Radiological manifestations of Systemic Lupus Erythematosus (SLE)

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Purpose

1- To review the physiopathology of Systemic lupus erythematosus (SLE), its clinical symptoms, diagnosis criteria and possible complications.

2- To know the radiological manifestations of SLE and be able to recognize them.

3- Correctly interpret the imaging findings within the illness context.

4- Consider the importance of imaging studies in SLE.

Methods and Materials

We reviewed the imaging studies performed on patients diagnosed with SLE over a 28 month period (January 2007 - May 2009) and the imaging findings present in them.

Multiple highly diverse radiological manifestations were obtained affecting different organs and systems: pleural effusion, pneumonia, pulmonary fibrosis, diaphragmatic dysfunction, pericardial effusion, arthropathy, cerebral infarction, kidney atrophy and failure, transplanted kidney.

We also reviewed the possible complications due to treatment (immunosuppressors, corticosteroids) such as infections by unusual germs and osteoporosis.

Results

SLE is a multisystem autoimmune disease of unknown origin characterized by the presence of antinuclear auto-antibodies, with an incidence of 7.3 cases per 100,000 habitants, with an approximate prevalence of 124 cases per 100,000 habitants. The disease is 10 times more frequent in women.
It can affect any organ and joints. Clinical symptoms vary according to organ(s) affected. SLE is diagnosed by the presence of at least 4 clinical-analytical criteria established by WHO (Table. 1).

Disease duration is variable and characterized by alternate periods of activity and remission. Disease severity is classically defined based on number of affected organs.

Imaging plays an important role in determining disease extension and severity. In cases where patients present less than 4 WHO criteria, radiological findings may assist in confirming SLE diagnosis.

The **ANTI-PHOSPHOLIPID SYNDROME** is present in 27-42% of SLE patients, characterized by appearance of recurrent vascular thrombosis and haematological alterations (thrombopaenia or haemolytic anaemia), associated with antiphospholipid antibodies (anticardiolipin and lupus anticoagulant). They may present recurring heart attacks, Budd-Chiari disease, thrombosis of dural venous sinuses, intestinal ischemia, and recurring pulmonary thromboembolism.

**RESPIRATORY SYSTEM:**

Respiratory system affection is frequent, approximately 50 to 60% of patients present symptoms of pleuropulmonary affection. The pleura, lung and respiratory muscles may be affected.

**Pleural effusion** is the most common manifestation. Radiological alterations of lungs in most cases are **badly defined patchy parenchymatous areas** affecting pulmonary bases. These areas are frequently due to infection although sometimes they represent acute lupus pneumonitis, alveolar haemorrhage or Bronchiolitis obliterans organizing pneumonia (BOOP).

- **Pleural effusion:** is the most frequent symptom, bilateral in half the cases (Fig. 1). They are usually small effusions.

- **Pulmonary infection:** very frequent, presenting 3 times greater risk of pneumonia than the general population. Immunosuppressor treatment increases the possibility of suffering infection. This infections may be due to common or uncommon germs (atypical pneumonia). A high prevalence of PULMONARY TUBERCULOSIS is also reported. Furthermore, atelectasis and respiratory musculature weakness predispose to pulmonary
parenchymatous disease. Recurring pneumonia may lead to bronchiectasis (Fig. 2, 3 and 4).

- **Diaphragmatic dysfunction**: present in 25% of patients. It manifests radiologically as diaphragm elevation, linear atelectasis may also be present. Clinical symptoms are dyspnoea and orthopnoea. Pulmonary function presents restrictive pattern. The pathogeny of this dysfunction is unknown (Fig. 5)

- **Acute lupus pneumonitis**: is rare, affecting 1 to 4% of patients. Clinical symptoms are similar to acute infectious pneumonia and thromboembolic disease. Due to damage of alveolar capillaries, oedema and haemorrhage occur, usually located in pulmonary bases, visualized in thorax radiological examinations as uni or bilateral patchy alveolar consolidations.

- **Pulmonary haemorrhage**: is a rare complication with high mortality (70-90%). It may be secondary to infection or uraemia or in relation to immune system alterations. Thorax X-rays shows bilateral acinar opacities. In patients with severe haemorrhage, examinations reveal large bilateral ground glass areas or multifocal consolidations.

- **Pulmonary fibrosis and chronic interstitial pneumonitis**: present in <3% patients. In thorax studies we can find architectural distortion, honeycombing areas, pleural thickening, and pulmonary fibrosis. It is important to differentiate this from acute alveolitis (it presents with ground glass areas without pleural thickening) (Fig. 6).

