CASE REPORT

Tuberculous lymphadenitis and borderline leprosy in a patient with isolated unconjugated hyperbilirubinaemia

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SUMMARY

A 35-year-old man was diagnosed with tuberculous lymphadenitis and multibacillary borderline tuberculoid leprosy. On investigation, isolated unconjugated hyperbilirubinaemia was detected and evaluation led us to conclude that the probable cause was Gilbert's syndrome. He was successfully managed by administration of chemotherapy for the treatment of both the mycobacterial infections, with no adverse effects on liver function tests.

BACKGROUND

Gilbert's syndrome is characterised by mild unconjugated hyperbilirubinaemia with, however, normal values for standard hepatic biochemical tests and normal hepatic histology other than a modest increase of lipofuscin pigment in some patients. Serum bilirubin concentrations are most often <3 mg/dL, although higher and lower values are both frequent. Its prevalence is approximately 8%.¹ Leprosy and tuberculosis co-infection has been reported in earlier studies.²⁻³ We report a case of co-infection with tuberculosis and leprosy in a patient with isolated unconjugated hyperbilirubinaemia (Gilbert's syndrome). To the best of our knowledge, this is the first case of co-infection of tuberculosis with leprosy in a patient with Gilbert's syndrome.

CASE PRESENTATION

A 35-year-old married man, a teacher, presented with a 4-month history of multiple swellings over the right side of his neck. The patient's history revealed that 1 year earlier he had been diagnosed with leprosy based on clinical examination and histopathological examination of skin biopsy. He was prescribed rifampicin and dapsone at the time. Later investigations revealed the presence of isolated unconjugated hyperbilirubinaemia, which was suspected to be secondary to haemolysis induced by dapsone, though G6PD levels were within normal limits. The dermatologist decided to stop dapsone and substituted it with clofazimine. Eight months later the patient was re-evaluated and his disease was reclassified as multibacillary borderline tuberculoid leprosy, for which he was prescribed ofloxacin by a dermatologist from outside our centre, in addition to the above two drugs. Ofloxacin is not a drug recommended for treatment of multibacillary leprosy⁴ and hence it was stopped when the patient reported to our centre. The patient was a non-smoker, did not drink alcohol and

had no history of tuberculosis. On general physical examination, he was moderately built and nourished, afebrile, his pulse rate was 70/min, with regular and good volume, respiratory rate 15/min, blood pressure 110/70 mm Hg. There were multiple lymph nodes in his right cervical region measuring between 2×2 cm and 3×3 cm. These were non-tender, matted and firm; the skin over the swelling was normal. Examination of chest, abdomen and other systems did not reveal any abnormality.

INVESTIGATIONS

A haemogram showed haemoglobin of 15 g/dL, total leucocyte count 6300/mm³, neutrophils 62%, lymphocytes 34%, monocytes 1% and eosinophils 2%. Reticulocyte count was 0.83%. Peripheral smear did not reveal any abnormality. Erythrocyte sedimentation rate was 35 mm in the first hour. Routine urine analysis was normal. Renal function tests, fasting blood sugar, serum electrolytes and lactate dehydrogenase were within normal limits. Total bilirubin was 2.9 mg/dL and direct bilirubin 1.6 mg/dL but other liver function tests including enzymes were within normal range. The serological tests for HIV, hepatitis A, hepatitis B and hepatitis C virus were negative. Chest roentgenogram and ultrasonography of the abdomen were normal. Histopathological examination of the cervical lymph node biopsy was suggestive of non-suppurative granulomatous lymphadenitis. Central caseous necrosis surrounded by an epithelioid cell layer and sporadic Langhans' giant cells were observed on histology suggestive of tubercular lymphadenitis.

DIFFERENTIAL DIAGNOSIS

Unconjugated hyperbilirubinaemia can be due to various causes, including Gilbert's syndrome, Crigler-Najjar syndrome type I and type II, drug-induced hyperbilirubinaemias and haemolytic anaemias.

TREATMENT

The patient was started on an antitubercular regimen (isoniazid, rifampicin, pyrazinamide and ethambutol) and chemotherapy for leprosy, after stopping ofloxacin; he was followed under the supervision of the dermatologist.

