Case Report

Pemphigus Vulgaris following ART pregnancy

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Abstract

Pemphigus vulgaris is a rare autoimmune disorder which affects the skin and mucous membrane. It affects both sexes equally. We had a patient who underwent ART treatment for infertility, affected by this disorder during treatment. Now she is in a dilemma to decide regarding the frozen embryos.

Key Words: Pemphigus vulgaris, Pregnancy, Infertility, Autoimmune, Acantholysis, ART, FET.

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Introduction

The word "Pemphigus" is derived from the Greek word "Pemphix" which means bubble or blister[1]. It is a group of chronic bullous disease and was named by Wichman in 1791. Common in all races, but more common in Jews[2]. Pemphigus in India tends to occur at a younger age and is more severe compared to Western countries[3]. The incidence of pemphigus is 0.09 to 1.8%[4,5]. Pemphigus vulgaris is a rare autoimmune, intraepithelial disorder affecting skin and mucous membranes(Fig 1). It presents as large flaccid bullae on a normal or erythematous base which break easily.

Fig 1 - Muco cutaneous lesions

They are mostly seen in oral mucosa, scalp, midface, sternum and groin[6]. In the oral cavity,the buccal mucosa and the hard palate are the commonest sites of involvement, followed by lips, tongue, floor of the mouth and gingiva in descending order of frequency[3]. It is mediated by circulating antibodies against keratinocyte cell surface. The auto antibodies target the proteins called desmogleins. The desmogleins are present in the outer layer of the skin.

Case report

Mrs.X, 29 yrs, married to Mr.Y, 30 yrs presented with primary infertility for 2½ yrs. She attained spontaneous menarche at 12 yrs of age and continued to have irregular induced cycles mostly with progestogens. Coital history was normal. She was on oral contraceptive pills(OCP) for 6 months for cycle regularisation 3yrs ago. Subsequent to OCP intake she had cerebral venous thrombosis(2008) diagnosed by MRI and had been treated with oral anticoagulants for 2 yrs.For fertility, she had attempted two cycles of Intra uterine insemination (IUI) elsewhere which failed. She underwent 3 cycles of IUI with clomiphene citrate 100mg and gonadotrophins, in our department which also failed.

As her multiple IUI attempts failed, she was planned for ART(August-2012) after clearance from Neurophysician. The protocol used was flare GnRH agonist protocol along with controlled ovarian hyperstimulation using highly purified urinary FSH. She had mild hyperstimulation and was monitored. Out of 26 oocytes obtained, the number of M II(mature) oocytes were 22. Intracytoplasmic sperm injection (ICSI) was done with husband's spermatozoa and 19 oocytes showed fertilization and all of them cleaved. Blastocyst transfer was done on D5 with 2 expanded blastocysts. The remaining 12 embryos, all blastocysts, were frozen. Micronised vaginal progestogens were given for luteal support and advised to do serum β hCG after 2 weeks to confirm pregnancy. It was a biochemical pregnancy and progestational support was stopped.

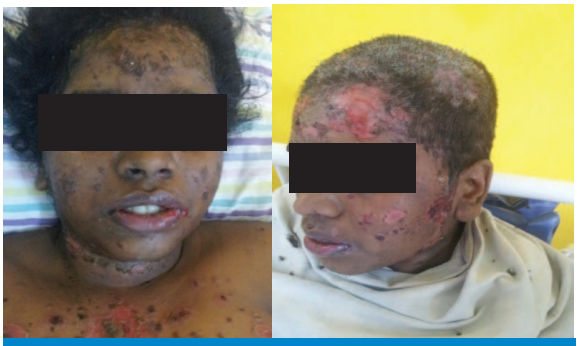

Fig 2 - Patient with muco cutaneous lesions in face, chest& scalp

After 4 months of ART/ICSI cycle, in Jan 2013 she underwent frozen embryo transfer (FET) after getting a neurophysician opinion regarding hormone

replacement treatment for FET. Programming of the endometrium was done with increasing doses of estradiol valerate and luteal support given with vaginal progestogens from D14(29th Dec 2012) of menstrual cycle. Embryos were thawed and 3 expanded blastocysts with survival rate of 1-70%, 2-20% were transferred. Luteal support continued with estrogens and progestogens. She was advised to do serum β hCG on 16.01.13, which showed positive result.

