SPLEEN AND LYMPH NODES

MUSEUM CATALOGUE

Department of Pathology, University of Adelaide, 2004

SPLEEN AND LYMPH NODES

INTRODUCTION

The spleen is flattened ovoid in shape and is located within the peritoneal cavity, its capsule being covered by mesothelium, in the left hypochondrium. It is closely related to the posterolateral aspect of the stomach and tail of the pancreas. Its normal weight in the adult is around 150gm and it measures approximately 12x7x3cm. It is confined within a capsule that contains blood vessels, lymphatics and nerves. The arterial supply to the spleen is via the splenic artery derived from the coeliac axis and the venous drainage is into the portal system via the splenic vein.

The primary function of the spleen is as a filter of blood but it also serves an immunologic function, being the largest lymphoid organ in the body. Macroscopically the spleen is seen to be studded with tiny 1-2mm white/grey flecks corresponding to the malpighian follicles or white pulp that is intimately associated with the splenic arterial circulation. A cylindrical cuff composed predominantly of T lymphocytes (periarteriolar lymphoid sheath) surrounds the central arteries. At intervals, the lymphoid sheaths expand into lymphoid follicles containing B lymphocytes. These transform into germinal centres upon antigenic stimulation. The white pulp contains a continually changing population of lymphocytes. The red pulp of the spleen is organised for blood filtration and contains thin walled vascular sinusoids, separated by the splenic cords of Billroth, which are spongelike, being composed of a loose network of reticular cells and fine collagen fibres, and numerous macrophages.

Lymph nodes are encapsulated ovoid structures with a pale cut surface and normally only measure several mm in diameter. Lymph containing lymphocytes, antigens and macrophages ready with antigens to present, enters in to the subcapsular sinuses, which communicate with the medullary sinuses. A variety of histopathologic patterns may develop in a reactive node depending on the antigens presented. These include follicular and paracortical hyperplasia, sinus histiocytosis, granulomatous inflammation and an acute lymphadenitis. As the immune response develops, the lymph node may enlarge. Neoplastic cells may also enter via the lymph and be filtered out in the subcapsular sinuses to proliferate and cause lymphadenopathy.

The pathology of spleen and lymph nodes is complicated by the fact that they are commonly involved in lymphoid malignancies and leukaemias, which have a complex classification entirely dependent on histological examination, and in the modern age by a plethora of other tests, including immunohistochemistry and flow cytometry. The macroscopic appearances are largely non-specific. The important things to develop are a good understanding of the differential diagnosis of lymphadenopathy and splenomegaly, as well as a basic understanding of the classification of lymphoid malignancies (see later).

Any comments on this catalogue are welcome. Please contact a member of the department.

HOW TO USE THIS CATALOGUE

This catalogue is to be used as a tool to develop your knowledge as well as provide an opportunity for revision.

It is divided into:

- Introduction and approach to specimens (pages 105-107).
- Index (pages 108-109). Examples of specific diagnoses can be found via the index.
- Core and classic disease processes (pages 110-121). This gives examples and discussion of core and/or classic diseases of the lymph nodes and spleen. These are the specimens that students should focus on being able to identify initially. However, it depends to some extent on what

you have covered in lectures and practical classes or resource sessions as to what you should know. Some of the specimens and discussion are directed more towards clinical medical students.

- Main catalogue (pages 122-132). This section covers the specimens in numerical order. Questions and/or comments accompany some of the specimens to help you expand your knowledge. In order to fit more specimens in the museum, not all of the pots are in numerical order on the shelves, and large specimens are often found on the bottom shelves.

You might find it useful to work quietly with a few friends and to have a few textbooks handy (e.g. pathology, medical, anatomy). As well as learning pathology, you will also find that you can learn and revise some anatomy and clinicopathological correlation from the specimens and information given.

You do not have to examine every specimen in the museum. However, just as in clinical practice, you will not become proficient in diagnosing something if you have only seen one case. Exposure to a variety of cases (specific diagnoses can be found via the index) to experience the variability in morphology will help your learning greatly. In general the red and blue dots on the pots indicate basic and straightforward pathology, whereas yellow dots tend to indicate less readily diagnosable conditions. This is not a hard and fast rule, and you will find yellow dot specimens turning up in resource sessions/practical classes and even exams, if they represent classic pathology.

