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REVIEW

Splenomegaly: Investigation, diagnosis and management

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SUMMARY

Splenomegaly is a feature of a broad range of diseases, and presents to clinicians in many fields. This review examines the aetiology of splenomegaly in the developed world, and describes a logical approach to the patient with splenomegaly. In some patients, extensive radiological and laboratory investigations will fail to yield a diagnosis: these cases of "isolated" splenomegaly are not uncommon and can be particularly challenging to manage. The risks of serious underlying disease must be balanced against the risks of invasive investigations such as splenic biopsy and diagnostic splenectomy. We discuss the options in isolated splenomegaly and their evidence base, and incorporate them into a management strategy to aid the clinician in cases of diagnostic difficulty.

Introduction

The patient with splenomegaly can present as a diagnostic challenge to a wide variety of clinicians. The list of conditions associated with splenomegaly is extensive, and as noted by William Osler in 1908, "nearly all diseases of the spleen are of a secondary nature".[1] A patient presenting with splenomegaly may therefore have a collection of symptoms, signs and test results that are common to various diseases: some benign and self-limiting, some infective and others malignant. The clinician must adopt a systematic approach to identify serious disease, whilst minimising unnecessary investigations and anxiety for the patient. A century after Osler, this review examines the tools that are available in this diagnostic pathway, and suggests a safe management strategy for those challenging patients with isolated splenomegaly.

Defining splenomegaly

The "gold-standard" definition of splenomegaly is splenic weight: the normal adult spleen weighs about 50–250 g, and this decreases with age.[2] This can clearly only be established at splenectomy or post mortem examination, and it is surprisingly difficult to establish a practical clinical definition of splenomegaly.

The clinical finding of a palpable spleen was previously considered to be evidence of splenic enlargement,[3] but up to 16% of palpable spleens have been found to be of normal size on radiological assessment.[4] While clinical examination can be convincing in massive splenic enlargement, radiology is often needed to confirm the diagnosis. A single radiological definition of normal splenic size has not been adopted, and the assessment is often partly subjective.[5–7]

On ultrasound examination, "craniocaudal length" is used most often to measure splenic size; this correlates well with splenic volume, particularly when the right lateral decubitus position is adopted.[5] However, the quoted upper limit of normal varies from 11 to 14 cm.[6,8] Other ultrasonographic indicators of splenomegaly include an anteroposterior measure greater than two thirds of the distance between the anterior and posterior abdominal wall,[6] or complex formulae can be used to estimate splenic volume.[7] With CT examination, splenic length, the "splenic index" (product of length, depth and width) and the sum of volumes of consecutive scan slices have all been used.[6] Radiological confirmation of splenomegaly may therefore depend both on the radiologist's preferred method and a degree of subjective judgement. A maximum length of 13 cm is a typical limit.

Aetiology and epidemiology of splenomegaly

The conditions associated with splenomegaly are shown in Table 1. There is limited recent information from developed countries on its epidemiology. Looking at unselected healthy populations, the prevalence of a palpable spleen in college freshmen was found to be 2.9% in 1966; none of these subjects developed malignant disease at follow-up of 10 years.[9] Prospective studies in unselected medical outpatients found palpable spleens in 2–5.6% of patients, with an unknown aetiology after basic investigations in 25–41% of cases.[3] In many of these patients splenomegaly was not confirmed radiologically. More recent small studies describe

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Table 1
Diseases associated with splenomegaly.

Category	Groups	Examples
Infection	Acute	Infectious mononucleosis, viral hepatitis, septicaemia, typhoid, cytomeglalovirus, toxoplasmosis
	Subacute/chronic	Tuberculosis, subacute bacterial endocarditis, brucellosis, syphilis, HIV
	Tropical/parasitic	Malaria, leishmaniasis, schistosomiasis
Haematological	Myeloproliferative	Myelofibrosis, chronic myeloid leukaemia (CML), polycythaemia vera, essential thrombocytosis
	Lymphoma	Non-Hodgkin lymphoma (NHL), Hodgkin lymphoma
	Leukaemia	Acute leukaemia, chronic lymphocytic leukaemia (CLL), hairy cell leukaemia, prolymphocytic leukaemia
	Congenital	Hereditary spherocytosis, thalassaemia, HbSC disease
	Others	Autoimmune haemolysis, megaloblastic anaemia
Congestive		Cirrhosis, splenic/portal/hepatic vein thrombosis or obstruction, congestive cardiac failure
Inflammatory	Collagen diseases	Systemic lupus erythematosus, rheumatoid arthritis (Felty's)
	Granulomatous	Sarcoidosis
Neoplastic		Haemangioma, metastases (lung/breast carcinoma, melanoma)
Infiltrative		Gaucher's disease, amyloidosis
Miscellaneous		Cysts

