

## Gynaecomastia During Antituberculosis Chemotherapy with Isoniazid

Sir,

Isoniazid is an essential drug in antituberculosis chemotherapy and widely used as an effective drug in all antituberculosis drug regimens. The serious adverse reactions during isoniazid therapy are rare and include hepatitis, peripheral neuropathy, cutaneous reactions and mental changes etc. Gynaecomastia caused by isoniazid is very uncommon and so far only few reports are published. We present a case of isoniazid induced gynaecomastia during intermittent chemotherapy for the first time.

A 42-year-old male patient was diagnosed to have tuberculosis of cervical lymph nodes. He received category III regimen under Revised National Tuberculosis Control Programme (isoniazid 600 mg, rifampicin 450 mg, pyrazinamide 1500 mg, thrice weekly for two months followed by isoniazid 600 mg and rifampicin 450 mg, thrice weekly for four months). After three months treatment, cervical lymph nodes almost disappeared but patient complained pain in left mammary region after four months, while receiving only isoniazid and rifampicin. In next one week a painful and gradually increasing swelling appeared around left nipple. A somewhat small painless swelling was also noticed in left nipple area. The swelling was visible, 6x8 cm on left side, soft but tender and not fixed to the underlying structures. The temporal association with antituberculosis therapy led to a presumptive diagnosis of isoniazid induced gynaecomastia. Isoniazid was discontinued and daily rifampicin, ethambutol and ciprofloxacin were started. The breast swelling did not increase further.



Fig. 1 : Photograph of patient showing gynaecomastia during antituberculosis therapy with isoniazid.

The external genitalia and secondary sexual characters of patient were normal. Routine investigation of blood and urine, x-ray chest, USG abdomen and other organ functions were normal. His endocrinological workup including 24 hr urinary 17-ketosteroids, plasma estradiol, hCG, LH, FSH, testosterone & prolactin etc did not revealed any abnormality. The gynaecomastia disappeared completely after six months.

Gynaecomastia is a benign enlargement of male breast tissue. Many commonly used drugs can cause drug induced gynaecomastia, however it is very uncommon with antituberculosis drugs.<sup>2</sup> Apart from isoniazid, only ethionamide and thiacetazone<sup>3</sup> have been incriminated in causing gynaecomastia. The first two reports on isoniazid induced gynaecomastia were published in French literature in 1953 and 1976. One of these report described painless gynaecomastia during four months daily therapy with isoniazid (600 mg/day). A recent report published in English literature described bilateral painful gynaecomastia after four months daily therapy with 300 mg isoniazid.<sup>1</sup> Our patient also developed bilateral painful gynaecomastia after four months therapy with isoniazid but in a thrice weekly regimen containing 600 mg of isoniazid under direct observation.

Clinically significant drug induced gynaecomastia may be due to an imbalance between the circulating estrogens and androgens. Defective androgen receptors may also contribute to gynaecomastia.<sup>2</sup> It has been hypothesized that isoniazid causes disturbance in vitamin B6 complex activation in liver leading to alteration in the estrogen-androgen metabolism. Another possible mechanism is refeeding gynaecomastia due to recovery from a chronic disease with improved nutrition in debilitating patients.<sup>1</sup>

Our case highlight painful gynaecomastia during intermittent isoniazid therapy and treating physicians should be aware of it. In mild form, same therapy should be continued and in severe reaction, alternate regimen may be considered.

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### REFERENCES

1. Khanna P, Panjabi C, Maurya V, Shah A. Isoniazid associated, painful, bilateral gynaecomastia. *Indian J Chest Dis Allied Sci* 2003;45:277-79.
2. Thompson DF, Carter JR. Drug-induced gynaecomastia. *Pharmacotherapy* 1993;13:37-45.
3. Chunhaswasdikul B. Gynecomastia in association with administration of thiacetazone in the treatment of tuberculosis. *J Med Assoc Thai* 1974;57:323-27.