Anti-tumour necrosis factor treatment and pregnancy: the way is open

Sirs,

We read with interest the case report by Scioscia and others on "Intentional etanercept use in pregnancy . . . " (1). Unfortunately, they missed our earlier report of 4 such cases some 4 years ago (2). We wish to update our experience to include now 2 women who have given birth to 2 children each under similar conditions.

Given that autoimmune rheumatic diseases disproportionately affect women of childbearing age, the safety of new drugs regarding birth defects, miscarriages or pre-term delivery is of concern. All anti-TNF agents are pregnancy category B, suggesting that as human data in not available, therapy should be avoided in pregnant or breastfeeding women (2). In our clinic, with 250 women receiving anti-TNF treatment in the years 2002-6, four women with severe intractable arthritis successfully conceived and maintained their pregnancies to full term while under continuous anti-TNF treatment, as previously described in detail (3). Since then we have adopted a policy of not discouraging selected anti-TNF patients from pregnancy and supporting them throughout their pregnancies; two of the original 4 have successfully conceived and maintained second pregnancies under continuous anti- TNF treatment.

Case 1

A 30-year-old nulliparous woman with an eleven-year history of seronegative erosive rheumatoid arthritis (RA) unresponsive to methotrexate (MTX) and hydroxychloroquine had received infliximab and azathioprine for 2 years prior to her first pregnancy (azathioprine, though relatively ineffective for arthritis, was continued so as to improve anti TNF therapy, possibly reducing anti-drug antibodies.) She responded quite well to treatment with infliximab at a dose of 3 mg/kg in combination with azathioprine, with residual low grade synovitis remaining in her metacarpophalangeal joints (MCPs) only, with both erythrocyte sedimentation rate (ESR) and C-reactive protein (CRP) near normal. She continued therapy until she delivered a fully healthy child at week 39. After 3 years of this treatment her disease flared despite infliximab increase to 5 mg/kg and infliximab was switched to etanercept. She had received etanercept and azathioprine for 1 year prior to becoming pregnant for a second time. She continued therapy until Caesarean section, due to preeclampsia, at 36 weeks, delivering a fully healthy child.

Case 2

A 27-year-old nulliparous woman with a ten-year history of severe erosive polyarthritis typical of RA but leucopenia, rash and serologies – low complement and positive anti DNA and anti-cardiolipin – consistent with lupus, "rhupus", conceived spontaneously to first successful pregnancy after two failed IVF pregnancies while under etanercept mycophenolate mofetil treatment. Treatment with etanercept only was continued throughout the uneventful pregnancy until Caesarean section, due to premature rupture of membranes at week 37, delivering a fully healthy child. After 3 years, and a failed trial of adalimumab, she became pregnant for a second time. She continued etanercept therapy until she delivered a fully healthy child at week 39 by elective Caesarian section.

For these women disease control was problematic, but their pregnancies were important and valued. Intensive consultations on the potential effects of anti-TNF agents on pregnancy were conducted before they became pregnant. In all cases, treatment was continued throughout pregnancy with close monitoring until delivery of a fully healthy child. The newborn babies were entirely well and remain so, with one to 5 years follow-up.

While most of the reports to date on anti TNF treatment suggest their apparent safety (1-5), a recent study suggest that that treatment with anti TNF agents at the time of conception may be associated with increased risk of spontaneous abortion; but the contributory role of disease severity and other anti-rheumatic agents cannot be excluded (6).

We believe that properly selected and properly monitored women, in whom these drugs are essential to control their arthritis and yet desire to have children, can be encouraged to proceed, with caution, on the basis of the currently available data: the way is open.

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