asymptomatic young men in whom significant, persistent splenomegaly was detected on clinical and radiological examination, with normal investigations including bone marrow, liver and rectal biopsies.[10] Since many of these patients remained well for over 10 years, there does seem to be a group of individuals with benign splenomegaly, but the prevalence is not clear.

The frequency and causes of splenomegaly have now been studied retrospectively in US hospital inpatients.[11–13] The estimated incidence from 1963 to 1995 was 0.3% of admissions and a diagnosis was reached in 98%, but 12% required a diagnostic splenectomy.[11] Of all patients with splenomegaly, haematological disease was found in 16–66%, hepatic disease in 9–41%, infectious disease in 9–36%, congestive or inflammatory disease in 4–10% and primary splenic disease (e.g. storage disease) in 1–6%.[11–13] Within the haematological disorders, the most common diagnoses were lymphoma (16–44% of all splenomegaly), CML (8–29%), haemoglobinopathy (7–25%), CLL (0–20%) and myelofibrosis (9–16%).

The causes of splenomegaly vary between hospitals in the same country,[12] but differences between developing and developed countries are even more striking. 11–45% of massive splenomegaly in Africa is due to Tropical Splenomegaly Syndrome of malarial origin, and up to 30% is due to schistosomiasis.[14]

Assessment of the patient with splenomegaly

Clinical assessment begins with a thorough history and examination. The history may elicit symptoms of pressure effects from the enlarged spleen, such as left hypochondrial discomfort or early satiety. There may be symptoms of cytopenias due to hypersplenism: a syndrome comprising splenomegaly; anaemia, leucopenia and/or thrombocytopenia; compensatory bone marrow hyperplasia; and improvement after splenectomy (if performed). General systemic symptoms such as fever, sweats, weight loss or lymphadenopathy suggest haematological, malignant, infectious or inflammatory disease. A thorough systemic enquiry is essential to recognise multi-system disorders such as the collagen diseases and sarcoidosis. The past medical history may suggest the cause of splenomegaly, though further investigations will be indicated if the presentation is unusual (e.g. massive splenomegaly in a patient with mild congestive cardiac failure). A family history should be carefully elicited, such as of malignancy or anaemia, while remembering that individuals with autosomal recessive conditions like Gaucher's disease often have no affected family members. Risk factors should be identified for liver disease, particularly alcohol intake, and for infectious diseases (travel, sexual contacts, intravenous drug use, exposure to animals and predisposition to infective endocarditis).

Physical examination will typically confirm palpable splenomegaly, depending on the degree of enlargement and body habitus. General examination may reveal fever, lymphadenopathy, anaemia, signs of hepatic or inflammatory disease, stigmata of endocarditis, or involvement of any other organ system. The difficulty with splenomegaly is that many signs and symptoms that may be elicited are common to various conditions. Most patients require at least preliminary laboratory and radiological investigations, as shown in Table 2. This list is not exhaustive, and additional investigations may be indicated by specific clinical findings.

Even if initial assessment does not identify the cause of splenomegaly, certain parameters may narrow the differential diagnosis. In studies of inpatients with splenomegaly, haematological diseases were positively associated with lymphadenopathy, massive splenomegaly and "cytoses" (erythrocytosis, leucocytosis, thrombocytosis, marked left shift of the neutrophilic leucocytes or marked reticulocytosis).[12] 84% of cases with progressive splenic enlargement were associated with haematological disease, predominantly malignancy.[11] Infectious diseases showed positive associations with fever, and hepatic diseases with abnormal liver

Table 2
Initial investigations in the patient with splenomegaly.

