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The management of lupus in young people

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INTRODUCTION

Juvenile onset systemic lupus erythematosus (JSLE) accounts for 20% of all SLE presentations. It most commonly develops around adolescence. It is a serious and complex autoimmune disease that, although requiring specialist care, will benefit from the active involvement of general practice.

THE FACTS ABOUT JSLE

JSLE is a chronic autoimmune disease that can affect any part of the body including skin, joints, and the major organs. It most commonly presents around adolescence (median age at diagnosis 12–14 years). The female preponderance is less marked in adolescents than in adults.[1]

JSLE patients have a more aggressive disease than adults. They have higher rates of organ involvement including renal and liver disease, are more likely to die in the acute phase of the illness, and sustain more organ damage. In contrast with some juvenile arthritis patients, JSLE patients do not 'grow out' of the disease. They will therefore have a lengthy disease duration and incur a great burden of medication and its unwanted effects.

JSLE patients are still about 18 times more likely to die than their peers (standardised mortality rate [SMR] JSLE 18.3, confidence interval [CI] = 11.8 to 28.3), in contrast with adults (SMR 3.1, CI = 2.6 to 3.9).[1] Deaths usually relate to active JSLE with organ involvement, often in the context of suboptimal treatment adherence. Counselling patients with organ involvement about the controllable but serious nature of the illness is difficult but essential.

WHEN TO SUSPECT JSLE AND WHAT DIFFERENTIAL TO CONSIDER

JSLE symptoms are highly variable from a relatively mild disease such as a rash with joint pains and fatigue, to a life-threatening illness. The American College of Rheumatology (ACR) diagnostic criteria[2] include typical rashes, joint pains, renal or haematological disease, in the presence of auto-antibodies, but patients often present with symptoms not listed within these criteria, including non-specific constitutional symptoms such as fatigue, fevers, or weight loss. A facial butterfly rash may be present in up to 50% of patients. Alopecia and Raynaud's phenomenon are common. Alternative initial diagnoses include idiopathic thrombocytopenic purpura, haemolytic anaemia, auto-immune hepatitis, juvenile idiopathic arthritis, infection, other connective tissue disease, and haematological malignancy, and the work-up must reflect this broad differential.

An initial limited screening blood test in suspected cases may include full blood count, erythrocyte sedimentation rate (ESR), anti-nuclear antibody (ANA), and a urine dipstick. If these are negative/normal, the diagnosis of JSLE is highly unlikely. However, a referral should never be delayed in an unwell patient pending test results.

MODERN MANAGEMENT OF JSLE

The aim of treatment is to induce clinical remission or low disease activity, while minimising side effects and preventing damage, to enable the young person to reach their potential. Medications include steroids (for example, prednisolone), hydroxychloroquine, azathioprine, methotrexate, mycophenolate mofetil, cyclophosphamide, and biologic therapies such as rituximab.[3] Where GPs agree to prescribe and monitor medications, they must be supported with clear written guidelines from hospitals and have reliable, rapid access for advice on issues arising.

Regardless of which treatment is chosen, hydroxychloroquine is usually also added as it is protective against organ damage, diabetes, thrombotic events, ischaemic heart disease, and dyslipidemia. It may have a protective effect on survival.[4] In addition to pre-screening, it is important that patients

Box 1. Useful links and further reading[1]

For doctors

- Centre for Adolescent Rheumatology (http://www.centre-for-adolescent-rheumatology.org/)
- UK JSLE Study Group (https://www.liverpool.ac.uk/translational-medicine/research/ukjsle/about/)
- Arthritis and Musculoskeletal Alliance, Standards of Care Documents (http://arma.uk.net/resources/standards-of-care/)
- British Society for Rheumatology (https://www.rheumatology.org.uk/)
- Flint J, Panchal S, Hurrell A, *et al*. BSR and BHPR guideline on prescribing drugs in pregnancy and breastfeeding — Part I: standard and biologic disease modifying anti-rheumatic drugs and corticosteroids. *Rheumatology (Oxford)* 2016; **55(9):** 1693–1697.
- Flint J, Panchal S, Hurrell A, *et al*. BSR and BHPR guideline on prescribing drugs in pregnancy and breastfeeding — Part II: analgesics and other drugs used in rheumatology practice. *Rheumatology (Oxford)* 2016; **55(9):** 1698–1702.

