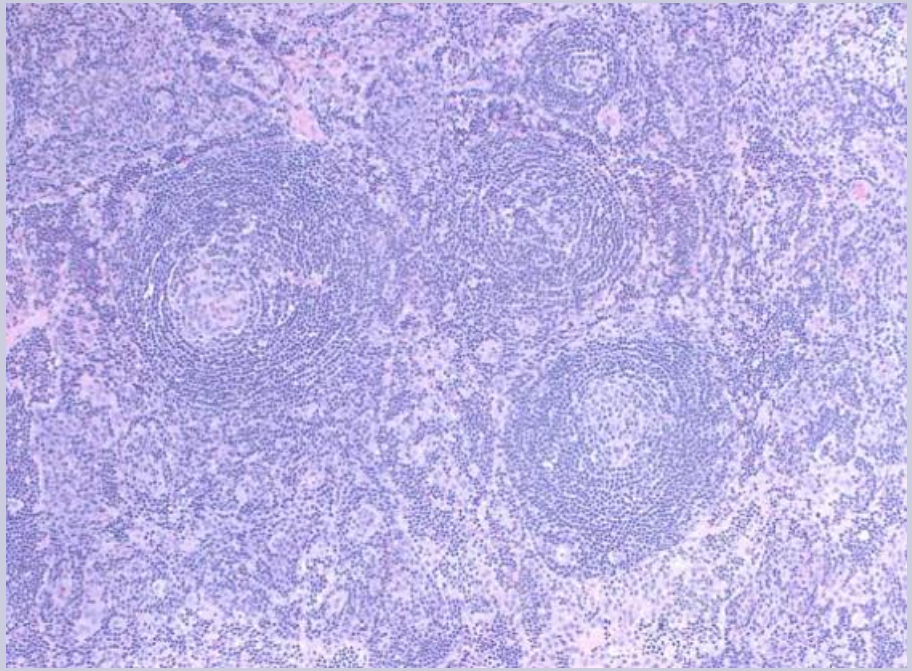
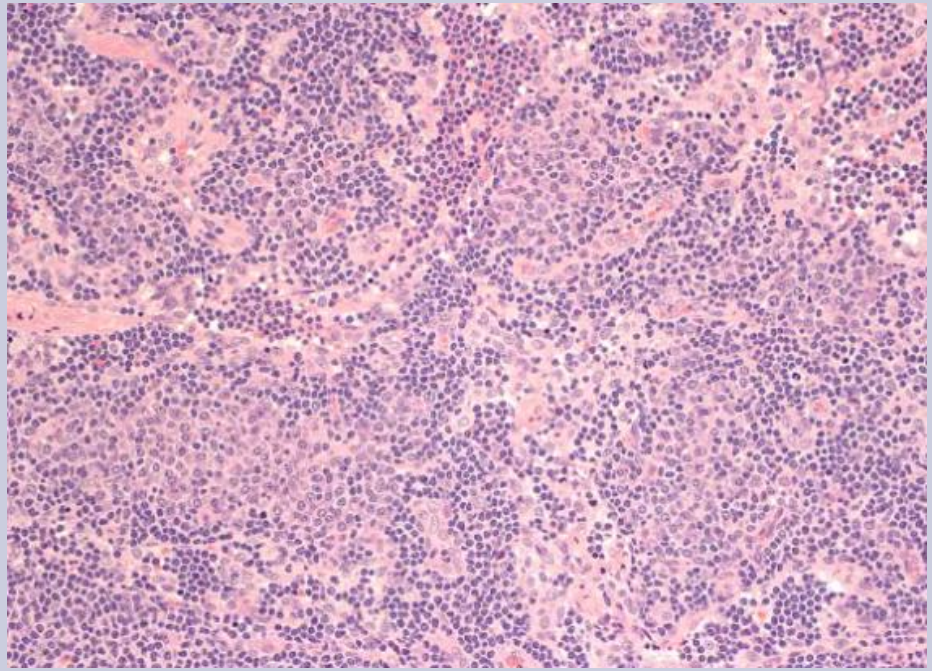
Histopathology



Regressed germinal centers with ‘onion skinning’



