Psychosis in a young female – a diagnostic and therapeutic challenge

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Psychosis secondary to lupus can lead to diagnostic and therapeutic challenges particularly when there is lack of autoantibodies. The condition is a recognized feature within the spectrum of ACR-defined neuropsychiatric disorders occurring in SLE.[1,2] As illustrated in the case reported below, early diagnosis and treatment can lead to favourable responses.

Case report

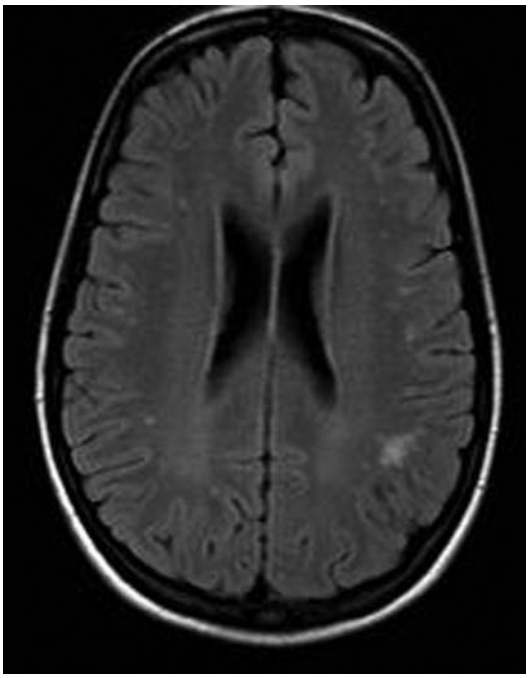
A 25-year-old Caucasian woman presented to the emergency department via urgent GP referral with a week-long history of deterioration in mental state typical of acute psychosis. The patient appeared extremely anxious and disorientated with paranoid delusions and bizarre ideation. She mentioned hearing voices and being unable to sleep or eat properly. She described hallucinations, thought withdrawal and inability to carry out simple tasks of daily living. She appeared to have impaired memory and concentration and lack of complete insight regarding her current state although she was asking for help continually.

Prior to deterioration she had been fit and well with no history of drug use. She lived with her parents and had a twin brother who was well. There was no known family history of medical or psychiatric illness and she was in a stable relationship with her boyfriend.

The initial impression was of an acute psychosis and she was discharged home on olanzapine (5 mg twice daily) with plans for close community mental health follow-up. However, within a few days she was admitted acutely to the psychiatric ward as her condition worsened and she developed Parkinsonian-like signs with stooped posture, shuffling gait and masked facies. Her thought processing had worsened with slowness and increased paranoia. Physical examination was normal including blood pressure (115/70 mmHg) and fundoscopy. Initial biochemical and microbiology screening was also normal apart from a raised creatinine kinase level (1295 IU/L). There was no history of seizures. Ferritin was normal and atypical infection screening including toxoplasma, treponema pallidum, lyme and HIV was negative. Autoantibody screen, including ANA, ANCA, anti-cardiolipin, serum ACE, immunoglobulins, dsDNA and complement levels were negative. Thrombophilia screen (including lupus anticoagulant) was normal. A porphyria screen was also negative. She was reviewed by a neurologist who was concerned that she had an underlying organic cause for the psychosis and may have developed extrapyrimidal side-effects from anti-psychotic therapy. An MRI brain and lumbar puncture were thus organized. The MRI revealed high intensity signals in the subcortical white region and left parietal region (Figure 1). CSF examination was normal. An incidental screening chest radiograph revealed small pneumothoraces and a subsequent high resolution computed tomography scan of the thorax confirmed these and revealed small scattered pulmonary nodules (Figure 2). Further testing showed the ck-mb level was 23.7 (ref range 0–3.5). An echocardiogram was performed which showed right ventricular hypokinesia.

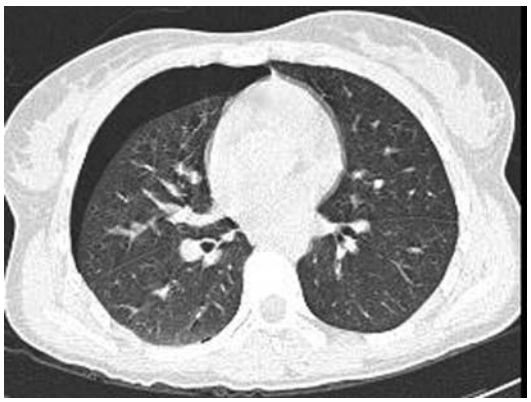
The combination of psychosis with an MRI appearance compatible with SLE and evidence of lung and myocardial involvement led to a clinical suspicion of of seronegative lupus. Despite detailed screening no metabolic or infective causes were evident. Thus, after extensive discussion with neuroradiologists, neurologists and

