Case Report

Isoniazid induced Gynaecomastia

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Abstract

Gynaecomastia is very uncommon due to anti tuberculosis drugs. We describe this event in a 48-year-old male patient who received antituberculosis chemotherapy with isoniazid, rifampicin, ethanmbutol and pyrazinamide for right sided pleural effusion. After three months of treatment, he developed painful bilateral gynaecomastia. Gynaecomastia disappeared completely after stopping the isoniazid. Various mechanisms leading to gynaecomastia are also briefly discussed.

Key words: *Gynaecomastia, Isoniazid.*

Introduction

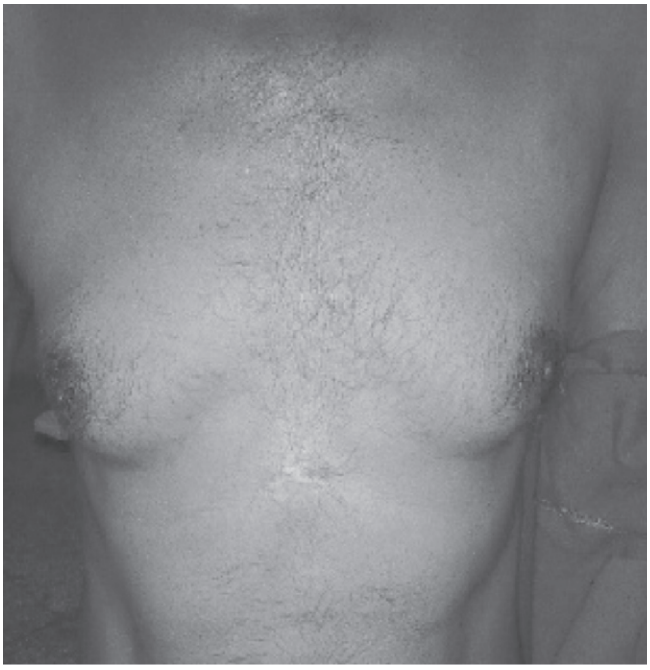
Isoniazid is an important drug in antituberculosis chemotherapy. It has been widely used as an effective drug for last so many years in all anti tuberculosis drug regimens. The serious adverse reactions with isoniazid therapy are very uncommon and include hepatitis, peripheral neuropathy, cutaneous reactions and mental changes etc.1 Gynaecomastia due to isoniazid is extremely rare with only few reports published in English literature2-4. This report describes an additional case of this type in view of its rarity and awareness among the treating physicians.

Case report

A 48-year-old male patient was diagnosed to have right sided pleural effusion. The pleural fluid investigations including fluid cytology and biochemistry suggested the tuberculous etiology. He was put on category-I regimen under revised national tuberculosis control programme (isoniazid 600 mg, rifampicin 450 mg, ethambutol 1200 mg, pyrazinamide 1500 mg, thrice weekly for two months followed by isoniazid 600 mg and rifampicin 450 mg, thrice weekly for four months). After two months of treatment, the pleural effusion part responded with the therapy but patient started complaining pain in right mammary region while receiving only isoniazid and rifampicin. In subsequent week patient noticed a painful swelling around the right nipple that gradually increased in size and became tender. A similar painful swelling was also noticed in the left nipple area. Both the swellings were visible, soft, but tender and not fixed to the underlying structures (Figure 1). He denied use of over the counter drugs,

Legends for Photograph

Figure 1: Photograph of patient showing bilateral gynaecomastia (front and lateral view).



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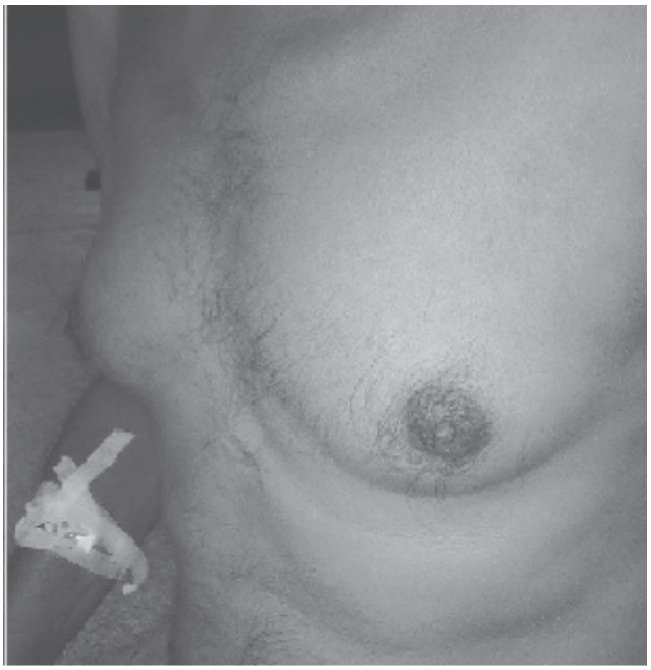