In most patients	In selected patients (depending on clinical features)
Haematology	
Full blood count	Direct antiglobulin test
Peripheral blood film	Reticulocyte count
ESR	Malaria blood film
Clotting screen	Haemoglobin electrophoresis/HPLC
Biochemistry	
Urea and electrolytes	Serum ACE
Liver function tests	Serum protein electrophoresis
C-reactive protein	Urine Bence Jones protein
Bone biochemistry	
Serum LDH	
Vitamin B12, red cell folate	
Microbiology	
Monospot test	Peripheral blood cultures
Serology: hepatitis B/C	Sputum microscopy, culture and AAFB
	Mantoux test
	Serology: HIV, CMV, toxoplasmosis, brucella
Immunology	
Auto-antibodies incl. ANA	
Rheumatoid factor	
Radiology	
Ultrasound/CT abdomen	Ultrasound abdomen with duplex-Doppler studies
Plain chest radiograph	CT chest, abdomen and pelvis
	Transthoracic/transoesophageal echocardiogram
Bedside	
Urine dipstick (protein, blood)	

ESR: erythrocyte sedimentation rate; HPLC: high-performance liquid chromatography; LDH: lactate dehydrogenase; ACE: angiotensin-converting enzyme; AAFB: acid and alcohol-fast bacilli; and ANA: anti-nuclear antibodies.

function tests, hepatomegaly, and thrombocytopenia or leucopenia.[12] All patients with the combination of splenomegaly and lymphadenopathy had serious associated diseases, most often haematological malignancy. While none of the associations are so specific that other diagnoses can be excluded, these features may nonetheless contribute to the clinician's overall diagnostic impression.

Radiology of the spleen

Radiology has four major roles in the investigation of splenomegaly: confirmation of splenic size; evaluation of splenic architecture; assessment of other organs affecting the differential diagnosis; and in certain patients, radiologically-guided biopsy.

Even in palpable splenomegaly, radiological assessment is usually necessary to quantitate the abnormality, as discussed above. The main modalities used are ultrasound and CT (Fig. 1). Imaging also delineates the architecture of the enlarged spleen, and distinguishes between focal lesions, either single or multiple, and diffuse splenomegaly. Focal lesions may be neoplastic (lymphoma, metastasis, other tumours); infective (bacterial abscess, tuberculosis, histoplasmosis, fungal); vascular (haematoma, angioma); granulomatous (sarcoidosis) or cysts. In some conditions, clinical features and initial imaging will establish the diagnosis (e.g. a history of trauma and haematoma), but imaging findings specific to a single disease are uncommon. In the context of focal lesions for example, differentiation of malignant tumours from benign lesions can be impossible.[6,15] Most commonly the spleen is diffusely enlarged, and specific findings must be sought elsewhere.

Important information is also gained from the characteristics of other tissues, and this will frequently dictate the imaging modality used. In liver disease, ultrasound will not only demonstrate hepatic echogenicity, but the use of duplex-Doppler parameters can identify congestive splenomegaly.[16] In malignant disease, CT is usually essential to identify enlarged lymph nodes, primary tumours or other metastases. Sarcoidosis, tuberculosis and other inflammatory disorders may also be suggested by patterns of multi-system involvement. Magnetic resonance imaging is used infrequently, but can be valuable for certain focal and diffuse abnormalities.[17] For example, about 10% of patients with portal hypertension have splenic Gamna Gandy bodies on T2-weighted MRI.

In summary, the first-line choice of imaging modality varies between patients. Ultrasound is portable and does not involve ionising radiation. It will confirm the presence of splenomegaly, distinguish focal lesions from diffuse enlargement, and can support a diagnosis of congestive splenomegaly. CT is more reproducible, and evaluates other organs where a systemic disorder is suspected.

Second-line investigations

In some patients, clinical assessment and/or first-line investigations will either reveal the diagnosis or direct subsequent diagnostic tests. For example, a peripheral blood film suggestive of myeloproliferative disease prompts a bone marrow biopsy and testing for the JAK2 V617F mutation. Immunophenotyping of abnormal peripheral blood cells confirms the diagnosis of some acute and chronic leukaemias. Identification of lymphadenopathy can be followed by biopsy, particularly where clinical features favour malignancy over self-limiting infection.

In those in whom findings from the initial assessment are non-specific, the clinician must decide how intensively to investigate further. In most patients (except those who are young and asymptomatic with mild splenomegaly and no other findings), a bone marrow aspiration and trephine is a reasonable second-line investigation. This can reveal myeloproliferative or lymphoproliferative disorders, infectious or inflammatory disease such as tuberculosis, leishmaniasis and sarcoidosis. Liver biopsy can be considered if hepatic lesions are identified, if liver function tests are very abnormal, or if granulomatous disease is suspected.[18]

The patient with splenomegaly sometimes remains undiagnosed despite undergoing the above. We will refer to such patients as having "isolated splenomegaly", although other investigations may not be entirely normal (for example, there may be cytopenias or abnormal liver function tests). The management of these patients is considered in the remainder of this review.

