


Rheumatology 2012;51:193–195
doi:10.1093/rheumatology/ker287
Advance Access publication 7 October 2011

Fluorodeoxyglucose positron emission tomography in juvenile systemic lupus erythematosus with psychiatric manifestations: relation to psychopathology and treatment response in two cases

Sir, Psychiatric manifestations in JSLE are not uncommon, and they often pose diagnostic and therapeutic challenges. MRI of the brain is frequently without abnormalities [1]. [18F]-fluorodeoxyglucose positron emission tomography (FDG PET) detects relative reductions in regional cerebral glucose metabolism, and has been suggested as a more sensitive diagnostic tool [1, 2]. We describe two cases of JSLE with CNS involvement presenting as psychosis and catatonia, respectively. In the absence of MRI abnormalities, FDG PET showed marked metabolic disturbances, which differed between patients and were normalized with successful treatment.

Case 1, a girl, adopted from China, at the age of 10 years was diagnosed with SLE, based on the presence of exanthema, arthritis, vasculitis, nephritis, anaemia, lymphopenia and positive tests for ANAs and anti-DNA antibodies. She was initially treated with mycophenolate and CSs (peroral and intermittent intravenous bolus infusion). After 4 months, she was admitted due to recurrent episodes of psychosis with delusions (e.g. convinced that the parents would eat her) and visual hallucinations (claiming that the bed had teeth), accompanied by severe anxiety, agitation, self-mutilation and aggression. Combination treatment with rituximab and various antipsychotics had little effect. A lumbar puncture (LP) showed an increased IgG index and no signs of infection. An electroencephalogram (EEG) recorded during symptoms was without signs of epileptic activity. MRI with angio sequence was normal except for a small subcortical white matter lesion in the right frontal region, which was not considered a plausible cause of the clinical symptoms. FDG PET showed hypermetabolism in the basal ganglia (Fig. 1). Treatment with CYC, 500–1000 mg/m² every 4 weeks, was initiated, and after 6 months the CNS symptoms were reduced to rare panic attacks, while the nephritis showed only modest improvement. A second, third and fourth FDG PET scan showed gradual normalization of the glucose metabolism over a period of 2 years. She continues to have some learning disabilities.

Case 2 is a boy, 16 years old, Indian, with no known predisposition for mental illness. The diagnosis of SLE was based on discoid lupus (diagnosed by a dermatologist 6 months before admission to our department), anaemia, arthralgia, nephritis and positive tests for anti-dsDNA antibodies and ANAs. CNS symptoms, which began acutely and before the initiation of treatment, included confusion, anxiety and incoherence and latency of speech. Treatment with mycophenolate and CSs was started. LP showed an increased IgG index. EEGs were initially normal but later showed abnormal frontotemporal low-frequency activity (1–2 Hz). MRI with angio sequence was normal. FDG PET showed frontoparietal hypometabolism (Fig. 1). He rapidly developed a universal rigidity with waxy flexibility, i.e. his arm would remain in the position in which it was placed, and he was increasingly unresponsive and unable to cooperate. Treatment with CYC, 500–1000 mg/m² every 4 weeks, improved all but the CNS symptoms. The diagnosis of catatonia was made, based on immobility, mutism, posturing, rigidity and waxy flexibility. He was treated with clonazepam, 1–5 mg/day, with only modest improvement of the catatonia. After 2 months the decision was made to start electroconvulsive therapy (ECT). He was given 12 treatments following an adult dosage protocol, with clinical improvement occurring immediately after the first treatment. Four weeks after the last treatment, he was able to attend school normally. FDG PET showed complete recovery from the earlier findings. He has no CNS sequelae.

In these two cases of juvenile CNS-SLE, FDG PET showed patterns of dysmetabolism that normalized with treatment, and thus provided an important alternative to MRI. FDG PET findings differed in association with differing symptomatologies, showing striatal hypermetabolism in the psychotic girl and frontoparietal hypometabolism in the catatonic boy. With respect to the former, it could be speculated that the hypermetabolism was caused by inflammation [1], which may also interfere with neurotransmitter function. In that context, it is interesting that an increased striatal dopaminergic activity has been hypothesized to cause an aberrant attribution of salience to external stimuli, which in turn underlies the formation of psychotic features such as delusions [4]. With respect to the latter, the hypometabolism could be caused by microangiopathy and consequent ischaemia [1]. The neurobiological background for catatonia is not known, but changes in frontoparietal blood flow and metabolism have been found, albeit in different subregions than observed here [5, 6]. Catatonia has been described in several case reports of both paediatric and adult SLE patients [7, 8]. In the majority of cases, catatonia respond to benzodiazepines and/or ECT [9]. However, cerebral vasculitis is a relative contraindication to ECT, and care should be taken to optimize anti-inflammatory efforts before starting treatment. We conclude that FDG PET should be considered in SLE with CNS affection, that ECT should be considered for catatonia in SLE, and that
further studies on the relation between CNS symptoms and FDG PET findings in SLE is warranted.

**Rheumatology key message**
- This case report illustrates the role for FDG PET in JSLE with psychiatric manifestations.

