13. PROGRESS OF PREGNANCIES IN A PATIENT WITH PREVIOUSLY TREATED THROMBOTIC THROMBOCYTOPAENIC PURPURA AND LUPUS

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Introduction: The combination of TTP, lupus, and pregnancy in a diagnosis list is enough to make the heart flutter in even the most experienced clinician and the perception that complications will be severe in pregnancy is high. We report two successful pregnancies in a 29 year old British-Asian lupus patient with previously treated TTP in adolescence. Pregnancy outcomes in women who have recovered from severe acquired thrombotic thrombocytopaenic purpura (TTP) and then become pregnant are not well documented, even less so if they develop lupus and subsequently become pregnant. This case illustrates that this unusual sequence of conditions expected to predispose to an increased rate of obstetric complications and foetal loss can be overcome using conventional medications and carefully co-ordinated multi-specialty care.

Case description: We report here the case of a 29 year old British-Asian woman who was diagnosed with acquired TTP at the age of 15 requiring intensive care admission, treatment with plasma exchange and steroids. A full autoimmune serology was negative at the time. Three years later, she had a refractory relapse of her TTP requiring multiple treatments including plasma exchange, intravenous vincristine and Rituximab. She concurrently developed intermittent inflammatory joint pain and severe lethargy and investigations were consistent with a new diagnosis of lupus with positive ANA, positive Crithidia and double stranded DNA antibodies and low C3 and C4 complement levels. Her extractable nuclear antigen profile included only a positive RNP antibody. She had regular infusions of fresh frozen plasma (Octoplas). She required a second course of Rituximab very soon afterwards due to inadequate response and unfortunately developed a hypersensitivity reaction. She developed tonic clonic seizures and rash which was attributed to worsening TTP with a mild persistent renal impairment and increasing proteinuria attributed to lupus nephritis but platelets were considered too low for renal biopsy. She was therefore commenced on steroids and intravenous cyclophosphamide with an early conversion to low dose oral cyclophosphamide due to poor vascular access for three months. She had a good response and was switched to myophenolate mofetil (MMF) as a maintenance drug with an ACE-inhibitor for renal protection. She remained stable over a period of 3 years with MMF, perindopril, simvastatin and a reducing course of prednisolone. In 2011, hydroxychloroquine was added. She had increasing proteinuria but had no signs of nephrotic syndrome, and both her lupus and TTP remained quiescent. At the age of 23, our patient was seen in a pre-pregnancy clinic and her MMF was stopped and changed over to azathioprine in preparation for a planned pregnancy. At the same time, perindopril was changed to Nifedipine and was started on aspirin to prevent pre-eclampsia. She conceived naturally the following year. She was monitored regularly in combined Obstetric Immunology/Rheumatology Clinics and monitored for hypertension and recurrence of thrombocytopenia and lupus; despite persistent proteinuria (up to 94.1mg/mmol), she otherwise had an uneventful pregnancy delivering at 37 weeks gestation. Her proteinuria continued to worsen after delivery, and the plan was to change back to perindopril. However, she became pregnant again quickly and had a miscarriage at 8 weeks gestation. Her proteinuria progressed and she was recommenced on perindopril. She again conceived naturally and was switched back to Nifedipine with Labetalol for hypertension. Clexane was both added. She delivered her second baby successfully. Post second delivery, her renal function worsened again and she subsequently had proteinuria in the nephrotic range although there were no clinical features. A year later, she underwent a renal biopsy due to persistent proteinuria which showed relatively mild class IV lupus nephritis S (A/C) (active and chronic lesions: diffuse segmental proliferative and sclerosing lupus nephritis) with minimal chronic damage. She has been maintained on MMF, hydroxychloroquine and low dose prednisolone. Her TTP has not recurred since late 2007. Overall, our patient has had two healthy babies from three pregnancies despite early treated TTP and lupus.

Discussion: When a patient already has a diagnosis of TTP, pregnancy is predicted to increase the risk of thrombotic microangiopathic relapse and thereby to increased maternal and foetal complications. It is also well established that both lupus and pregnancy are also predisposing factors for developing TTP. TTP is a thrombotic microangiopathy, caused by deficiency of or reduced activity of the von Willebrand factor (VWF) cleaving protease ADAMTS13. Childhood onset TTP can be either inherited or acquired. Inherited forms are usually associated with low levels of the ADAMTS13 (ADisintegrin-like And Metalloprotease with Thrombo-spondin repeats, 13) protease whereas acquired cases are associated with increased antibody inhibitor to the protease. Up to a quarter of acute TTP episodes are associated with pregnancy and the puerpurium. In women with hereditary ADAMTS13 deficiency, TTP can occur during pregnancy, and is associated with foetal loss. Recent work has shown that in acquired TTP, reduced ADAMTS13 activity levels and the presence of anti-ADAMTS13 antibodies denote risk factors for poor pregnancy outcomes in women. Such women have an increased occurrence of lupus, as well as hypertension, albuminuria, and depression. In the case of our patient, she had increased levels of immunoglobulin (IgG) inhibitors of the ADAMTS-13 protease (30% of normal) – already a significant risk factor in both developing lupus, and complications during pregnancy. She would have therefore have been predicted to be more at risk of TTP relapse, particularly during pregnancy. Despite this, treatment with potent, but conventional immunosuppression helped keep her in remission, and most likely contributed to keeping her lupus at bay. It is reassuring to know that successful treatment of TTP can minimise the recurrence of thrombocytopenia and ensure good control of lupus. Our case highlights how successful and fairly uncomplicated pregnancies can be achieved and carried to term

Key learning points: Fertility can be preserved with aggressive management of TTP with cyclophosphamide in young patients. TTP preceding a lupus pregnancy is generally regarded as high-risk but need not be if the TTP and lupus are in remission and the woman is on appropriate drugs for pregnancy. Our case illustrates an unusual sequential progression of TTP, lupus and relatively uncomplicated pregnancy managed in close co-operation by multiple specialist teams.