For patients

- Lupus UK (https://www.lupusuk.org.uk/)
- Children's Arthritis Trust (http://childrensarthritistrust.org.uk/)
- Arthritis Research UK (http://www.arthritisresearchuk.org/)
- Arthritis Care (https://www.arthritiscare.org.uk/)

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have annual screening for retinal toxicity, especially after 5 years of exposure. All patients should use daily high-factor sunblock as UV light may trigger a flare and medications such as azathioprine increase risk of skin cancer.[4] Tight blood pressure control predicts kidney survival.

GP PRESENTATION OF AN ADOLESCENT WITH JSLE FEELING GENERALLY UNWELL

For non-specific symptoms such as fevers with arthralgias or a rash, the clinical differential diagnosis will be between an SLE flare, an infection, or a drug reaction. Clinically differentiating these is challenging. Infection causes an elevated ESR and C-reactive protein (CRP); SLE flares usually have high ESR but normal CRP. High titres of double-stranded DNA or low-complement C3 and C4 levels may also be helpful SLE disease activity markers.

Headaches are a common reason for presentation and may represent simple headaches or migraine but may also represent CNS lupus or an infectious aetiology. GPs should have a low threshold to refer, especially if there are other features of active SLE or constitutional symptoms.

Fatigue, sleep disturbance, and chronic pain are common and difficult symptoms to address. Mood disorder, methotrexate, anaemia, active disease, and physical deconditioning usually contribute. Screening for treatable causes (for example, anaemia, thyroid disease, lupus activity markers), minimising offending drugs, supporting physical reconditioning (paced reintroduction to exercise), psychological support, and a pain management programme may all be required.

CONTRACEPTION AND PREGNANCY

It is extremely important to discuss family planning and contraception with JSLE patients as drugs such as mycophenolate are teratogenic and unplanned pregnancies are high risk for both mother and fetus. It is important to avoid oestrogen containing oral contraceptives if the patient has antiphospholipid antibodies or a history of venous thrombosis. Other SLE patients may be offered combined contraceptive medications.

Fertility is not altered in most patients with SLE due to the disease itself. However, almost one-quarter of JSLE patients require treatment with cyclophosphamide which is gonadotoxic, and high cumulative doses in younger JSLE patients may eventually impact on their fertility.

Complications during pregnancy may be maternal, such as lupus flares (three times more likely), worsening renal impairment, hypertension, pre-eclampsia, or thromboembolism. Fetal risks include miscarriage, preterm birth, intrauterine growth restriction, and neonatal lupus syndromes.[5]

ADOLESCENCE AND 'TRANSITION'

Normal adolescent demands include not only school and vocational planning, increasing peer and changing family dynamics, and striving for independence but also risk taking and sexual development. In addition to all of this, JSLE patients must negotiate numerous additional tasks including hospital attendance, blood tests, managing repeat prescriptions, and taking medications. Both the disease and its treatment may affect appearance (for example, growth, acne, hair loss, rashes) at a time where fitting in with peers is crucial. The disease and its treatment can affect energy and mood.

Transition to adult health care is stressful for patients, parents, and healthcare professionals alike. High non-attendance and non-adherence rates, with general disengagement, may ensue, with resultant flares and damage. The GP may be the only link to continuity during this time. GPs must advocate for the young person and their family with the new hospital or team, and also advocate for the team around the importance of attendance and adherence. Colleges and schools may not have any understanding of the barriers faced by the young person. Letters of support can be hugely beneficial.

THE FINAL WORD

JSLE remains a serious and chronic illness. Although specialist care is required, the value of an involved GP cannot be overstated. The GP offers continuity of care and insight into local and family dynamics. By embracing a shared-care approach to management, teams in primary and hospital care empower these young people to reach their potential in health, education, employment, and family life.

Helpful information for healthcare professionals and patients can be accessed online (Box 1).

Provenance

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Competing interests

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