The aetiology of isolated splenomegaly

Retrospective reviews of patients who have undergone diagnostic splenectomy are most informative in the aetiology of isolated splenomegaly. As these patients were felt to warrant diagnostic splenectomy, they are quite a different group from the asymptomatic young men with splenomegaly detected at routine examinations previously described.[9,10] Table 3 shows the variable proportion of patients found to have haematological malignancy at diagnostic splenectomy: 0–80%.[19–25] These patients had undergone extensive conventional investigations, including bone marrow biopsy and sometimes liver biopsy. Other common

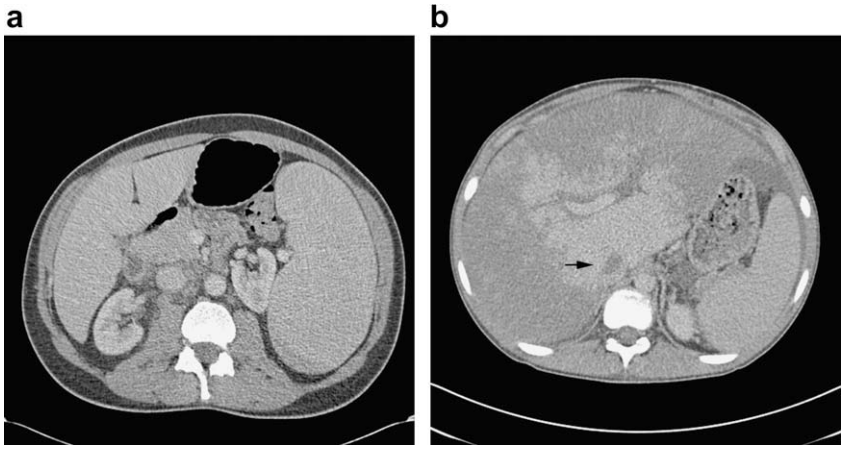

Fig. 1. The use of CT in splenomegaly. (a) Contrast-enhanced axial CT image in a patient with hairy cell leukaemia. There is massive splenomegaly with antero-medial displacement of the left kidney. (b) Contrast-enhanced axial CT image in the venous phase. There is poor enhancement of the peripheral liver and a filling defect in the IVC (arrow). Contrast enhancement of the caudate lobe is preserved due to separate, direct drainage into the IVC. This is Budd–Chiari syndrome, one of the few causes of splenomegaly that has diagnostic imaging appearances.

Table 3
Findings at diagnostic splenectomy for splenomegaly.

Study	*n*	% Haematological malignancy	% Non-diagnostic	
Hermann et al.[19]	52	31	0	
Goonewardene et al.[20]	13	0	54	1 "Non-diagnostic" developed lymphosarcoma at 21 months
Knudson et al.[21]	28	0	75	1 "Non-diagnostic" found to have lymphoma at 2 years
Cronin et al.[22]	10	80	10	
Kraus et al.[23]	122	59 for "splenomegaly" 33 for "splenic mass"	5	
Carr et al.[24]	18	39	0	
Pottakat et al.[25]	41	37	0	Study from India. Tuberculosis in 12%

diagnoses included "congestive" splenomegaly, sarcoidosis and splenic cysts.

Most early studies described patients in whom no diagnosis was made at splenectomy. Dacie et al. followed up 10 such patients with neutropenia, thrombocytopenia, anaemia and gross splenic enlargement, in whom splenic histology showed no evidence of overt lymphoma. Nine years later, four had developed malignant lymphomas, while the others showed no related disease.[26] In contrast, other studies of similar patients found that very few developed lymphoma, with up to 60% remaining healthy after splenectomy and prolonged follow-up.[21] This particularly applied to young patients (mean age 28 years), who had mild cytopenias but were asymptomatic, and often had a recent history of infection.

