Takayasu's Arteritis & Pregnancy: A Review

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Abstract

Takayasu's arteritis (TA) is a well known yet rare form of large vessel vasculitis. TA commonly effect women in childbearing age of Asian origin. The etiology remains speculative but current literature supports autoimmune basis for TA. Suppression of inflammation and preservation of vascular competence form the basis of the treatment. The basic disease appears to be unaffected by pregnancy, inflammatory activity and haemodynamic status improves with pregnancy, but the high arterial pressure and the pre-eclampsia constitute main maternal complications. The foetal complication is intrauterine growth. Therefore, obstetricians are faced with the dilemma of optimal management in pregnancy. The optimum management of these women involves conception during the remission period, antenatal care provided by multidisciplinary team (involving rheumatologist), continuation of low dose steroids through out the pregnancy, early detection, treatment of hypertension and curtailing the second stage of labour for better maternal and foetal outcome.

INTRODUCTION

Takayasu's arteritis (TA) is a primary arteritis of unknown cause, which occurs in the women of the childbearing age. The mean age of presentation of TA is usually in the second and third decade of life [1,2,3] with a greater prevalence in Asian women, it occurs sporadically throughout the world. It is more common in women than men (8:1), and the peak incidence is in the second and third decades [4] .

Takayasu's disease was first described in 1908 by two Japanese ophthalmologists, Takayasu's and Onishi, who observed retinopathy occurring with absent limb pulses. Nowadays it is recognized as a rare (2-3 per million) inflammatory disease of the vascular tree, principally affecting major vessels such as the aorta, its branches and the pulmonary arteries [5,6] .

The disease preferentially involves the elastic arteries including the aorta and its major branches. Typical histopathological changes consist of disruption of the elastic fibers of the vessel wall, inflammatory cell infiltration with occasional granulomatous reaction, fibrotic thickening of the adventitia and intimal thickening.

The disease is characterized classically by a triphasic course, commencing with an initial active phase of constitutional symptoms such as malaise, weight loss, fever, myalgias and arthralgias, and is associated with an increase in acute phase reactants (e.g. C-reactive protein CRP or Sedimentation rate ESR). This progresses to a second stage with symptoms of cerebral, visceral or extremity ischemia before resulting in a final 'burnt-out' quiescent phase of fibrosis. Unfortunately, these 'typical' symptoms are seen in only 33 per cent of all patients and the severity and progression of vessel involvement are extremely variable. [7]

The American College of Rheumatology criteria for the diagnosis of Takayasu's arteritis are as follows [8] :

Figure 1

1.	age of onset <40 years
2.	claudication of an extremity
3.	decreased brachial artery pulse
4.	blood pressure difference between two arms of >10 mm Hg, bruit over subclavian artery or aorta and arteriogram abnormality

The presence of three or more of these criteria demonstrates a sensitivity of 90.5 per cent and a specificity of 97.5 per cent.

New angiographic classification of Takayasu's arteritis, Takayasu's conference 1994 [9] .

Figure 2

Type	Vessel involvement
Type I	Branches from the aortic arch
Type IIa	Ascending aorta, aortic arch and its branches
Type IIb	Ascending aorta, aortic arch and its branches, thoracic descending aorta
Type III	Thoracic descending aorta, abdominal aorta, and/or renal arteries
Type IV	Abdominal aorta and/or renal arteries
Type V	Combined features of types IIb and IV

According to this classification system, involvement of the coronary or pulmonary arteries should be designated as C (+) or P (+), respectively.

Ishikawa defined clinical groups based on the natural history and complications of the disease [10] .The four most important complications were defined as Takayasu's retinopathy, secondary hypertension, aortic regurgitation, and aneurysm formation, each being graded as mild/moderate or severe at the time of diagnosis.

Ishikawa clinical classification of Takayasu's arteritis [10]

Figure 3

Group	Clinical features
Group I	Uncomplicated disease, with or without pulmonary artery involvement
Group IIA	Mild/moderate single complication together with uncomplicated disease
Group IIB	Severe single complication together with uncomplicated disease
Group III	Two or more complications together with uncomplicated disease

TREATMENT

A substantial minority of patients with Takayasu's disease are asymptomatic. Treatment in the initial phase is with steroids with or without cytotoxic agents. This induces remission in approximately 80% of all patients although 50% of those subsequently relapse and require a further course of steroids. Subsequent treatment is limited to angioplastic or surgical correction of the stenosis or aneurysms.

The disease tends to be self-limiting in 20% of patients while in a similar percentage the disease remains persistently active. There is also increasing evidence that occult inflammation may continue to occur despite clinical evidence of a remission. The presence of retinopathy, aortic regurgitation and significant aneurysm indicate the worst prognostic factors. The commonest causes of death are heart failure, myocardial infarction and stroke. [11]

In general, steroid therapy is recommended in cases where inflammatory signs such as an elevated sedimentation rate, elevated C-reactive protein and a high white blood cell count are present.