BASIC APPROACH TO SPLEEN AND LYMPH NODE PATHOLOGY SPECIMENS

This is similar to that for all specimens and includes the famous rules:

- Read the clinical history if given, it will often provide relevant information
- Always look at the front of the pot first (i.e. the one with the number and the dot) but always make sure to look at the back and sides as well
- Determine what tissues are present if possible
- Identification of and description of the abnormality.
    - Is the organ of normal size, too small or too large?
    - Is the abnormality focal, diffuse (involving the entire organ, region or tissue) or multifocal? The lesion itself should then be described.

To describe a specimen you need to be able to use the correct terminology to communicate the nature of the pathology that is present.

Spleen

Normal size or enlarged?

When faced with a spleen the first decision to make is whether the spleen is normal in size or enlarged. If enlarged, is it diffusely enlarged or does it contain focal masses of tumour?

If diffusely enlarged, can you still see the areas of white pulp? The white pulp is often effaced in leukaemic infiltration, as the leukaemic cells infiltrate and the red pulp and overrun the white pulp. Is the white pulp expanded or more prominent than normal (giving a miliary appearance)? Preferential involvement of the white pulp may occur in CLL, certain non-Hodgkin's lymphomas and certain cases of Hodgkin's lymphoma (as lymphocytes will preferentially home in to the white cell areas).

Large tumour masses in the spleen may be caused by lymphoma (Hodgkin's or non-Hodgkin's) or metastases.

Focal lesion

These are single abnormalities that anyone can point to with confidence and say "This is the abnormality". With focal lesions, remember the things to consider in the description are:

- Colour: What colour is it? Is it all one colour or is it many colours (variegated)? Does it look homogenous (all the same the whole way through)? Patchiness in colour or discoloured greyish areas in a tumour suggest necrosis.
- Size: You can give a measurement but don't get too obsessive
- Shape
- Consistency: This is of course difficult when the specimen is in a pot and you are unable to touch it, and who would want to anyway? But even just by looking you can get some idea: Does it look solid? Does it look friable (as if it's falling to pieces?) or are there holes in it or bits missing to suggest necrosis?
- Margins: Margins can be a help in determining if a lesion is benign or malignant. Malignant lesions typically have diffuse/irregular or infiltrative margins, however, sometimes rapidly growing malignant tumours or metastases may have deceptively well defined margins. Benign lesions tend to have well defined or encapsulated (surrounded by a band of fibrous tissue) margins, however, some benign lesions may have poorly defined edges. In practice there are few benign lesions of the spleen and lymph nodes.
- Infarcts are a common focal lesion of the spleen. They are pale, often subcapsular and may have irregular margins.

Multifocal

This means that there is more than one distinct lesion within the specimen. All the above comments regarding the description of focal lesions apply here as well.

Lymph nodes

The main abnormalities to look for in lymph nodes are enlargement and the appearance of the node on cross section (e.g. is there necrosis?). Sometimes adjacent nodes appear stuck together, suggesting their involvement by an invasive malignancy.

Limits to diagnosis on macroscopic examination

In all cases a diagnosis is given, but it is important to realize that sometimes the final diagnosis was only made based on the clinical history and histological examination. Distinction cannot often be made macroscopically between the Hodgkin's and non-Hodgkin's lymphomas and even often with leukaemic infiltration.

There have been many changes in the histological diagnosis and classification of lymphomas and leukaemias, and as some of the cases are very old, the diagnosis given may be out of date or incorrect, as the histology has not been reviewed.

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LYMPH NODES

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CORE AND CLASSIC DISEASE PROCESSES

LYMPH NODES: LYMPHADENOPATHY

CASE 637

Clinical information
No clinical history is available.

Describe the specimen
The specimen consists of a mass of greatly enlarged lymph nodes, some of which appear matted together. One has been cut in cross section to reveal uniform fleshy tan tissue, with no haemorrhage or necrosis.

What is the diagnosis?
Lymphadenopathy

Comment
This was reportedly Hodgkin's disease (diagnosed histologically) involving the cervical nodes. On macroscopic examination alone, all one can say is that the nodes are greatly enlarged. Such massive lymphadenopathy is probably neoplastic in nature.