This time again she achieved pregnancy but she developed bullous skin lesions 2 days after pregnancy confirmation and diagnosed as pemphigus vulgaris (Fig 2) on clinical examination. Nikolsky's sign was positive. She was given topical application and waited for ultrasound for confirmation of clinical pregnancy. Scan at 6 weeks confirmed a biochemical pregnancy. She discontinued progestogen. Then she was started on oral steroids and continued for 3 months. She temporarily stopped medications for one month as there was no formation of new lesions. But she had a relapse and developed blisters all over the body, turned into raw areas, developed painful oral ulcers, dysphagia and fever with chills. She was admitted for 20 days and treated with steroid infusion and immunosuppressant. Diagnosis was confirmed by histopathology with Tzanck smear. She was advised to take chronic steroid therapy. Hormones-estrogens and progestogens as one of the causative factor for PV was discussed with the couple by the dermatologist.

She was reviewed in our department in November 2013.Since progestogens were incriminated in the appearance of the skin lesions, patient was worried about further treatment.

Following options were discussed:

1.Repeat FET if she is permitted another HRTschedule
2. Surrogacy with frozen embryos if pregnancy is not permitted for the patient.
Currently she is on steroid infusion thrice a month, immunosuppressant and calcium.

Discussion

Most of the autoimmune diseases occurs more frequently in women than in men and this is because of the possibility of influence of sex hormones over development of autoimmunity. During pregnancy, changes occur in the levels of estrogens and progesterones dramatically and also in cortisol, norepinephrine and dehydroepiandrosterone. This partially influences profound immunological changes throughout pregnancy and during postpartum period. These changes are very essential to accommodate the semiallogeneic fetus and include immunosuppressive and immunoregulatory processes[6].

Pemphigus vulgaris is an autoimmune bullous dermatosis. Desmoglein 3 is found in desmosomes and auto antibodies are formed against it[1]. Apart from genetic factors, immunological factor is required to trigger pemphigus vulgaris. It also coexists in other autoimmune problems such as myasthenia gravis and lupus erythematosus[6]. The 3 primary subsets of pemphigus include pemphigus vulgaris, pemphigus foliaceus and paraneoplastic pemphigus[7].

Each type of Pemphigus has distinct clinical and immunopathologic features. Pemphigus vulgaris accounts for approximately 70% of pemphigus cases. PV if not treated is a life threatening disease. The mortality rate is 5-15%[8]. Secondary infection is the most common cause of death. As it is a lifelong disease, needs prolonged treatment. When steroids are started, improvement can be seen within few days. The oral blisters heal slowly. Further formation of blisters is stopped in 2-3 weeks. Complete healing however takes time[9]. Lifelong low dose medication is required for some. Diagnosis is by Tzanck smear preparation which is simple, rapid, patient friendly and non-invasive. Hence it can be used instead of immunofluorescence testing for early pemphigus[10].

Because of its autoimmune nature like systemic lupus erythematosus, it gets precipitated or aggravated during pregnancy[11]. Our patient had flare-up of disease during the period of early pregnancy while on progestogens.

Apart from hormones, early pregnancy, stress can also trigger PV. This is a rare presentation of Pemphigus vulgaris which occurred due to hormones in a ART cycle.

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Sir Robert Hutchison's Petition and the Medical Humanities

From inability to let well alone
From too much zeal for the new and contempt for what is old
From putting knowledge before wisdom, science before art, and
Cleverness before common sense;
From treating patients as cases;
And from making the cure of the disease
More grievous than the endurance of the same,
Good Lord, deliver us.'

-Sir Robert Hutchison (1871- 1960)