- **Bronchiolitis obliterans organizing pneumonia (BOOP)**: is rare in these patients, though it may be the first symptom of SLE. It presents in imaging studies as multiple alveolar and interstitial pulmonary opacities, frequently bilateral, which may be migratory and usually with periphery predominance. Corticoid treatment improves many radiological findings.

- **Pulmonary arterial hypertension**: more frequent in patients with associated antiphospholipid syndrome due to recurring pulmonary thromboembolism. In 14% of patients it is secondary to chronic interstitial pulmonary disease.

**CARDIOVASCULAR SYSTEM:**

*HEART DISEASE*

SLE may affect: myocardium, pericardium, heart valves and coronary arteries.
- **Valve affection**: is the most common SLE heart symptom. It can be seen in 18-74%. It is more common in patients with associated antiphospholipid syndrome. Valvular infection may range from slight valve thickening to Libman-Sacks endocarditis, characterized by formation of granular growths which may be associated with valvulitis and lead to valvular destruction.

- **Pericardial effusion**: exudative pericardial effusion and pericarditis occurs in 17-50% in SLE patients. Clinical symptoms and electrocardiograph findings are critical in its diagnosis. In a contrast CT we can see abnormal thickening and enhancement of the pericardium and pericardial effusion (Fig. 7).

- **Myocarditis**: myocarditis is an infrequent SLE symptom and may be clinically silent in over half the cases. It presents with a myositis with lymphocyte and neutrophil perivascular infiltration, which may lead to global dysfunction of left ventricle.

**VASCULAR DISEASE**

- **Atherosclerosis**: is a multifactor problem. The death rate due to coronary disease in SLE patients is 9 times the general population. Atherosclerosis may be accelerated due to corticosteroid treatment, hypertension (secondary to kidney disease) and vasculitis.

- **Vasculitis**: is the most important SLE symptom, usually starting with minimal vasculopathy yet finishes producing pathological elements like fibrinoid necrosis in small arteries, arterioles and capillaries diffusely. Moreover, a very active endotheliopathy occurs associated with the antiphospholipid syndrome generating a microangiopathy, which may lead to symptoms of varied magnitude in any organ, with particular importance in the central nervous system (CNS) where ischemic lesions secondary to vasculitis can be observed.

- **Deep vein thrombosis (DVT)**: they present a greater risk than the general population of suffering from this, particularly those with associated antiphospholipid syndrome.

**GENITOURINARY SYSTEM:**

Kidney affection is frequent in SLE. Nephritis is asymptomatic in almost all lupus patients and its classification is basically histological. SLE auto-antibodies react against the surface antigens of glomeruli, mesangial matrix or basal membranes, resulting in a
deposit of immunocomplexes in the glomeruli. Subsequently, cytokines are released leading finally to glomerular necrosis and fibrosis which lead to kidney failure.

Patients with chronic kidney failure may need dialysis and in some cases kidney transplant (Fig. 8, 9 and 10).

Kidney disease imaging findings in SLE are non-specific. Kidney size depends on duration of their affection (longer the time smaller the size). With ultrasound, kidneys affected by the disease usually appear hyper-echogenic.

The renal vein may present thrombosis, although infrequent and is usually secondary to hypercoagulability due to the nephritic syndrome. Patients with associated antiphospholipid syndrome are at greater risk.

With kidney failure, the parathyroid glands experiment hyperplasia, generally due to phosphate retention and resulting reduction seric calcium concentration. Secondary hyperparathyroidism made cause renal osteodystrophy (Fig. 11).

MUSCULOSKELETAL SYSTEM:

Approximately 80% of SLE patients present non-erosive non-deforming symmetrical polyarthritis affecting hand, wrist, knee and shoulder joints. 10% will have irreversible deformities, metacarpal-phalangic joint dislocations (Fig.12), likewise swan neck and "boutonniere" (Jaccoud Syndrome) deformities.

In hand X-rays we can see pericapsular oedema representing synovitis around the small joints. Juxtaarticular osteoporosis can be seen.

Carpal instability is diagnosed in 15% of patients. This entity is demonstrated on confirmation of distance increase (>3mm) between scaphoid body and lunate and rest of the carpal bones in a wrist X-ray done with radiolunar deviation.

Osteonecrosis or avascular necrosis may be presented, particularly in patients receiving intravenous corticosteroids. The femoral head is the most affected followed by the humeral, femoral condyle and tibial plateau.

Fractures due to insufficiency are a diagnosis to be considered in these patients, since many are treated with corticosteroids. These fractures may not be visible in X-rays due
to the osteoporosis. MRI enables early detection of these fractures which manifest with a signal increase in T2 sequence (due to bone marrow oedema).