The overall 5-year survival rates were 96.5%, 94%, and 80.3%, for the groups I, II & III respectively. Patients with a single mild complication or no complication at diagnosis had a five year event free survival of 97%, compared with 59.7% in patients with a single severe or multiple complications. No deaths occurred in patients in groups I and IIA, whereas19.6% of patients in groups IIB and III died during follow up, mostly from cerebrovascular disease and cardiac failure. [12]

TAKAYASU'S & PREGNANCY

Fertility is not adversely affected and pregnancy does not appear to exacerbate the disease, inflammatory activity and the haemodynamic status may improve with pregnancy although development of blood pressure is not uncommon in pregnancy. However, pregnancy should be considered in remission period [13] .

Whenever possible, women should be assessed preconceptually. This gives them the opportunity to make an informed decision based on their individual risks prior to proceeding with a pregnancy. It enables appropriate adjustments or stoppage of cytotoxic drugs to be made prior to conception (including commencement of folic acid) and optimal timing of pregnancy. Combined contraceptive pill is generally avoided as there is increased theoretical risk of thromboembolism. However, progesterone only pill or depot injections or intra uterine devices can be recommended.

Baseline investigations should be taken as part of the evaluation and should include full blood count, C-reactive protein and renal function. Apart from base line investigations Doppler ultrasound and Magnetic resonance imaging of the carotids & other major vessels involved should be performed to assess the severity of the disease and echocardiogram to assess the ejection outflow in the pregnancy around 28 weeks gestation. From various studies [14,20] quotes around 5-15 % first trimester loses including therapeutic termination for severe T A (group III & IV with renal involvement)

ANTENATAL CARE

Antenatal care should be provided by a multidisciplinary team that includes an obstetrician, midwife, radiologist, hematologist, anaesthetist, cardiologist and rheumatologist.

All the women should be booked as early as possible.

Steroids can be used safely during pregnancy in the low doses [21] . Women should be carefully monitored from first trimester. The frequency of clinic visits depends upon need, but we advise a minimum of monthly until 28 weeks, fortnightly to 36 weeks and then weekly. Maternal complications [22] are superimposed pre-eclampsia (60%), congestive cardiac failure (5%), cerebral haemorrhage (5%) progressive renal impairment [23] and fetal complications include growth restriction and this can be predicted on the basis of following table [14] .

The maximal score is 8. There appears to be a cut-off point at score 4. Thus a score of 4 or above indicates a baby at high risk for growth retardation, early treatment with antihypertensive drugs has shown to improve fetal outcome.

All women should receive regular growth scans. Uterine artery Doppler ultrasound scans, performed at 20 and 24 weeks of gestation, provide a predictor for uteroplacental function and help to identify women with the highest risk pregnancies, who should be monitored more intensely thereafter. In spite of the limitations of clinical, ultrasound and umbilical artery Doppler assessment, the knowledge of reduction in growth helps to predict the failing placenta and thereby allows the planning of early delivery. Apart from hypertension, there were no major obstetric problems and no maternal deaths directly related to pregnancy.

Pregnancy can continue till term and induction of labour is considered in the presence of superimposed pre eclampsia or hypertension. Elective Caesarean at term is indicated for severe disease (retinopathy, arterial aneurysms, and aortic regurgitation [13] . Hypertension in the second stage of labour is a risk factor for cerebral haemorrhage; shortening this stage by use of low forceps delivery or vacuum extraction appears to be a reasonable solution. [14,22]

The anaesthetic management of a parturient suffering from this arteritis is important involvement of anaesthetist at an early gestation to make plan depending upon needs and risks involved regarding the regional anaesthesia. It is necessary for these women who are on long term Prednisolone to have usual doses of dexamethasone or betamethasone if they are at risk of preterm delivery.

Patients should be informed regarding the genetic predisposition in some families, the majority of which demonstrated by BW52 human lymphocyte antigen [24] mode of transmission to the child is not clear. Subsequent pregnancies if conceived in the remission period should not pose threat, however in severe disease early management by steroids and immunosuppressants has good outcome and termination or sterilization is only a last option.

DRUG THERAPY IN PREGNANCY

Drug therapy requires a careful assessment of the risk/benefit ratio for the patient. Low dose steroid (usually Prednisolone) is often the mainstay of therapy during pregnancy and if she is in remission cytotoxic drug (Azathioprine) is with drawn. Prednisolone is metabolized by the placenta and thus not transmitted to the fetus except at high doses. In event of blood pressure anti hypertensive medication (methyl dopa or nifidipine) should be started at an early gestation for better maternal and foetal outcome [14] . Azathioprine crosses the placenta but is not converted to its active metabolites by the immature fetal liver. Thus, the risk of congenital anomalies is small. Breastfeeding is avoided in patients who are on Azathioprine due to the theoretical risk of immunosuppression as infant's liver changes Azathioprine into its active metabolites. We recommend Thromboprophylaxis in these patients as they might be associated with anti phospholipids antibodies (aPL) especially the patients from oriental origin, however it's association with aPL is universal [15,16,17,18,19] .

CONCLUSION

Fertility is not adversely affected and pregnancy does not appear to exacerbate the disease, T A should have a medical screening prior to conception. Medical management of a pregnancy patient with T A does not differ significantly from a non-pregnant patient. Multidisciplinary management is essential for satisfactory clinical outcome during pregnancy and their blood pressure should be strictly controlled for a favorable maternal and fetal outcome and the mode of delivery should be planned.

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