There are a number of causes of lymphadenopathy:
Reactive lymphadenopathy

- 2ndary to local inflammation or infection in the area of drainage e.g. nasopharyngeal, genital, skin, tuberculosis
- systemic infections e.g. infectious mononucleosis, HIV/AIDS, 2ndary syphilis, rubella, measles
- non-infective systemic disease e.g. rheumatoid arthritis, SLE, sarcoid
- response to 'foreign' material e.g. silica, lipid
- certain drugs
- other

Neoplastic lymphadenopathy

- lymphomas
- leukaemic infiltration
- metastatic
    - carcinomas, melanomas and germ cell tumours readily metastasise to lymph nodes
    - sarcomas don't metastasise to lymph nodes so readily
    - tumour cells are filtered out in the subcapsular sinus, subsequently grow and ultimately extend outside the node. Presence of extra-nodal extension indicates worse prognosis
    - other

Lymphadenopathy may be localised or systemic depending on the process.

SPLEEN: SPLENOMEGALY - GENERAL

CASE 4192

Clinical information
No clinical history is available.

Describe the specimen
The specimen is of a greatly enlarged spleen and a small separate piece of grossly thickened and haemorrhagic ureter.

What is the diagnosis?
Splenomegaly

Comment
This is a case of so called Egyptian splenomegaly or bilharzia where splenomegaly results from portal hypertension secondary to hepatic fibrosis caused by infection with certain species of the helminth Schistosoma. The disease is common in Africa. Occasional cases developed in Australians who fought in North Africa in both world wars. The worm causing the disease needs a freshwater snail host. The larvae released from the snail swim through fresh water and penetrate human skin whence they gain access to the vasculature and migrate to various regions of the body. Once within the body they develop into adult forms and lay eggs, triggering a massive granulomatous inflammatory response with fibrosis. There are 5 major species that affect humans and various manifestations develop depending on the specific infection.

Like lymphadenopathy, splenomegaly may be caused by a wide variety of diseases.

What are the causes of splenomegaly?
Causes include:

- Infection e.g. malaria, infectious mononucleosis, tuberculosis, leishmaniasis
- Vascular: portal hypertension, congestive cardiac failure
- Autoimmune haemolytic anaemias
- Autoimmune/connective tissue disease: rheumatoid arthritis, SLE, sarcoid
- Infective endocarditis
- Amyloidosis
- Genetic storage diseases
- Neoplasia
    - Lymphoma
    - Extramedullary haemopoiesis or direct infiltration in leukaemia
    - Angiosarcoma
    - Metastases

What are the potential complications of splenomegaly?
Hypersplenism and rupture in certain cases. Infarction may also occur.

SPLEEN: INFARCTION

CASE 3934

Clinical information

A 30-year old woman was admitted complaining of shortness of breath, frequency of micturition and swelling of her legs nine weeks after a miscarriage at 6 months gestation. There was no history of significant previous illness. On examination she was febrile with a temperature of 39.4C, her BP was 200/140, there were old haemorrhages in the fundi, she had a moderately enlarged heart, signs of oedema in both lungs and an enlarged liver. She developed rigors on the day before she died.

Describe the specimen

The specimen consists of a moderately enlarged spleen. On the periphery are two pale wedge-shaped lesions.

What is the diagnosis?

Splenomegaly with infarction

Comment

The cause of this woman's illness was not established though she had a very high blood pressure and heart failure. Autopsy apparently revealed no vegetations on the cardiac valves but the lungs contained multiple infarcts and kidney sections showed focal, mainly glomerular lesions.

What are the causes of splenic infarction?

Causes include:

- Embolism
- Thrombosis e.g. in vasculitis, sickle cell disease
- Leukaemic infiltration (infarction thought to be caused by subendothelial infiltration of splenic vessels by neoplastic cells leading to thrombosis)

SPLEEN: RUPTURE

CASE 23913

Clinical information
This 64-year old woman had vague symptoms of loss of appetite and lassitude for about 6 months. When first seen she had hepatosplenomegaly with a Hb of 32g/L and a raised white cell count with occasional myeloblasts. She died after the diagnosis of acute myeloid leukaemia was made.

Describe the specimen
The specimen shows a cut section of a mildly enlarged spleen with overlying diaphragm. There is a large recent perisplenic haematoma between the two. The splenic parenchyma appears homogenous with loss of white pulp markings and there are patchy areas of pallor in keeping with recent infarction.

What is the diagnosis?
Acute leukaemic infiltration of the spleen with infarction and splenic rupture

What are the causes of splenic rupture?
The main cause is major abdominal trauma. Spontaneous splenic rupture or rupture with minimal trauma is a complication of splenomegaly due to certain causes e.g. leukaemic infiltration, infectious mononucleosis.