herbal products, alcohol or any other medications apart from prescribed regimen recently. The isoniazid was discontinued. Patient was reassured and was shifted to rifampicin and ethambutol based therapy for the next 3 months. The breast swelling did not increase further. After one month of stopping isoniazid, the pain subsided and the swelling started reducing in size. At the end of three months, the swelling completely disappeared. No other obvious cause on detailed evaluation (normal genital and thyroid examination with normal secondary sexual characteristics) led to a presumptive diagnosis of isoniazid induced gynecomastia due to the temporal association with anti tuberculosis therapy. This diagnosis was based on probable (WHO-UMC causality categories) role of isoniazid in causing gynecomastia.

Discussion

Glandular enlargement of the breast in male is known as gynecomastia. Gynaecomastia is a benign enlargement of male breast due to an increase in the duct tissue and periductal stroma. Normally, gynecomastia occurs in the neonates, during puberty and with aging as a physiological phenomenon5. Imbalance in androgen or estrogen action in the breast tissue through variety of mechanisms leads to pathological gynecomastia. Drug induced gynecomastia is one such mechanism seen commonly in clinical practice. Many drugs including atenolol, amidarone, anabolic steroids, busulfan, cimetidine, cyclophosphamide, diazepam, digoxin, estrogens, haloperidol, ketoconazole, methyl dopa, metoclopramide, omeprazole, opioids, penicillamine, phenothiazine, phenytoin, protease inhibitors, spironolactone, theophylline, testosterone, etc has been listed in the drug induced gynaecomastia6.

Although the incidence of drug induced gynecomastia varies from 20 to 25%, only occasionally the antituberculosis therapy is incriminated to cause gynecomastia despite its use for last so many decades5. Gynaecomastia due to antituberculosis drugs is extremely rare. Apart from isoniazid, only thiacetazone and ethionamide have been incriminated as a cause of gynaecomastia7, 8. The first report on isoniazid induced gynaecomastia was published in French literature in 19539. There are only few published reports in English literature on gynaecomastia with isoniazid2-4. Our patient also developed bilateral painful gynaecomastia after two months of therapy with isoniazid in a thrice weekly intermittent regimen containing 600 mg of isoniazid under direct observation. Such a report during directly observed treatment with intermittent isoniazid therapy is further rare in the literature4.

Pathological gynecomastia most commonly occurs due to imbalance between androgen and estrogen or because of increased aromatase activity in the adipose tissue leading to excess estrogen. Prolactin at time may be involved in the genesis of gynecomastia through negative feedback on gonadotropin hormone release10. Other possible mechanism such as defective androgen receptors may also contribute to gynaecomastia. The exact mechanism of isoniazid induced gynaecomastia is currently not known. It has been hypothesized that isoniazid causes disturbance in vitamin B6 complex activation in liver leading to alteration in the estrogen-androgen metabolism.3

Drugs are important and not uncommon cause of gynaecomastia in clinical practice and should always be included in the evaluation as the possible cause. Diagnostic evaluation however should be

individualized on the basis of clinical suspicion. Treatment of gynaecomastia should be directed at the underlying cause when identified. Most cases are benign and can be managed by explanation, reassurance and observation as done in our case. The reversible nature of gynaecomastia and no other associated morbidity strongly supports the need for the discontinuation of offending drug and observation rather than subjecting further evaluation or definitive management.

In conclusion, our case highlight that painful gynaecomastia may occur with isoniazid and treating physicians should be aware of this phenomenon. Such cases can be managed simply with reassurance and withdrawing the culprit drug without the need for unnecessary diagnostic evaluation.

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