

Azoospermia in a Patient Receiving Interferon Alpha for a Stage III Melanoma

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Sir,

The effects of interferon- α on fertility have not been thoroughly investigated. Recently it has been found that low-dose interferon- α does not have a negative effect on male fertility based on the modifications of serum inhibin B concentration (1).

CASE REPORT

A 38-year-old man was receiving interferon- α 2a at a daily dose of 9 million units (MU) 3 times a week for a stage III cutaneous melanoma. He had been treated for 5 years because of an intercurrent lymph node relapse. Other medications included salazopyrine 2–3 g daily for ulcerative colitis. Three months after interferon therapy was finished, he was referred to our hospital for evaluation of apparent infertility. The patient and his wife, who already had 2 children, decided to use contraception during interferon treatment. The patient denied a history of viral orchitis, trauma, exposure to radiation and other environmental hazards such as microwaves, ultrasound and chemicals (heavy metals and nematocides). A seminogram revealed azoospermia. Hormonal examination showed normal values of luteinizing hormone (LH): 3.9 mU/ml, and testosterone (4 ng/ml), but increased levels of follicle-stimulating hormone (FSH): 14.6 mU/ml. One year after stopping interferon- α treatment, the patient is still azoospermic and hormonal values have not varied significantly.

DISCUSSION

The effect of interferon- α in testicular function has not been clearly elucidated. Studies in animals showed conflicting results. In one report the expression of interferon- α in transgenic mice yielded to degeneration of spermatogenic cells and complete atrophy of the seminiferous tubules (2). Other authors reported that subcutaneous injections of interferon- α increased sperm production and serum testosterone levels in rodent models, therefore it was concluded that interferon- α might improve spermatogenesis, being a new approach for the management of male infertility (3). Its use in humans has been proposed for cases of idiopathic infertility (4) and prophylaxis of sterility after mumps orchitis (5). Yamamoto & Miyake (4) treated 4 patients with idiopathic infertility (3 with oligozoospermia and one with azoospermia) by intramuscular injections of interferon- α at a daily dose of 3 MU for 5 days per

week. All patients showed a marked improvement in sperm density and motility with the exception of the azoospermic patient, who had less impressive results. On the other hand, Foresta & Varotto (6) have observed spontaneous improvement of seminal indices in a group of men with idiopathic oligozoospermia, which raises some questions about the therapeutic benefit of interferon- α . Moreover, it has been shown that the level of interferon- α in the seminal fluid of oligozoospermic men is significantly higher than that of normozoospermic men (7).

The increased level of FSH in our patient is explained by the loss of inhibitory feedback due to the absence of sperm cells. Salazopyrine has been described as a cause of oligozoospermia and decreased sperm motility. The infertility produced by its metabolite, sulphapyridine, is reversible in a few months after stopping the therapy (8). There is no temporal association between the administration of salazopyrine and the development of infertility in our patient, as he had two healthy children after 4 and 6 years of continuous treatment. This is an exceptional case in that most patients diagnosed with melanoma do not entertain plans for future parenthood. Whether interferon- α may lead to sterility through an unknown mechanism or potentiate the toxicity of other drugs such as sulphasalazine remains to be investigated. Further studies are necessary to assess the effects of interferon- α on fertility.

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Annular Erythema Associated with Essential Thrombocythemia

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Sir,

Annular or figurate erythema often occurs in association with several diseases, including Sjögren's syndrome, subacute lupus erythematoses, fungal infections, *Borrelia* infections and even malignant disease of internal organs. However, in many cases of annular erythema, it is difficult to determine the underlying disease causing the skin lesion, even with careful examination. We present a case of annular erythema associated with essential thrombocythemia.

CASE REPORT

A 69-year-old man presented with a 5-year history of pruritic erythematous plaques on his trunk and extremities. He had been suffering from essential thrombocythemia for 20 years. Physical examination revealed annular or arcuate erythema on his back, thighs and knees. The lesions appeared as thumb-head-sized erythema. They gradually became larger and formed irregularly-shaped annular plaques with central healing. Each lesion persisted for approximately one week.

Laboratory findings were as follows: red blood cell count, $3.73 \times 10^{12}/\text{l}$; hemoglobin, 95 g/l; white blood cell count, $5.5 \times 10^9/\text{l}$; platelet count, $5.4 \times 10^{11}/\text{l}$ (normal, $1.5\text{--}3.5 \times 10^{11}/\text{l}$). Liver and renal function tests and urinalysis were within normal limits. Anti-nuclear antibody and anti-SSA and anti-SSB autoantibodies were negative. A skin biopsy showed a superficial perivascular infiltrate composed of lymphocytes. The patient's condition was complicated by repeated thrombocythemia during the course of his disease. The platelet count

increased to a maximum of $9.72 \times 10^{11}/\text{l}$, and spontaneously returned to the normal level. An interesting fact is that skin lesions stopped recurring when the platelet count dropped below approximately $3 \times 10^{11}/\text{l}$.

DISCUSSION

In the present case, skin lesions seemed to be associated with increased platelet count. Although the underlying mechanism for this is unknown, Tsuji (1) has demonstrated the presence of CD41a (GPII b/III a complex) on lesional vascular walls, suggesting the contribution of chemical mediators released from adhered, activated platelets in erythemas associated with essential thrombocythemia.

Cutaneous manifestations of essential thrombocythemia include erythromelalgia, acute febrile neutrophilic dermatosis and thrombotic diseases (2, 3). The present case, together with that of a previous report (1), strongly suggests that annular erythema is one of the important skin features that indicate the presence of thrombocytoses such as essential thrombocythemia.

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