What are the complications of splenic rupture?
Haemorrhage, if severe → hypovolaemic shock.

SPLEEN: DIFFUSE ENLARGEMENT IN AMYLOIDOSIS

CASE 12396

Clinical information

The patient was a woman aged 54 who had peripheral oedema and breathlessness for 18 months. At her last admission there was oedema and increasing albuminuria. Serum proteins were low but high globulin suggested multiple myeloma. Bence-Jones protein was negative. Venograms of the inferior vena cava and renal veins were normal. She died suddenly 2 weeks later from massive cerebral infarction.

Describe the specimen

The specimen consists of a kidney and a slice of spleen. The spleen is mildly enlarged and its cut surface shows poor demarcation between the white and red pulp. The kidney is slightly small and pale with reduced demarcation between cortex and medulla. There are also several broad shallow cortical scars suggestive of chronic pyelonephritis.

What is the diagnosis?

Amyloidosis of the spleen and kidney

What is this condition and how does it arise?

- amyloid is a pathologic extracellular protein with a characteristic fibrillary ultrastructural appearance
- the protein differs depending on the cause/associated disease but its formation appears to be related to immunological mechanisms
- it deposits in basement membranes, vessel walls and connective tissue and is seen as amorphous eosinophilic material on light microscopy. It characteristically demonstrates 'apple green birefringence' on a Congo red stain
- organs/sites of deposition depend on the underlying disease association. It may involve multiple organs or a single organ. The function of the organ will deteriorate with progressive amyloid deposition.
- affected organs are usually mildly enlarged and firm
- the prognosis in patients with systemic amyloidosis is poor
- there are multiple biochemically distinct forms
    - AL/primary amyloid
        - associated with 'plasma cell dyscrasias', especially multiple myeloma
        - composed of immunoglobulin light chains, usually lambda type
        - usually deposits in multiple organs
    - AA/secondary amyloid
        - occurs in occasional cases of various systemic chronic inflammatory conditions and tumours e.g. inflammatory bowel disease, tuberculosis, rheumatoid arthritis, Hodgkin's lymphoma, renal cell carcinoma
        - synthesized from serum amyloid associated protein (SAA), a normal protein produced by the liver
        - usually deposits in multiple organs
    - CNS amyloid
        - A- eta protein derived from amyloid precursor protein (APP), a normal protein found in neurones
        - seen in senile plaques and vessel walls in Alzheimer's disease and in vessel walls in congophilic angiopathy

- Various other types

What type of amyloid is this patient likely to have and why?
This patient may well have had AL/primary amyloid that developed secondary to excessive light chain production and deposition in multiple myeloma.

What is Bence Jones protein?
Bence Jones protein is the name given to the monoclonal light chains present in the urine (having been filtered through the glomerulus), present in up to 75% of cases of multiple myeloma.

Why did this patient develop proteinuria and oedema?
As well as causing chronic renal failure (which this patient is not reported to have), renal amyloidosis can cause the nephrotic syndrome (which this patient appears to have). Deposition of amyloid in the glomeruli can result in massive proteinuria with resultant hypoalbuminaemia and subsequent oedema.

Why was a venogram of the inferior vena cava and renal veins performed?
Renal vein thrombosis can occur in association with the nephrotic syndrome.

SPLEEN: DIFFUSE ENLARGEMENT WITH EFFACEMENT OF THE WHITE PULP IN LEUKAEMIA

CASE 24949

Clinical Information
This man was 68 years of age. A diagnosis of acute myelomonocytic leukaemia was made 11 months before his death. He was treated with cytotoxic drugs and transfusions. On his final admission he was markedly anaemic with clotting defects and haemorrhages in both optic fundi.

Describe the specimen
The specimen consists of a massively enlarged spleen containing a number of peripheral, wedge-shaped infarcts with pale or grey centres and haemorrhagic rims. Elsewhere, the splenic parenchyma appears homogenous with loss of white pulp markings.

What is the diagnosis?
Splenomegaly and infarction in acute leukaemia

Why may the spleen, liver and lymph nodes enlarge in leukaemias?
Leukaemic cells circulating in the blood are filtered out to some extent in the reticuloendothelial organs including spleen, liver and lymphoid tissue, causing their enlargement. In some leukaemias, extramedullary haematopoiesis may also occur in these organs (particularly spleen).