There are a few recent reports of the findings in unselected patients undergoing diagnostic splenectomy.[23–25] These show more clearly the types of haematological malignancy found. In a study of 122 patients, the commonest diagnoses were marginal zone lymphoma (17% of diagnostic splenectomies for splenomegaly); large B-cell lymphoma (10% of splenectomies for splenomegaly; 29% of splenectomies for splenic mass); and follicular lymphoma (2% of splenomegaly).[23] Compared to earlier series, those from the last decade have much lower rates of splenectomy failing to yield a diagnosis: 0–5%.[23–25] The difference could be interpreted as suggesting that most of the earlier "non-diagnostic" splenectomies would have a diagnosis made by modern histological and/or molecular techniques. Some could have had a lymphoma that was not detected histologically, with a long remission induced by splenectomy as a therapeutic procedure.[24] However, indications for splenectomy have changed over time, and many of the "non-diagnostic" procedures performed previously may now not be performed at all (if patients are young and asymptomatic, for example).[21,24]

In summary, while there is a significant rate of identifying lymphoma at diagnostic splenectomy, many patients presenting with isolated splenomegaly and non-diagnostic preliminary investigations will not have malignancy. Other factors must guide subsequent management, for which there are three principal options: watchful waiting, splenic biopsy and diagnostic splenectomy.

"Watch and wait" strategy

There is unfortunately little evidence indicating what factors suggest benign self-limiting disease, or "idiopathic" splenomegaly. In early studies of diagnostic splenectomy, no clinical or laboratory findings predicted which patients would have lymphoma rather than idiopathic splenomegaly.[27] Generally, young asymptomatic patients with a recent history of infection had no serious disease at splenectomy or follow-up, even in the presence of mild cytopenias.[21] In more recent studies reporting higher rates of lymphoma, all patients were symptomatic prior to splenectomy.[24] It is also important to note that while some patients with isolated splenomegaly will have a low-grade lymphoproliferative disorder, in many cases no treatment would be indicated unless the patient is symptomatic.

Patients in whom it may be reasonable to adopt a watch and wait strategy include those who are young, with mild splenomegaly. They should be well with no constitutional symptoms such as fever, weight loss or night sweats, unless these are of short duration and there is a strong suspicion of acute viral illness. There should be no symptoms suggesting disease in other systems such as the chest or gut. Lymphadenopathy should be minimal, unless biopsy has shown convincing reactive histology. The blood count could be normal, show very mild cytopenias, mild neutrophilia or thrombocytosis with a reactive blood film picture, or a polyclonal lymphocytosis. In these selected patients it may be appropriate to monitor the patient and the spleen size over the course of weeks to months.

If there is progressive splenic enlargement, new symptoms or clinical signs, or progressive blood count abnormalities, then the patient should be reassessed. Preliminary investigations should be repeated, and if the diagnosis remains unclear the abnormal spleen may need direct assessment. The options here are splenic biopsy and diagnostic splenectomy.

Splenic biopsy

Two techniques have been described for biopsy of the spleen: fine-needle aspiration (FNA) and core biopsy. Splenic FNA was first reported in 1916 in the diagnosis of leishmaniasis, and has now been used in the staging of malignancy,[28,29] in the evaluation of focal splenic lesions and diffuse splenomegaly.[15,30–34] It can diagnose infectious diseases such as tuberculosis, malaria, and fungal infections, and non-infectious diseases including sarcoidosis, amyloidosis and storage disorders.[30,31] Overall the procedure seems safe, many studies reporting no complications.[15,28,32,33] Others have described transient pain in up to 10%, bleeding (1–3% in large studies), and occasional pneumothorax and need for splenectomy.[29,34]

Sensitivity and specificity rates of splenic FNA are not frequently reported because limited numbers of patients undergo a further biopsy, diagnostic splenectomy or post mortem examination to establish whether the correct diagnosis was made on FNA. A study in which 21 cases had subsequent histological confirmation found a sensitivity of 68.8% and specificity of 100%; another series of 78 patients reported rates of 86.4% and 97.5%, respectively.[32,34] However, there is considerable heterogeneity between studies in the types of lesion biopsied, and in whether the patients studied had a pre-existing malignant diagnosis; other studies do not specify this information. These factors have a significant impact on the clinical utility of splenic FNA, which therefore varies widely: for example, rates of biopsies being inadequate for diagnosis vary from 1.3% to 34% in published series.[28,30] Overall, splenic FNA seems most useful in patients with focal splenic lesions, where malignancy can often be distinguished from benign disease,[28] but much less helpful in the investigation of undiagnosed diffuse splenomegaly.[33]