There are some plasma cell aggregates in the interfollicular regions

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Case study 5

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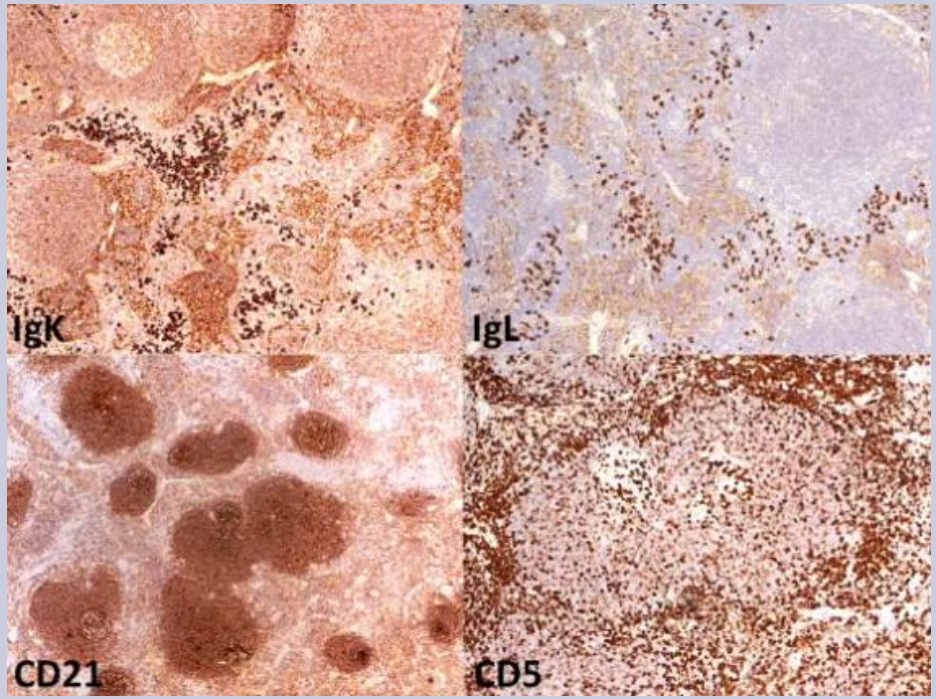
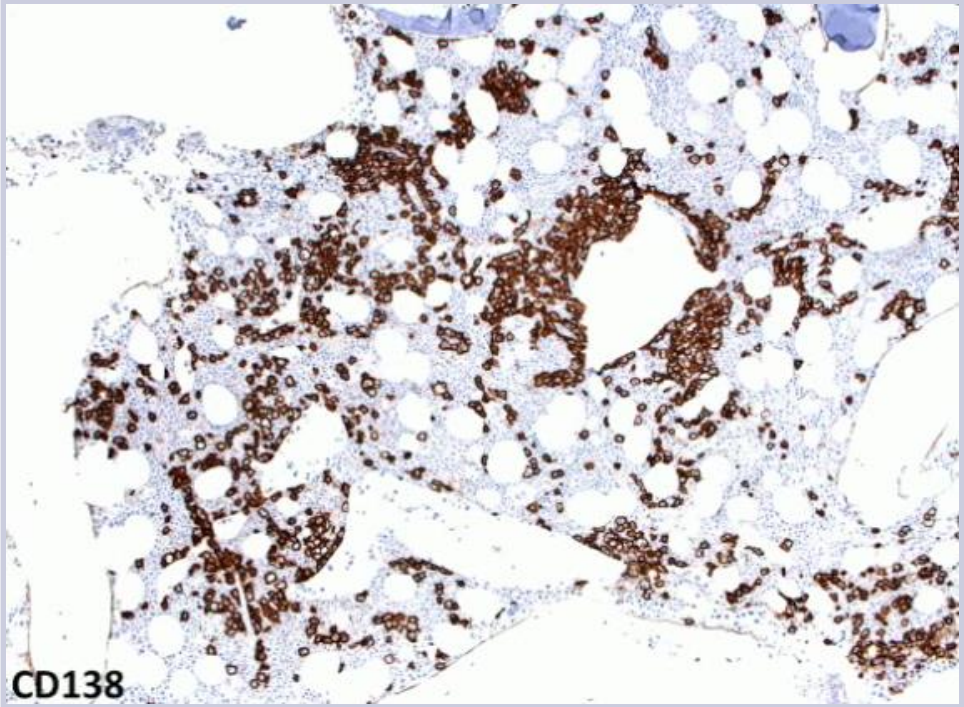
Histopathology



- 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)