Comment
Note that the tiny nodules of white pulp are not visible. This is typical with leukaemic infiltration. The leukaemic cells preferentially invade and expand the red pulp, with obliteration of the white pulp and the cut surface develops a homogenous brick red appearance. While chronic lymphocytic leukaemia may also give this picture, the cells of this disorder sometimes preferentially involve the white pulp (being lymphoid), thus causing expansion and prominence of the white pulp macroscopically (e.g. specimen 12323).

Splenic involvement is common in leukaemias, the cells being filtered out in the red pulp. The degree of involvement however is variable depending on the type. Splenomegaly may cause hypersplenism. In chronic myeloid leukaemia, extramedullary haemopoiesis may contribute to the splenomegaly and the spleen can be massive.

Infarcts also not uncommonly arise in spleens infiltrated with leukaemic cells, thought to be due to subendothelial infiltration of splenic vessels by cells leading to thrombosis.

SPLEEN: DIFFUSE ENLARGEMENT WITH EXPANSION OF THE WHITE PULP

CASE 50398/82

Clinical information
The patient was a man aged 55.

Describe the specimen
The specimen consists of the spleen which is enlarged and the white pulp is unusually prominent.

What is the diagnosis?
Splenomegaly with prominence of the white pulp.

This appearance may be caused by a variety of lymphoproliferative diseases: non-Hodgkin's lymphoma (some types), Hodgkin's lymphoma (some types) and chronic lymphocytic leukaemia. Histologically this case was said to be a type of non-Hodgkin's lymphoma.

What macroscopic patterns of disease can lymphoma cause in the spleen?
Lymphomas, depending on the type, may cause diffuse enlargement, expansion and prominence of the white pulp (miliary pattern) or large tumour masses. The white pulp is preferentially involved as the cells are lymphoid in nature.

Of course miliary TB may also affect the spleen which could look similar macroscopically and disseminated tiny abscesses can also cause such a miliary pattern (although there may not be so many of them).

How is non-Hodgkin's lymphoma classified histologically?
There have been numerous histologic classification systems over the years. Currently the recently developed WHO classification is favoured (you don't have to learn it). This divides up the different types based on cytologic, architectural and immunocytochemical features. Not all T and B lymphocytes are the same, they have different characteristics depending on their level of differentiation and activation. The phenotype of the neoplastic cells in the different non-Hodgkin's lymphomas closely recapitulates that of lymphocytes at these differing stages of differentiation and activation.

How is non-Hodgkin's lymphoma classified clinically?
The different histologic types are classified into low, intermediate or high grade (International Working Formulation) depending on their likely clinical behaviour and response to treatment. Low grade lymphomas tend to progress slowly but are difficult to cure. Paradoxically patients with aggressive tumours often do well, since the tumour cells proliferate rapidly and respond well to chemotherapeutic drugs.

In what tissues may non-Hodgkin's lymphoma arise?
Whilst probably most non-Hodgkin's lymphomas arise in lymph nodes, they can arise anywhere, including brain, breast, bone marrow, intestine and lung.

What are some of the different types of non-Hodgkin's lymphoma? (The following is mainly for interest, although clinical medical students should a have basic knowledge of a few of the commoner types).

Small lymphocytic lymphoma

This type typically arises in middle aged and elderly persons and is disseminated at presentation but progresses slowly. The cells resemble mature B lymphocytes. Some cases have a leukaemic element and

there is a close relationship between these tumours and chronic lymphocytic leukaemia. After some years, this disease typically transforms into a more aggressive lymphoid neoplasm.

Follicular lymphomas

Follicular lymphomas are B cell neoplasms that recapitulate the architectural and cytologic features of the normal secondary lymphoid follicle or germinal centre, generally being predominantly composed of cells with small-cleaved nuclei. They are usually seen in middle aged and elderly people. Disease is typically generalised at presentation but patients can live many years with their disease. These tumours ultimately may transform into a more aggressive type, usually diffuse large cell lymphoma. In the majority of the follicular lymphomas there is a characteristic chromosomal translocation t(14:18) which results in movement of the bcl-2 gene from chromosome 18 to the immunoglobulin heavy chain gene region on chromosome 14. This results in over-expression of the bcl-2 protein (which has anti-apoptosis functions) with implications for the control of programmed cell death.