**Supplementary data**
Supplementary data are available at Rheumatology Online.

**Disclosure statement**: The authors have declared no conflicts of interest.

Anders Jørgensen¹, Ian Law², Susan Nielsen³ and Martin B. Jørgensen¹

¹Psychiatric Centre Copenhagen, Rigshospitalet, ²Department of Clinical Physiology, Nuclear Medicine and PET and ³Department of Pediatrics, Copenhagen University Hospital, Rigshospitalet, Copenhagen, Denmark. Accepted 11 July 2011

Correspondence to: Anders Jørgensen, Psychiatric Centre Copenhagen, University Hospital of Copenhagen, Rigshospitalet, Blegdamsvej 9, DK-2100 Copenhagen, Denmark. E-mail: anders.01.joergensen@regionh.dk

**References**
Wells' syndrome (eosinophilic cellulitis) secondary to infliximab

Sir, George Wells first described this syndrome in 1971 as a ‘recurrent granulomatous dermatitis with eosinophilia’ [1]. It is an uncommon inflammatory dermatosis of unknown aetiology, with few cases reported worldwide. Wells’ syndrome is characterized by a pruritic rash, which usually follows a relapsing and remitting course, and distinct histology showing an infiltrate of eosinophils within the dermis. Pruritus can be intractable and unresponsive to anti-histamines. Affected individuals typically present with erythematous plaques over a 2- to 3-day period and plaques usually resolve without scarring over 2–8 weeks [2]. This condition is rarely associated with systemic involvement, but peripheral blood eosinophilia is common [3]. We describe the case of a woman treated with infliximab for RA who developed Wells’ syndrome.

A 69-year-old woman with seropositive RA of 18 years duration presented with a 6-month history of an intensely pruritic intermittent rash over her back and abdomen (Fig. 1). The rash had appeared 1 week after an infliximab infusion, following which infusions were withheld for 12 weeks. The rash then remitted and another infliximab infusion was given; consequently, the rash returned. The patient complained of disabling pruritus, despite the use of various anti-histamines and topical emollients, but systemically was well. The patient had received infliximab infusions every 6 weeks for almost 9 years for control of RA. She had also been taking oral prednisolone since diagnosis. There had been no change in her usual medications and she could not recall receiving any recent courses of antibiotics or over-the-counter medications. There was no recent foreign travel or history of insect bites or stings. There was also no suggestion of latent malignancy or infection upon systemic enquiry. Clinical examination showed an extensive rash over her trunk and back and skin-coloured papules with an erythematous rim. Investigations revealed a mild peripheral eosinophilia of $0.67 \times 10^9$ cells ($0.04–0.4 \times 10^9$ cells/l) and slightly elevated inflammatory markers. The eosinophil count had been intermittently mildly elevated for some months, with the total percentage of eosinophils of 5.3% at its peak (1–4%). A punch biopsy of a posterior lesion was performed. Histology showed a dense infiltrate of lymphocytes, histiocytes and abundant eosinophils in the dermis, perivascular areas and around sweat glands, consistent with Wells’ syndrome (Fig. 2).

Seven clinical variants of Wells’ syndrome have been documented: plaque type, annular granuloma-like, urticaria-like, papulovesicular, bullous, papulonodular and fixed drug eruption-like [3]. The pathophysiology of the lesions in Wells’ syndrome remains unknown. It has been suggested that excess production of IL-5 occurs, which drives eosinophilic accumulation in a local Th2 immune response [4]. A variety of triggering factors have been identified, such as insect bites or stings [5], chronic inflammatory diseases [6] and neoplasias. More commonly it is idiopathic, drug-related, or associated with immunological, myeloproliferative or infectious disorders [7]. Although a distinct entity, it has been suggested that Wells’ syndrome may be associated with rare multisystem eosinophilic disorders, such as Churg–Strauss syndrome and hypereosinophilic syndrome [7]. Prognosis for Wells’ syndrome is excellent and most patients recover without difficulty, although lesions may recur later. The patient was treated with topical steroids and infliximab was

---

References:

1. George Wells first described this syndrome in 1971 as a ‘recurrent granulomatous dermatitis with eosinophilia’ [1].

2. Wells’ syndrome is characterized by a pruritic rash, which usually follows a relapsing and remitting course, and distinct histology showing an infiltrate of eosinophils within the dermis. Pruritus can be intractable and unresponsive to anti-histamines.

3. Affected individuals typically present with erythematous plaques over a 2- to 3-day period and plaques usually resolve without scarring over 2–8 weeks.

4. Histology showed a dense infiltrate of lymphocytes, histiocytes and abundant eosinophils in the dermis, perivascular areas and around sweat glands, consistent with Wells’ syndrome.

5. Seven clinical variants of Wells’ syndrome have been documented: plaque type, annular granuloma-like, urticaria-like, papulovesicular, bullous, papulonodular and fixed drug eruption-like [3].

6. The pathophysiology of the lesions in Wells’ syndrome remains unknown. It has been suggested that excess production of IL-5 occurs, which drives eosinophilic accumulation in a local Th2 immune response [4].

7. A variety of triggering factors have been identified, such as insect bites or stings [5], chronic inflammatory diseases [6] and neoplasias. More commonly it is idiopathic, drug-related, or associated with immunological, myeloproliferative or infectious disorders [7].

8. Although a distinct entity, it has been suggested that Wells’ syndrome may be associated with rare multisystem eosinophilic disorders, such as Churg–Strauss syndrome and hypereosinophilic syndrome [7].

9. Prognosis for Wells’ syndrome is excellent and most patients recover without difficulty, although lesions may recur later. The patient was treated with topical steroids and infliximab was.