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Case study 5

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

Return to case study menu

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

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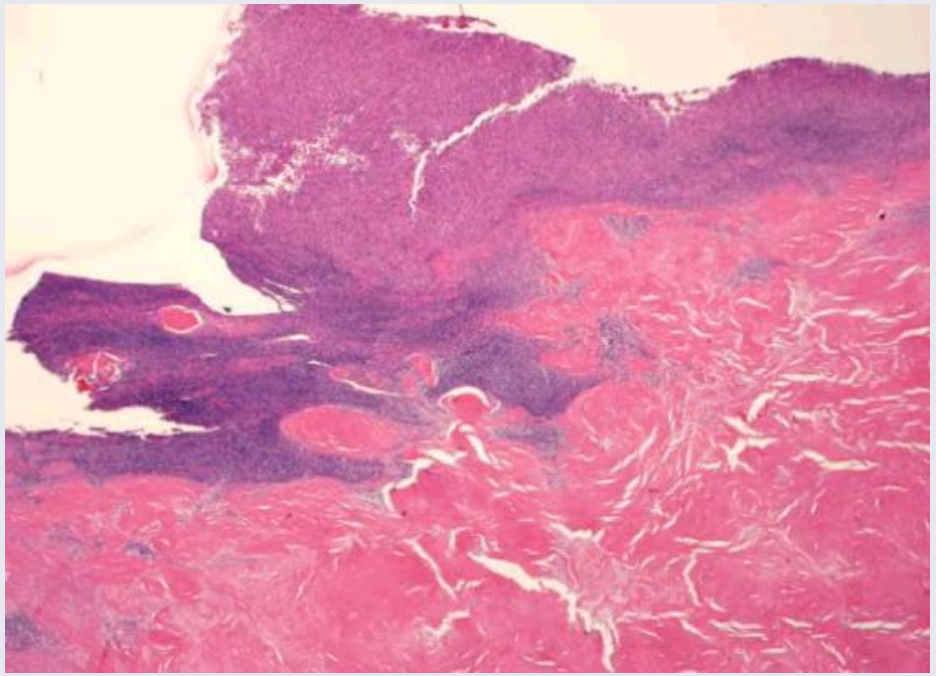

- Three distinct components
- Peripheral hyalinising sclerosis
- Inner layer of lymphoid tissue reminiscent of CDHV with dysplastic FDCs
- Central area of high-grade sarcoma

Case study 6

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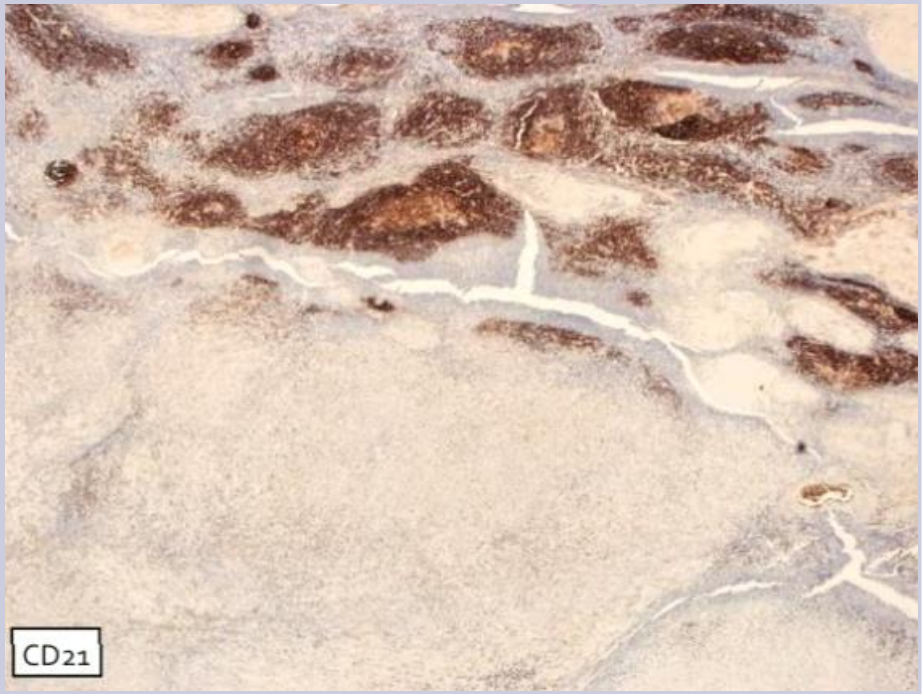
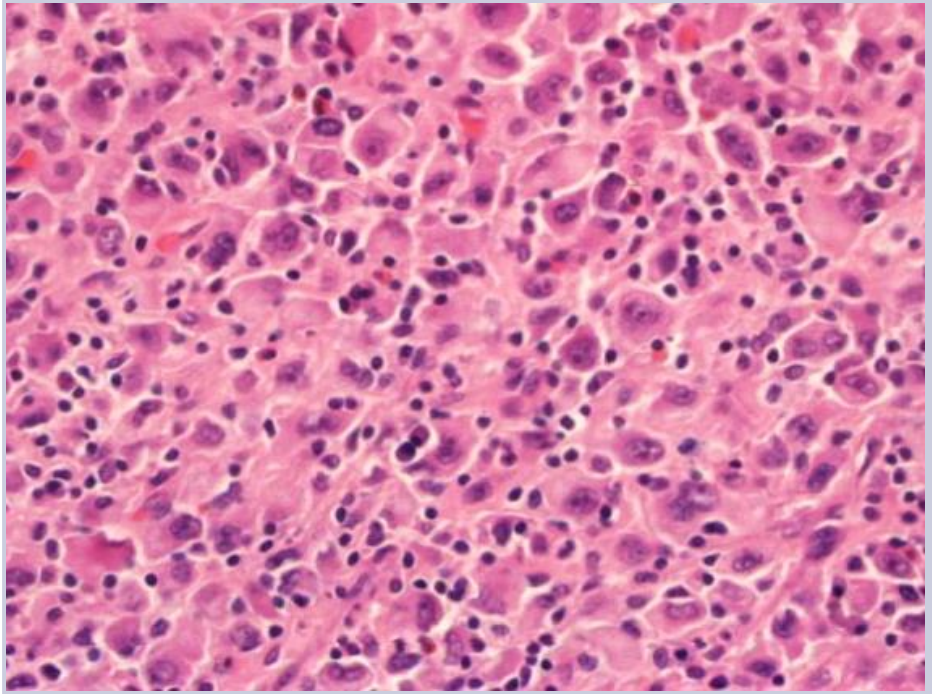
Histopathology