They are predisposed to septic arthritis and osteomyelitis. Radiological examinations show progressive bone destruction, periostitis and joint effusion.

Ligaments may present instability and laxitude.

**GASTROINTESTINAL SYSTEM:**

SLE may affect any part of the gastrointestinal system. Non-specific abdominal pain is present in 10-37% of patients.

Due to immunosuppressor treatment infection response is reduced and leukocytes and fever may not appear with infection.

The most common findings are:

- Hypomotility of lower oesophagus.

- Focal or diffuse pancreatitis: occurs in 8-28% of patients. It may be due to vasculitis, ischemia of small pancreatic vessels, deposit of immunocomplexes or a combination of any. Chronic pancreatitis is frequent and may be asymptomatic.

- Intestinal ischemia: the gastrointestinal tract is particularly susceptible to small vessel vasculitis, especially in the upper mesenteric artery distribution territory. Patients with associated antiphospholipid syndrome may present thrombosis, so they have an increased risk of suffering intestinal ischemia.

**CENTRAL NERVOUS SYSTEM (CNS):**

Affects 30-40% of patients. Neurological complications worsen SLE prognosis, and causes 19% of deaths by lupus.

CNS affected by SLE at origin is angiopathic, however other mechanisms also participate in the CNS illness such as direct autoimmune neural damage, demyelination and thromboembolism.
Vascular affection can be divided into:

- Large vessel disease: i.e. ischemic infarcts of arterial territories (Fig. 13 and 14).

- Small vessel disease: it presents with small cortical or deep grey substance infarcts. Anatomopathological analysis of these vessels shows marked endothelial hyperplasia and intimal fibrosis, leading to occlusion, which is described as lupus vasculitis.

- Venous sinus thrombosis and deep brain vein thrombosis, more common in patients with antiphospholipid syndrome due to its hypercoagulability.

Brain ischemia and infarct may be related to coagulopathy (secondary to antiphospholipid syndrome) accelerated atherosclerosis due to corticosteroids, vasculitis or cardiogenic thromboembolism in Libman-Sacks disease.

In MRI studies we can frequently find small multifocal lesions in white substance, generally in relation to gliosis or vascular demyelination. There is another form of white substance affection called "migratory edema", manifesting radiologically as hyperintense lesions in T2 sequences, which may change in size and location in time (Fig. 15 and 16).

The most common imaging finding is cerebral atrophy (Fig 17).

Intracranial haemorrhage occurs in 42% of patients with uraemia, thrombocytopenia and hypertension. In younger patients the presence of intracranial bleeding in the absence of trauma or clotting is unusual and should suggest SLE affection of the CNS (Fig. 18 and 19).

The prevalence of subarachnoid haemorrhage due to intracranial aneurism breakage is higher than in the general population due to risk factors presented (vasculitis, hypertension, accelerated atherosclerosis).

Brain abscesses may appear, although rare in the absence of AIDS, intravenous drug abuse or diabetes. In patients with Libman-Sacks' endocarditis septic embolism risk is greater due heart valve affection. The usual location of abscesses is the frontal and temporal lobes. With CT imaging we can see a hypodense mass with ring contrast enhancement. Patients being treated with corticosteroids are at greater risk for opportunistic infections (Candida, Nocardia).
SLE patients have a higher risk of aseptic meningitis due to non-steroid anti-inflammatories (NSAIDs), therefore treatment with these drugs is contraindicated.

Viral or bacterial meningitis, viral encephalopathy, seizures, delirium or sensorial alteration may present similarly. In these cases, it is very difficult to differentiate clinically and radiologically whether affection is due to SLE or treatment (Fig. 20, 21 and 22).

**TREATMENT**

There is no cure for SLE and complete remissions are extremely rare, therefore, treatment is aimed at reducing acute attacks.

*SLE not potentially fatal:

- Analgesics

- Antimalarials (Hydroxychloroquine, chloroquine, quinacrine)

NSAIDs are contraindicated as SLE patients have a greater risk of suffering aseptic meningitis, an increase in seric transaminases, hypertension and kidney failure.

*SLE potentially fatal:

The treatment base of any potentially fatal SLE manifestation or, which might damage an organ are CORTICOSTEROIDS.

Cytotoxic/immunosuppressor agents are recommendable for treating generalized lupus erythematosus.

**TREATMENT DERIVED COMPLICATIONS / SIDE EFFECTS**

- **CORTICOSTEROIDS**:

  Their use is associated with high infection risk. Patients treated with corticosteroids are particularly susceptible to opportunist infections.
Osteopenia prevalence in SLE patients is 25-46% and osteoporosis 4-33%. Most of the bone mass loss is due to corticosteroids (Fig. 23).