The problem of false-negative results is greatest in the diagnosis of NHL and Hodgkin lymphoma; indeed, the question of whether lymphoma can be reliably diagnosed on FNA has been debated before, typically in relation to lymph nodes.[35,36] Sampling error or the co-existence of benign and malignant cells can cause confusion between reactive and neoplastic lesions. If sufficient material is obtained, immunophenotyping by flow cytometry and immunocytochemistry can be employed; these techniques have

improved the discrimination between different histological subtypes of lymphoma with splenic FNA.[37] However, FNA is still unreliable in the diagnosis of Hodgkin lymphoma and T-cell lymphomas, in grading follicular NHL, and in differentiating transformation of follicular lymphoma from diffuse large B-cell lymphoma.[29,35,36]

These limitations are illustrated by a recent study of 156 splenic biopsies (83.9% FNA alone; others had an additional core biopsy).[29] Seventeen patients had false-negative findings, of which 13 had lymphoma. The accuracy of FNA for diagnosing NHL was 84%, but only 69% of lymphomas could be subclassified despite flow cytometry, surface marker studies and immunostaining. The sensitivity for diagnosing Hodgkin lymphoma was 50%.

Overall, while FNA can suggest and sometimes confirm a diagnosis, a negative result clearly does not exclude pathology. Any non-diagnostic, suspicious or negative biopsy should be followed by another diagnostic procedure, particularly if there is a clinical suspicion of lymphoma.

Splenic core biopsy has been used more recently.[38–43] The technique was described in 1985 in 32 patients who required staging of lymphoma, investigation of systemic symptoms or splenomegaly.[38] Bleeding was a complication in four patients (12.5%), requiring splenectomy in one, with slight or moderate pain in 50%. Smaller needles have been used since, and while bleeding is reported in up to 10% in some recent series,[39] many others report no complications.[40–42] An Italian multi-centre review of 398 splenic biopsies found no difference in complication rates between core and FNA biopsies.[43] Core biopsy has been used to diagnose a wide range of infectious, benign and malignant conditions (Fig. 2). Specimens are adequate for diagnosis in up to 90%, often permitting subtyping of lymphomas, but false-negative results do still occur.[39–41] The Italian study found similar diagnostic accuracy for splenic core biopsy and FNA overall (88.3% and 84.9%, respectively), but better accuracy for the diagnosis of lymphoma with core biopsy than FNA (90.9% and 68.5%).[43]

When considering the place of core biopsy in the investigation of isolated splenomegaly, the studies share many limitations with those of FNA: patient numbers are small, many look at focal splenic lesions rather than splenomegaly, and many patients already have a malignant diagnosis. Overall, both techniques represent a safe option for patients with isolated splenomegaly who require a diagnosis, potentially avoiding diagnostic splenectomy. Experience with core biopsy is more limited, but it has advantages if lymphoma is suspected.

Diagnostic splenectomy

The yield of diagnostic splenectomy has been discussed above. The use of this procedure has declined as other modalities of diagnosis have improved, and there are consequently very few recent data on complication rates specific to diagnostic surgery. One recent study from India reported a 41% incidence of postoperative complications and 2.4% mortality.[25] Elective splenectomy is now most often performed therapeutically for non-malignant disease, but splenectomy in the context of splenomegaly has traditionally been considered a riskier procedure. Early studies of splenectomy for massive splenomegaly demonstrated complication rates of up to 56% and mortality rates up to 14.7%.[44] A retrospective review of 135 splenectomies for haematological malignancy in 1996 found a complication rate of 63% for patients with spleens weighing more than 2000 g, and 29% for those less than 2000 g.[45]

Recent studies report more positive outcomes. Laparoscopic splenectomy was previously contraindicated in splenomegaly, but its use is now widespread and associated with lower morbidity, transfusion rate and shorter hospital stay than open splenectomy.[46] When compared to laparoscopic splenectomy for normal-sized spleens, some studies have found no difference in transfusion rate, length of stay, severe morbidity or rate of conversion to open splenectomy for enlarged spleens, although accessory incisions are needed more frequently.[47] "Massive" splenomegaly has been associated with increased morbidity: a study in 2003 found that splenic weights over 1000 g were associated with significantly longer postoperative stays, higher conversion rates, and a 14-fold greater risk of postoperative complications.[48] Nonetheless, others describe increasing success with laparoscopic splenectomy in this situation, with the conversion rate falling from 33% prior to 1999 to 0% in 2004 and 2005, and no reoperations or mortality.[49] This also reflects introduction of the hand-assisted laparoscopic splenectomy (HALS) technique, which facilitates mobilisation and removal of the spleen without morcellation (particularly important in diagnostic splenectomy).[50,51]

