Living With Vasculitis

Fertility and Vasculitis

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Introduction

Vasculitis activity and its therapy are potential threats to the fertility of patients with vasculitis. Loss of fertility is an important consequence of the disease, but the risks of this occurring can be considerably reduced with newer forms of treatment. As a chronic disease, vasculitis also causes psychosexual and relationship problems due to effects on self-esteem and mental well-being. Chronic kidney disease is a common consequence of renal vasculitis and the depressed kidney function itself affects fertility in both women and men.

Fertility in women

The major threat to women is cyclophosphamide exposure. This drug is used to control vasculitis activity and is directly toxic to the ovaries. This can result in permanent infertility, also known as primary ovarian failure. In addition to loss of menstrual periods, amenorrhea, blood levels of the hormones FSH and LH are elevated. Primary ovarian failure is related to the total amount of cyclophosphamide administered and to the age of the patient. Data from lupus nephritis suggests that a total cyclophosphamide exposure of 14-20g results in infertility in over 50% of women aged over 32 years. The risk of infertility in those under 32 years is lower, around 10% in one series. These risks can also be reduced by using short-term regimens or by intravenous pulse as opposed to daily oral administration. Three months of oral cyclophosphamide leads to an exposure of 9-14g, and an equivalent six dose course of intravenous pulse cyclophosphamide, 5-7g. Even if infertility is not induced, less severe ovarian damage leads to earlier menopause. Drugs that temporarily suppress ovarian function, such as zolodex, are used to reduce the risk of cyclophosphamide toxicity. Rituximab has been shown to be as effective as cyclophosphamide and can be used when cyclophosphamide avoidance is desirable.

Following cyclophosphamide withdrawal and return of a normal menstrual cycle, women can conceive and have children. There have been concerns that cyclophosphamide, through damage to DNA in the unfertilised egg, results in an increase in birth defects but this has not proved to be the case. However it is advisable to wait at least six months between stopping cyclophosphamide and attempting to conceive.

Women have a finite number of eggs and once lost, they cannot be replaced. For this reason, in cancer therapy, egg harvesting and preservation or even, preservation of ovarian tissue for subsequent re-implantation, can be considered when drugs toxic to the ovaries are used. This is rarely feasible in vasculitis due to the tempo of the disease, the need for rapid institution of therapy and the potential complications of the procedures.

Being unwell with vasculitis interferes in a non-specific manner with menstrual cycles and can cause periods to stop, amenorrhea. This can be differentiated from ovarian damage by an ultrasound scan of the ovaries which demonstrates the presence of healthy oocytes (egg follicles) and by measuring
hormone levels in the blood. Periods will usually re-start spontaneously as the patient recovers. Direct damage to the ovaries or female reproductive tract by vasculitis is rare but has occurred.

The influence of other drugs should also be considered. Some immune suppressives, such as, methotrexate and mycophenolate mofetil, and thalidomide, damage the foetus and must not be used in pregnant women or those attempting to conceive. Certain antibiotics, such as rifampicin, interfere with the contraceptive pill. Anti-inflammatory drugs and high dose steroids also reduce fertility. The infective risks of the coil are increased in those receiving immune suppression. Sexually transmitted diseases can be more problematic in immune suppressed patients and Chlamydia Trachomatis can result in infertility in women.

**Fertility in men**

Cyclophosphamide directly affects sperm production in men but there is more potential for recovery by the generation of new sperm forming cells when cyclophosphamide is withdrawn. However sperm production does not usually recover to pre-treatment levels and healthy sperm counts can remain depressed. It is likely that, in combination with non-specific effects of chronic illness, cyclophosphamide reduces male fertility. An alternative immune suppressive used in vasculitis, methotrexate, also reduces sperm formation but has a lower risk of sustained effects after drug withdrawal.

In contrast to the difficulties of egg preservation in women, semen preservation is quite feasible in men and can be considered before cyclophosphamide is commenced. It can be hard to advise on this, especially if there is a cost to the patient involved, because the risks of infertility are probably quite low with current cyclophosphamide regimens and if infertility occurs it is more likely to be partial rather than complete. Testosterone therapy has also been used to protect the testes from cyclophosphamide toxicity.

The testicles can be directly attacked by vasculitis in polyarteritis nodosa causing pain and swelling and subsequent loss of function. GPA (Wegener's) can affect the prostate gland but the effects on fertility are not well understood.

Drug effects, especially high dose steroids, vasculitic activity and chronic illness reduce testosterone levels that can lead to reduced libido and erectile failure. Testosterone levels in the blood are readily measured and testosterone supplementation can correct the problem.

**Conclusions**

The protection and preservation of fertility are important issues in the management of vasculitis. Much is known about the effects of cyclophosphamide in women although there is a shortage of information about the longer-term effects in men and in children. The potential dangers of this and other drugs should be discussed in detail before their use, but it should be remembered that cyclophosphamide has been a truly life saving drug in vasculitis and a balanced approach to assessing both risks and benefits is needed.

Many other factors will influence the fertility of vasculitis patients that include the consequences of vasculitic activity, ongoing medications and the patient's general state of health. Pre-conception counselling should be sort by women with vasculitis wanting children so that any risks to the mother, pregnancy or future baby can be discussed and appropriate plans made.

Information of fertility and contraception will be available from your GP or Practice Nurse. There are a number of assisted conception units throughout the country. It is possible to do an internet search for these under "assisted conception" and add the name of the city. However, further information in the form of a booklet "Birmingham Women's Fertility Centre - A Patient Guide" is available from the Birmingham Women's Fertility Centre. Contact is by completing the web form at: [http://www.bhamivf.com](http://www.bhamivf.com)