

Isoniazid-Induced Gynaecomastia

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Abstract

Isoniazid is a key component of anti-tubercular therapy (ATT) with various adverse drug reactions of which gynaecomastia is very rarely seen. Here in this article we describe a 50-year-old HIV-negative male with normal liver functions, hormonal profile, diagnosed as a case of tubercular chronic epididymo-orchitis and started on ATT with four drugs (HRZE) for the first two months and with RH in the continuation phase. After 4 months on Isonex the patient developed bilateral gynaecomastia which subsided after withdrawal of the drug.

INTRODUCTION

Isoniazid is still the most important drug worldwide for the treatment of all types of tuberculosis. The incidence of adverse reactions to isoniazid is approximately 5%; the most prominent of these reactions are rash, fever, jaundice, peripheral neuritis, cutaneous reactions and mental changes. Although isoniazid is implicated as a cause of drug-induced gynaecomastia^{1,2}, the literature is sparse. Even all the standard textbooks do not mention isoniazid as a cause of gynaecomastia. Regarding this, a search was made through various search engines on the internet but only few case reports were found.

CLINICAL RECORD

A 50-year-old male, HIV and Australia Antigen negative, with normal liver function and hormonal balance was diagnosed as a case of tubercular epididymo-orchitis (diagnosis was made on clinical examination, color doppler study of the scrotum, Mantoux positivity and FNAC).

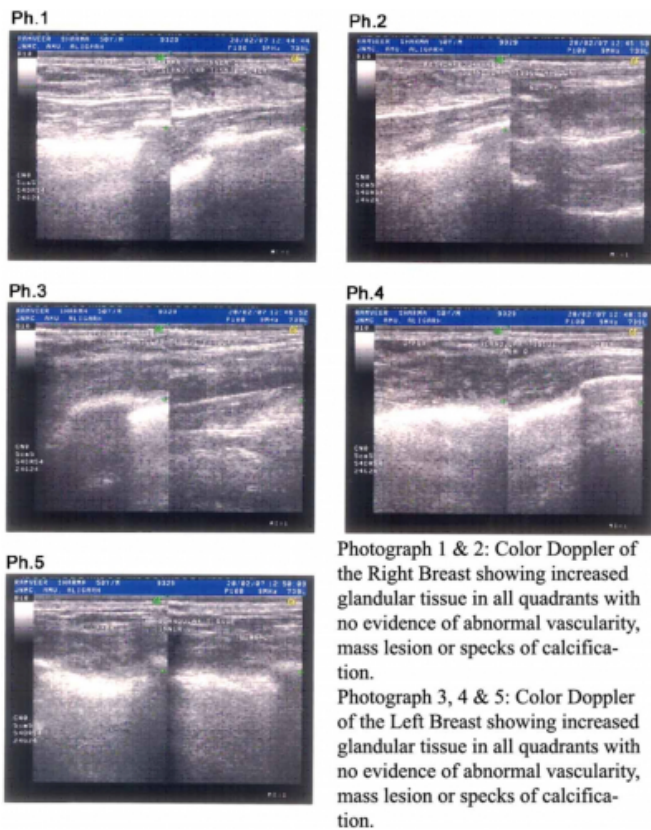
ATT was started with four drugs: Rifampicin-450 mg. Isoniazid-300mg, Pyrazinamide- 1500mg and Ethambutol-800mg for the first two months and then put in continuation phase with Isoniazid and Rifampicin.

After 4 months from the start of ATT, the patient noticed swellings around the nipple on both sides which were painless. On examination, diffuse visible swellings, non-tender, soft and not fixed to underlying structures were present on both sides but more marked on the right side. The secondary sexual characteristics and the external genitalia were evaluated but found to be normal. Endocrinological

referral and investigations revealed no abnormality. Hepatic and renal functions were within normal limits.

Color Doppler of the breast was done which showed increased glandular tissue in all quadrants of both breasts. There was no evidence of abnormal vascularity, mass lesion or specks of calcification. FNAC of the lump revealed tightly cohesive branching fragments of epithelium composed of small uniform oval cells with bland chromatin, myoepithelial cells – suggestive of gynaecomastia. The gynaecomastia subsided after withdrawal of Isoniazid after completion of six month of treatment.

Figure 1



DISCUSSION

Gynaecomastia^{4,5,6} is the growth of glandular tissue in male breasts. The term comes from the Greek words gyne and mastos, meaning female and breasts (feminine form), respectively, and roughly translating to female-like breasts. It is a benign condition that accounts for more than 65% of male breast abnormalities. Gynaecomastia is clearly differentiated from pseudogynaecomastia, which is an accumulation of excess fat in a male breast.

Many pharmacological agents^{7,8,9,10} can cause gynaecomastia. These drugs can be categorized by their mechanisms of action. The first type is drugs that act exactly like estrogens, such as diethylstilbestrol, birth control pills, digitalis, and estrogen-containing cosmetics. The second types are drugs that enhance endogenous estrogen formation, such as gonadotropins and clomiphene. The third types are drugs that inhibit testosterone synthesis and action, such as ketoconazole, metronidazole, and cimetidine. The fourth

types are those that act by unknown mechanisms, such as isoniazid, methyldopa, captopril, tricyclic antidepressants, diazepam, and heroin.

In 1953, when isoniazid became an integral part of antitubercular therapy, a report¹¹ from France implicated this drug as a cause of gynaecomastia. Another case was reported from France² which described painless bilateral gynaecomastia in a 52-year-old male on isoniazid for 4 months.

Similarly, our patient had bilateral painless gynaecomastia, which occurred after 4 months on treatment with isoniazid and subsided after withdrawal of the drug.

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