In recent studies specific to splenectomy with splenomegaly, complication rates of 6–22% and minimal perioperative mortality have been reported.[50,51] There are few data concerning long-term follow-up, and since splenectomy carries a risk of infection, this is important when considering diagnostic splenectomy in a previously healthy individual. In 1996 a review of 6942 patients, with a median follow-up of 6.9 years after splenectomy for any indication, found a 3.2% incidence of infection and 1.4% mortality rate.[52] These rates have fallen over time because of vaccination and prophylactic antibiotic regimens, and a more recent study of splenectomy for immune thrombocytopenic purpura identified no life-threatening infections after 434 patient-years of follow-up.[53]

It is worth considering whether splenectomy could bring benefits other than reaching a diagnosis. Splenectomy reverses the cytopenias associated with hypersplenism, regardless of underlying cause.[24,25] In haematological disease, splenectomy has also been used for palliation in symptomatic massive splenomegaly, and to induce remission in primary splenic lymphoma.[54] However, improved diagnostic and chemotherapeutic strategies have re-

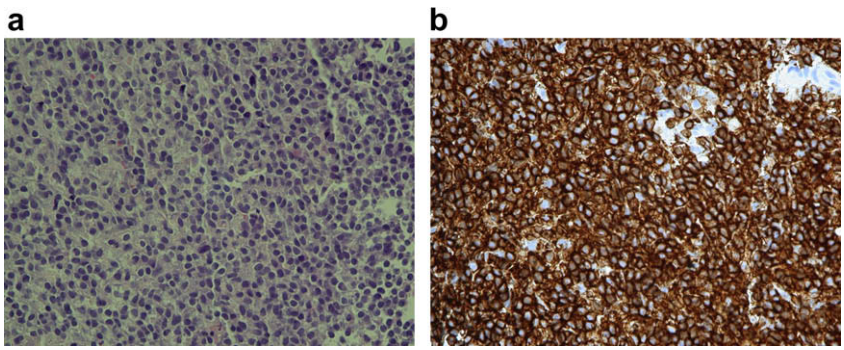

Fig. 2. Splenic core biopsy from a 69-year old patient with unexplained massive splenomegaly. (a) H&E stain showing a monomorphous population of lymphoid cells. (b) Immunostaining for CD20 (strongly positive). The diagnosis here was splenic marginal zone lymphoma. Images courtesy of Dr. T. Barker.

duced its use in lymphoma staging and treatment of diseases such as hairy cell leukaemia. The number of patients in whom the benefits of a diagnostic splenectomy truly outweigh the risks is relatively small. The procedure should only be considered in those in whom splenic biopsy is contraindicated or non-diagnostic and in whom a diagnosis is essential, especially in the presence of severe symptoms or cytopenias.

Conclusions

It is difficult to establish an evidence-based management strategy for the patient with splenomegaly, but certain conclusions are clear. The finding of splenomegaly should always be taken seriously, but the urgency of diagnosis depends on the individual clinical picture. Some patients with isolated splenomegaly will never develop signs of serious disease, and a "watch and wait" strategy can be advocated if there are no concerning features. In others a diagnosis becomes essential, and splenic biopsy is increasingly used in this situation to evaluate splenic pathology with minimal risk. Where this procedure is not available or non-diagnostic, the clinician must carefully review the differential diagnosis, clinical features and investigations, before deciding whether the benefits of diagnostic splenectomy outweigh the potential risks.

Practice points

The evaluation of splenomegaly hinges on a comprehensive clinical assessment, which guides the intensity of subsequent investigations.

Isolated splenomegaly can be associated with malignancy, but many patients develop no serious disease after long-term follow-up and watchful waiting is often appropriate.

Splenic biopsy is a safe, effective procedure for patients who require a diagnosis despite first- and second-line investigations.

Diagnostic splenectomy carries more risk and should only be considered in patients with significant symptoms and/or hypersplenism.

Conflicts of interest statement

None declared.

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