Diffuse large cell lymphoma

Diffuse large cell lymphoma has a diffuse architecture and the cells are large with large nuclei and prominent nucleoli. Most are of B cell type and the cells recapitulate a stage in the normal transformation of B cells into plasma cells. They present in adults, usually with localised lymphadenopathy, and although the prognosis is poor if untreated, good responses can be achieved with chemotherapy. They may arise de novo, from transformation of a low grade lymphoma (e.g. follicular) or sometimes in patients with T cell immunodeficiencies.

Mucosa Associated Lymphoid Tissue (MALT) lymphomas

These lymphomas are of B cell type and arise in epithelial tissues where lymphoid tissue may or may not normally be present. They usually arise in organs as a result of chronic inflammation, such as with Helicobacter-related gastritis in the stomach, or autoimmune disease, such as with Hashimoto's thyroiditis. Other sites of origin include the parotid gland and lungs. The cells are usually initially small, but transformation into a more aggressive large cell type may occur.

Burkitt's lymphoma

Burkitt's lymphoma is an aggressive B cell lymphoma. This disease is endemic in Africa, where it tends to occur in children or young adults and lesions in the jaw are common. Endemic African disease is strongly associated with Epstein-Barr virus and one of several characteristic chromosomal translocations may be present, resulting in excessive expression of the c-myc oncogene. In Western countries where this disease is sporadic or non-endemic, patients tend to present with intra-abdominal disease. These cases are less strongly associated with the Epstein-Barr virus. Burkitt like lymphomas also occur in patients with AIDS. The cells are fairly small and the architecture is diffuse. Apoptosis is frequent and the presence of scattered large macrophages with ingested cellular debris gives the classic 'starry sky' light microscopic pattern.

Anaplastic large cell lymphoma

Anaplastic large cell lymphoma is generally of T cell type and may occur in children or adults. The cells are large and very pleomorphic. A more indolent cutaneous form is also recognised.

SPLEEN: ENLARGEMENT BY TUMOUR MASSES

CASE 16064

Clinical information
The patient was a man aged 64.

Describe the specimen
The specimen consists of portions of the vertebral column, a mass of para-aortic lymph nodes, a slice of liver and a slice of spleen. The spleen is mildly enlarged and shows large pale tumour masses of varying sizes. The liver shows two tumour nodules. The lymph nodes are uniformly large and pale. Scattered pale infiltrates are also present in the body of the vertebrae.

What is the favoured diagnosis?
Lymphoma

Comment
This patient had previously been diagnosed with Hodgkin's disease. The macroscopic differential of the splenic masses includes non-Hodgkin's lymphoma, Hodgkin's lymphoma and metastatic malignancy. Leukaemias demonstrate more diffuse infiltration and don't form large tumour nodules. Metastases in the spleen are often better circumscribed than the tumour here (e.g. specimen 20008) and as just the reticuloendothelial tissues (liver, spleen, bone marrow and lymphoid tissue) are involved, lymphoma is favoured from the macroscopic appearances.

What macroscopic patterns of disease can lymphoma cause in the spleen?
Lymphomas, depending on the type, may cause diffuse enlargement, expansion and prominence of the white pulp (miliary pattern) or large tumour masses. The white pulp is preferentially involved as the cells are lymphoid in nature.

What is the neoplastic cell in Hodgkin's lymphoma? How prevalent are these in the tumours?
The neoplastic cell is the Reed-Sternberg cell (or Hodgkin and Reed-Sternberg cell). For a long time its exact nature was unknown (hence the term Hodgkin's disease) but recently it has been found that in the vast majority of cases they are derived from germinal centre B cells (hence the recent change in name to Hodgkin's lymphoma). There are various cytological variants. They are generally not the predominant cell type in the tumours, most of the cells being a mixture of non-neoplastic lymphocytes, eosinophils, macrophages and plasma cells.

What are the different histological types of Hodgkin's lymphoma?
- Nodular lymphocyte-predominant Hodgkin's lymphoma
- Classic Hodgkin's lymphoma
    - Lymphocyte rich
    - Nodular sclerosis (commonest)
    - Mixed cellularity
    - Lymphocyte depleted (rare)

Comment
Some types of Hodgkin's lymphoma have a strong EBV association.
The prognosis is primarily influenced by the stage (Ann Arbor system) and bulk of the disease and the presence or absence of B symptoms. The histological subtype is relatively less important, except for the lymphocyte depleted type that has a bad prognosis. However, the lymphocyte rich and nodular sclerosing

types generally present at an early stage so tend to have an extremely good prognosis and cure is obtained in many cases.