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Letter to the Editor

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Pregnancy in Takayasu Arteritis Patients Exposed to Anti-Tumour Necrosis Factor (Anti-TNF)-α Therapy

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Dear Editor,

In our clinic with 30/83 patients with Takayasu Arteritis (TA) receiving anti-Tumour Necrosis Factor (anti-TNF)-α agents in the years 2013-2014, two women successfully delivered while under therapy with Infliximab (IFX).[1] (Table 1).

	First Patient	Second Patient
Age at delivery (years)	35	27
Duration of TA (years)	5	10
Concomitant diseases	Ulcerative Colitis	\
Arterial involvement	Subclavian artery (left); common carotid artery (right and left); aortic arch; celiac tripod (Type V)	Carotid artery (right and left); anonima artery; subclavian artery (right and left); aortic arch (Type IIa)
Main previous manifestations	Upper and lower limbs claudication; carotidynia; *angina abdominis*	Low-grade fever; carotidynia; upper and lower limbs claudication
Infliximab	7 mg/kg from 05/2013	7 mg/kg from 02/2009 → 10 mg/kg from 10/2009
Therapy at conception	Mesalazine 1600 mg, prednisone 5 mg and AZA 100 mg daily	Prednisone 5 mg and AZA 100 mg daily
TADS before pregnancy	7/40	6/40
TADS after delivery	7/40	6/40
MRA post pregnancy	Reducing of the thickening of involved arteries	Unmodified (disease stability)
Delivery	elective CS for previous CS (37.5 wg, 2610 g)	elective CS for previous CS (38 wg, 3165 g)

TA: Takayasu Arteritis; TADS: TA Damage Score; CS: Caesarean Section; wg: weeks gestation

Table 1: Patients characteristics.

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First patient, a 35 year old woman with a diagnosis of ulcerative colitis since childhood, was diagnosed with TA in 2009. She had an uncomplicated pregnancy in 2004. When she planned a second pregnancy, she was receiving IFX7 mg/kg every-six-weeks plus chronic therapy (Table 1). At conception she had type-V-disease (generalized involvement of all aortic segments, thoracic and abdominal) based on angiography.[2] Magnetic Resonance Angiography (MRA) revealed thickening of the common carotid arteries, aortic-arch, sovraortic branches and a 30-40% stenosis of the celiac tripod. Positron Emission Tomography (PET) scan revealed increase vascular uptake in the thoracic aorta and the aortic-arch.[3] Azathioprine (AZA) was discontinued in the first 12 weeks gestation (wg) and IFX was discontinued at 28 wg, respectively. Aspirin was administered 100 mg daily until 35 wg. Echocardiography at 12 and 28 wg was normal and carotid ultrasonography at 24 wg was stable. Fetal growth, umbilical and placental flow was repeatedly normal at ultrasonography examination. Arterial blood pressure was consistent and well-controlled. At 37.5 wg she delivered a healthy child. IFX was started four weeks postpartum. MRA two months after delivery revealed significantly reduced thickening of involved arteries. TA Damage Score (TADS), a clinical score of TA damage, remained unchanged.[4]

Second patient, a 27 year old woman and a mother of a 8 year old son, was diagnosed with TA in 2004 and had received corticosteroids, cyclophosphamide followed by Methotrexate (MTX) and AZA with addition of IFX (7 and then 10 mg/kg) in 2009. MRA performed in 2013 was consistent with extensive and active arteritis: thickening of the common, right and left carotid arteries, occlusion of the right carotid artery, bilateral occlusion of the subclavian artery and thickening of the aortic-arch. PET-scan confirmed increased uptake of contrast media in the aortic-arch and brachiocephalic, left subclavian and left axillary arteries. At conception she had type IIa disease (involvement of the ascending portion of aorta and the aortic arch).[2] AZA was discontinued in the first 12 wg and IFX was stopped at 28 wg; aspirin 100 mg daily was administered until 35 wg. Blood pressure remained consistently normal. At 30 wg Erythrocyte Sedimentation Rate (ESR) and C-Reactive Protein (CRP) elevation in association with anemia were observed and the patient complained of carotidodynia. Prednisone was increased (15 mg) and then tapered. Echocardiography at 12 and 28 wg and carotid ultrasonography at 24 wg were consistent with TA stability. Ultrasonography repeatedly showed normal fetal growth, umbilical and placental flow. At 38 wg she delivered a healthy child. TADS score was stable during pregnancy. Histopathological analysis of the placenta revealed no arteritic feature. Breastfeeding was allowed. One month after delivery the patient discontinued the therapy and was lost to clinical follow-up for two months. She developed low-grade fever, carotidodynia, upper and lower limbs claudication in addition to high ESR and CRP. IFX was re-introduced with immediate benefit. MRA three months after delivery was consistent with disease stability.

TA mainly affects women during child-bearing years.[2] Preventing fetal toxicity due to treatments and disease progression during pregnancy is challenging. Furthermore, maternal complications, including arterial hypertension, pre-eclampsia and cardiovascular involvement can impact on maternal and fetal outcomes.[5] Relatively few TA pregnancies have been described without consensus on the optimal management of disease during pregnancy.

Anti-TNF agents, IFX in particular,[1] appear safe and effective in rheumatic patients during pregnancy. Here, we described two successful pregnancies of TA patients treated with IFX before conception and until 28 wg. Blood pressure remained optimal and the vascular inflammation/remodelling did not worsen.[6] Newborns were healthy. We followed the indication to discontinue IFX during the last trimester[6]: This approach seems to be safe for the mother and minimizes fetal exposition to the drug. The risk of infections is low. In our reported cases infections were not observed in postpartum period till one years follow-up of the babies. In infants exposed to infliximab in utero a normal antibody response to standard vaccinations is ensuring in the early childhood.[7] Live vaccines are recommended after 6 months of age in infants exposed to anti-TNF in utero.[8] To the best of our knowledge, this is the first report describing the use of anti-TNF agents in pregnant TA patients.

CONFLICTS OF INTEREST

The authors declare that they have no conflicts of interest.

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CONSENT

The patients have signed a generic informed consent.

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