Figure 1
MRI Brain (T2 FLAIR) showing high intensity signal lesions within subcortical white matter and single larger lesion in left parietal region



lupus experts the decision was made to treat our patient with pulsed cyclophosphamide (500 mg) and methylprednisolone (250 mg). She received a total of nine pulses as per the Lupus Institute recommended regime for neurolupus (first three at weekly intervals then three at fortnightly intervals and three at 3-weekly intervals). She tolerated the infusions well. Clinically, progress was initially slow but she did appear to improve in terms of comprehension and concentration. She was moved on to mycophenolate mofetil (1 g twice daily) as maintenance treatment which she also tolerated well. After six months inpatient stay on the psychiatric ward she was discharged home with day-care arrangements and reduced anti-psychotic requirements (olanzapine 2.5 mg nocte). Three days post discharge she had a witnessed tonic-clonic seizure lasting approximately one minute (no incontinence). She was thus commenced on an anti-epileptic (leviteracetam 500 mg twice daily) on advice from neurologists. MRI appearances remained unchanged and, importantly, there were no new lesions. Clinically, our patient thereafter made remarkable clinical progress and at a recent outpatient review, nine months since the initial psychotic episode, was reported to be almost completely back to her usual self.

Figure 2
HRCT thorax showing small scattered pulmonary nodules and pneumothoraces



Discussion and conclusion

Our patient was unusual in her initial presentation but psychosis can be one of the first manifestations of lupus. In a large series of SLE patients, psychosis at the onset of disease was described in one-third of cases.[3] It is usually reported occurring in association with cutaneous and haematological manifestations and active lupus markers, particularly high titres of ANA and/or dsDNA antibodies.[1] However, ANA negative lupus is a rare but recognized condition with a reported prevalence between 5–8.9%.[4]

ACR criteria for SLE can help with diagnosis but are not necessary to make a diagnosis of neuropsychiatric lupus. It is also recognized that the spectrum of neurological conditions seen in lupus is varied and there is still lack of agreement on uniform criteria.[5,6]

There is controversial evidence for autoantibodies that may be detectable in the serum or CSF of patients presenting with neuropsychiatric lupus. These include anti-neuronal antibodies, brain-lymphocyte cross-reactive antibodies, anti-ganglioside antibodies, anti-ribosomal P antibodies and anti-phospholipid antibodies.[7,8] Testing for the

first three is not widely available. Reported prevalence of anti-P is highly variable and influenced by factors such as ethnicity, sensitivity and specificity of the assays used and timing of analysis in relation to clinical event.[9,10] Our patient's CSF was sent to the USA for further analysis but unfortunately due to technical problems it was subsequently not possible to test it for specific antibodies. She was negative for antiphospholipid antibody which is reported in correlation with lupus (thrombotic episodes involving cerebral vasculature) although there are no convincing data to support its usefulness in the diagnosis of lupus psychosis.[11,12]

MRI abnormalities[2,13] in SLE patients have a varying reported prevalence (19–70%). T2 weighted images particularly with FLAIR sequencing to dampen CSF signals are better for highlighting areas of oedema. Focal neurological disease is often associated with predominantly fixed lesions in the periventricular and subcortical white matter within the territories of major cerebral blood vessels. However, these are a non-specific finding and also associated with hypertension, disease duration and age-related small vessel changes.

Diffuse neuropsychiatric presentations are often associated with transient subcortical white matter lesions and patchy hyperintensities in grey matter not confined to major cerebral blood flow regions. Similar findings may occur in posterior reversible encephalopathy syndrome (PRES) which has been reported to occur in SLE. Our patient presented with an altered mental state and MRI findings which can occur in PRES but did not manifest the more commonly reported symptoms of headaches and visual disturbance. She also had normal renal function and no history of hypertensive episodes or prior use of cytotoxic or immunosuppressive medication which are other reported associations.[14]

Other imaging findings in SLE include infarction, venous sinus thrombosis and myelopathy. Single photon emission computed tomography (SPECT) scans are sensitive in lupus in identifying abnormalities in regional cerebral blood flow. However, abnormalities are seen in up to 50% of SLE patients without neuropsychiatric manifestations.[2]

There is limited information on the long-term outcome of lupus psychosis. A follow-up study commented on patients with severe psychotic manifestations at onset having favourable prognosis long term.[1] Currently, no standardized treatment exists for lupus psychosis. Corticosteroids and various immunosuppressive regimes have been reported as beneficial.[1] Cyclophosphamide has been shown to be more effective in neuropsychiatric lupus compared to methylprednisolone alone.[15] Plasmapheresis may be added in refractory cases.[16] There are case reports of successful use of intravenous immunoglobulin.[17] Rituximab has also been found effective in some cases.[18] Mycophenolate has been effective in our patient in whom, due to gender and young age, long-term cyclophosphamide would not be ideal. However, there is limited evidence on its efficacy in neuropsychiatric SLE[19] and use may thus currently be restricted to those patients in whom cyclophosphamide is contraindicated or ineffective.[20] A small open label study has shown azathioprine to be useful in maintenance treatment of lupus psychosis following induction therapy with cyclophosphamide and steroids.[21]

In summary, our case proved to be a diagnostic and therapeutic challenge but ultimately led to a positive outcome for all involved.

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