



ISONIAZID INDUCED GYNAECOMASTIA - A RARE CASE REPORT

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ABSTRACT

Background: Gynaecomastia, a glandular enlargement of breast in males, due to Anti-Tubercular drugs is a very rare entity. There had been few studies showing isoniazid, ethambutol and thioacetazone are the drugs causing gynaecomastia. We present a case where gynaecomastia was seen in male patient after intake of isoniazid as part of treatment of tuberculosis. **Case Report:** A 31 year old man was diagnosed pulmonary tuberculosis, after doing sputum smear microscopy. After taking 3 months of Anti tuberculosis drugs, the patient felt swelling in Breast region presenting as painless bilateral gynaecomastia. Physical examination of external genitalia no abnormality and all secondary sexual characteristics were intact. Isoniazid was suspected as the reason for gynaecomastia and it was stopped. Consequently the breast swelling reduced, patient was reassured and Isoniazid was restarted to complete the treatment. **Discussion:** Adverse drug event management is a very important during the course of Anti tuberculosis therapy. In the above case, the gynaecomastia or the pain was subsided after stopping of the suspected drug. Gynaecomastia related to use of Isoniazid was first recognized in 1953. The mechanism of Isoniazid causing Gynaecomastia is not known. The plausible proposed mechanism is altered androgen-estrogen balance due to disturbance in pyridoxine metabolism. Defective androgen receptors may also contribute to Gynaecomastia. Other mechanisms might be refeeding Gynaecomastia which is caused by restoration of weight, Gonadotrophin secretion and gonadal function.

KEYWORDS: Isoniazid, gynaecomastia, Anti tubercular drug.

INTRODUCTION

Isoniazid was discovered in 1912 in Prague by Meyer and Malley as a part of docturnal work. In 1952 the use of inexpensive and safe Isoniazid came into use for treatment of Tuberculosis.^[1] Isoniazid is not only used in management of drug sensitive Tuberculosis but is also part of shorter Multidrug resistant TB Regimen and other atypical Mycobacterium infections. Isoniazid acts by inhibiting mycolic acid synthesis. Isoniazid has bactericidal effects both intracellular and extracellular and is well absorbed through gastrointestinal tract. Peripheral neuropathy, CNS irritation, depression, acute psychosis, encephalopathy, hepatitis are side effects known. Gynaecomastia is a very rare side effect associated with isoniazid. Here is the case presented with gynaecomastia induced by isoniazid.

CASE REPORT

A 31 year old male was suffering from cough of one month duration and had evening rise of temperature. He had loss of weight and appetite. When investigated, he was found to be smear positive on Zeihl -Neelson Technique on sputum sample. His Chest x-Ray was also suggested of TB. His Blood picture showed normocytic

anaemia with raised ESR. Based on Clinical findings, and investigations, he was started on Anti tuberculosis treatment with Isoniazid(600mg), Rifampicin(450mg), Pyrazinamide (1500mg) and Ethambutol(1200mg) alternate day as per Revised National Tuberculosis Control Program Protocol(RNTCP). After taking 3 months of Anti tuberculosis drugs, the patient felt swelling in Breast region presenting as painless bilateral gynaecomastia. Physical examination of external genitalia no abnormality and all secondary sexual characteristics were intact. He was investigated with mammography and Isoniazid was suspected as the reason for gynaecomastia and it was stopped. The diagnosis was based on probable role of Isoniazid causing gynaecomastia (WHO-UMS scale). Consequently the breast swelling reduced, patient was reassured and Isoniazid was restarted to complete the treatment.



Fig: 1: Picture bilateral gynaecomastia.

DISCUSSION

The above case report suggest that the culprit drug was Isoniazid. Glandular enlargement of breast in males is referred as gynaecomastia. Gynaecomastia due to Isoniazid is rare but non serious side effect.

The above case highlights the importance of recognizing the temporal association of this benign side effect of isoniazid therapy during the course of ATT that can be managed simply with reassurance and withdrawing the culprit drug, thus avoiding the need for unnecessary diagnostic evaluation.

True gynaecomastia is defined as glandular enlargement of breast tissue of more than 4 cm in men. It should always be differentiated from the pseudo gynaecomastia by demonstrating firm, fibrous cord-like tissue that is concentric with nipple-areola complex in true gynaecomastia by approximating thumb and forefinger together from either side of the breast during clinical examination.^[3]

Gynaecomastia is one of the most common breast problems in men and was first described by Paulus Aegineta (AD 625-690), who thought it was due to formation of fat. It can occur due to numerous causes which include developmental gynaecomastia, congenital causes like Klinefelter syndrome, hermaphroditism, enzyme defects of testosterone production, acquired causes like trauma, infection, torsion (twisted testicles), radiation, mumps, chemotherapy, malignancies like bronchogenic carcinoma, alcoholism, systemic causes like congenital Adrenal hyperplasia, cirrhosis, renal failure, thyrotoxicosis and drugs.^[4]

Drug induced gynaecomastia documented a temporal association of offending drug. Drugs that induce Gynaecomastia are spiranolactone (anti hypertensive), finesteride (anti androgen), retronavir(anti viral drugs), haloperidol(antipsychotic drugs), enalapril (calcium

channel blockers, cimetidine(H2 Blockers), methotrexate (chemotherapy drugs).^[5]

Anti tuberculosis drugs that can cause gynaecomastia include Isoniazid, thioacetazone and ethionamide.^[6] Gynaecomastia related to the use of isoniazid was first recognized in 1953 in France. In 1957, another case isoniazid induced Gynaecomastia was seen in Italy.^[4]

In most of the case reports cited, Gynaecomastia appeared at least 3 months of Isoniazid intake.^[7]

Pathological Gynaecomastia occurs due to imbalance between androgen and estrogen or because of increased aromatase activity in adipose tissue leading to excess estrogen. Prolactin at times may cause gynaecomastia through negative feedback on gonadotropin hormone release.^[8] Isoniazid causes gynaecomastia by altering the vitamin B6 complex activation in liver, leading to altered estrogen-androgen metabolism. It has also been postulated that isoniazid probably acts by phenomenon called "Refeeding Gynaecomastia," which is supposed to be caused by restoration of weight, gonadotrophin secretion and gonadal functions.^[9]

Adverse drug effects like gynaecomastia often embarrassment and emotional discomfort. Reassurance to the patient and removal of offending drug helps to complete treatment without interruption. Specific treatment might be required in case of pain and embarrassment. In such cases, surgery may be required.

In conclusion, the importance of this entity lies in the fact that recognition and withdrawal of the offending drug can lead to resolution of this problem.

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