B-cell follicles are based on CD21+ FDC meshworks



Sarcoma region

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Case study 6

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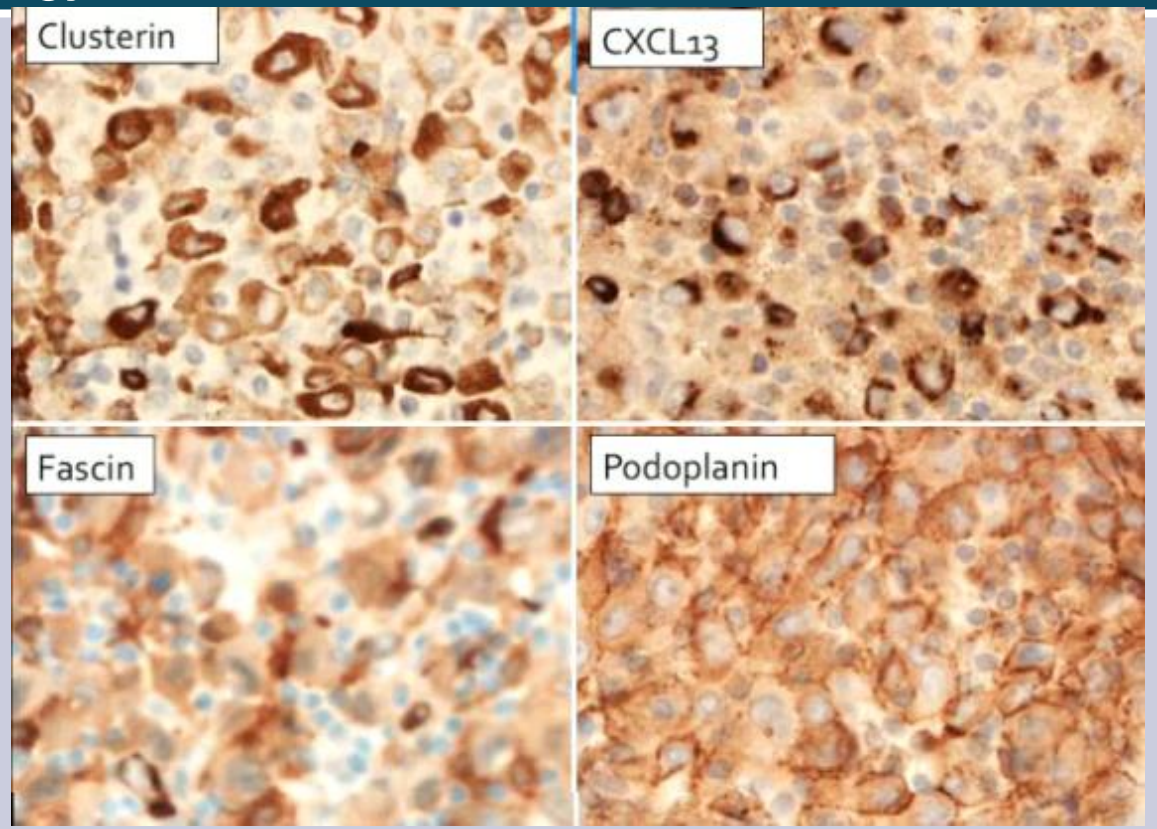
Histopathology



- 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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Case study 6

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

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