- **IMMUNOSUPPRESSORS:**

It has been noted the concomitant use of corticosteroids with immunosuppressors considerably increases the risk of opportunist infection. Patients may not present leukocytosis and fever with infection due to immunosuppressor treatment.

* **Cyclophosphamide.** Its main adverse effect is the appearance of neutropenia. It usually favours the appearance of bacterial and opportunist infections (nocardiosis, fungal infections), and reactivation of latent infections due to the Varicella zostervirus, M.tuberculosis or human papilloma virus.

* **Azathioprine.** Causes an important immunodepressor effect but less than cyclophosphamide. Administered jointly with steroids, increases the risk of infections like that due to the Varicella zoster virus, bacteraemia and interstitial pneumonia.

* **Methotrexate (MTX).** May cause bone marrow depression and alterations of humoral and cell immunity. Most of the opportunist infections observed with this drug appeared in patients who also received corticosteroids.

Images for this section:
<table>
<thead>
<tr>
<th>SLE DIAGNOSTIC CRITERIA (WHO)</th>
</tr>
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<tbody>
<tr>
<td>&gt; MALAR ERYTHEMA</td>
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<td>&gt; DISCOID SKIN LESION</td>
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<td>&gt; PHOTOSENSITIVITY</td>
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<td>&gt; MOUTH SORES</td>
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<td>&gt; NON EROSIVE ARTHRITIS</td>
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<td>&gt; SEROSITIS (PLEURISY OR</td>
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<tr>
<td>PERICARDITIS)</td>
</tr>
<tr>
<td>&gt; RENAL INVOLVEMENT</td>
</tr>
<tr>
<td>&gt; PSYCHOSIS OR SEIZURE</td>
</tr>
<tr>
<td>&gt; HAEMATOLOGICAL ALTERATIONS</td>
</tr>
<tr>
<td>&gt; IMMUNOLOGICAL ALTERATIONS</td>
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<td>&gt; POSITIVE ANTINUCLEAR</td>
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<td>ANTIBODIES</td>
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The presence of at least 4 of these criteria (simultaneous or not) can establish the diagnosis of SLE

Table 1
Fig. 1: Bilateral pleural effusion
Fig. 2: Pneumonia in lower right lobe and upper left lobe.
Fig. 3: Pneumonia in medial lobe.
Fig. 4: Bilateral pleural effusion and pneumonia in lower right lobe.
**Fig. 5:** Elevation of both hemidiaphragms (diaphragmatic dysfunction) and basal atelectasis.
Fig. 6: Initial stage pulmonary fibrosis.
Fig. 7: Pericardial and pleural effusion in patient with SLE.
Fig. 8: Male patient with SLE, kidney transplant. Diverticulitis in hepatic angle of colon.
Fig. 9: Male patient with SLE, kidney transplant.
Fig. 10: Kidney atrophy. Ascitis due to peritoneal dialysis.
Fig. 11: Renal osteodystrophy.
Fig. 12: Lupus arthropathy. Multiple metacarpal-phalange dislocations and osteoporosis.
Fig. 13: Non enhanced CT. Middle Cerebral Artery territory ischemic acute stroke.
Fig. 14: Non enhanced CT. Middle Cerebral Artery territory ischemic acute stroke.
**Fig. 15:** Severe SLE, 20 year old woman. MRI(FLAIR). Hyperintense areas in white brain substance.
Fig. 16: Severe SLE, 20 year old woman. MRI(FLAIR). Hyperintense areas in white brain substance.
Fig. 17: Severe SLE, 20 year old woman. Brain atrophy.
**Fig. 18:** MRI, T1 sequence Small bleeding in left cerebelous hemisphere.
Fig. 19: MRI, T2 sequence Small bleeding in left cerebelous hemisphere.
Fig. 20: Bacterial meningitis. Non enhanced CT. Multiple bilateral and symmetrical frontotemporal hypodense areas (probably edema).
Fig. 21: Bacterial meningitis. Signal increase in cortical sulci.
Fig. 22: Bacterial meningitis. Intense leptomeningeal enhancement in cortical sulci.
Fig. 23: 49 year old oman receiving corticosteroid treatment for SLE. Diffuse osteoporosis and wedging of several vertebrae.
Conclusion

SLE is a complex multisystem disease presenting many highly different radiological findings to be considered in all areas of radiology.

The radiologist must familiarize him/herself with the radiological finding spectrum of SLE and possible complications, since knowledge is crucial for correct imaging interpretation.

Imaging studies are necessary in many SLE cases, particularly for determining illness extension and severity.

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