OUTCOME AND FOLLOW-UP

The cervical lymph node enlargement resolved over 6 months of antitubercular treatment and the patient successfully completed the treatment. He

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was also declared cured of leprosy after successfully completing the multidrug therapy for multibacillary leprosy.

DISCUSSION

Although individually, tuberculous lymphadenitis, leprosy and Gilbert's syndrome are commonly seen in clinical practice in India, their concurrence in the same patient is uncommon. In such clinical situations where multiple diseases occur together, special attention needs to be paid to looking for drug interactions while using a multiple treatment regimen, avoiding certain drugs that can aggravate the other coexisting disease, and conducting more frequent laboratory and clinical monitoring. On the contrary, if care is not taken, unnecessary avoidance of important drugs can occur. In this case, initially the isolated unconjugated hyperbilirubinaemia was thought to be due to haemolysis but work-up conducted later made us conclude that it was probably due to Gilbert's syndrome. The diagnosis of Gilbert's syndrome can be confirmed by genotype analysis,⁵ fasting test, nicotinic acid test, phenobarbital test, radio-labelled chromium test, thin-layer chromatography and drug clearance test. In the present case, these tests were not available at our centre. The demonstration of a raised bilirubin level that is predominantly unconjugated, with normal liver enzymes and no evidence of haemolysis, is usually sufficient for diagnosing Gilbert's syndrome.⁶ This diagnostic confusion had compelled the treating dermatologist to substitute dapsone with clofazimine. However, such a change would not compromise the efficacy of the treatment regimen.⁴ Rifampicin was not considered as the cause of hyperbilirubinaemia as it was prescribed later.

Most of the case reports concerning such mycobacterial co-infection are of patients suffering from leprosy and pulmonary tuberculosis. In our case, extrapulmonary tuberculosis, that is, tuberculous lymphadenitis, occurred in a patient of leprosy. We could not conclusively prove the diagnosis of Gilbert's syndrome as the patient could not afford further investigations. However, the absence of evidence of haemolysis and review of the patient's previous medical records made us conclude that the probable cause of isolated unconjugated hyperbilirubinaemia was Gilbert's syndrome as all other tests were normal.⁷ In such patients there can be alteration in metabolism of drugs such as acetaminophen.⁸ Prescribers thus need to be careful while prescribing for such patients who are on multidrug therapies and need a drug for some other ailment.

Learning points

- ▶ Coexistence of tuberculous lymphadenitis, leprosy and suspected Gilbert's syndrome mandates extreme caution to avoid drug interactions while using multiple drug regimens and necessitates frequent clinical and laboratory monitoring.
- ▶ Unconjugated hyperbilirubinaemias due to drug-induced haemolysis will require withdrawal of important drugs such as dapsone, whereas these agents can be cautiously used in conditions such as Gilbert's syndrome; hence careful evaluation of unconjugated hyperbilirubinaemia in a patient with concurrent tuberculosis and leprosy is important.
- ▶ Patients with conditions such as Gilbert's syndrome can have altered metabolism of commonly used drugs, for example, acetaminophen; hence caution is warranted during their use as antipyretics in tuberculosis.

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Competing interests None.

Patient consent Obtained.

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REFERENCES

- 1 Wolkoff AW. The hyperbilirubinemias. In: Fauci AS, Braunwald E, Kasper DL. eds. *Harrison's principles of internal medicine*, 17th edn. New York: McGraw-Hill, 2008:1929.
- 2 Agarwal DK, Mehta AR, Sharma AP, et al. Coinfection with leprosy and tuberculosis in a renal transplant recipient. *Nephrol Dial Transplant* 2000;15:1720.
- 3 Prasad R, Verma SK, Singh R, et al. Concomitant pulmonary tuberculosis and borderline leprosy with type II lepra reaction in a single patient. *Lung India* 2010;27:19–23.
- 4 World Health Organization. WHO Model Prescribing Information: Drugs Used in Leprosy. <http://apps.who.int/medicinedocs/en/d/Jh2988e/5.html> (accessed 31 Jan 2014).
- 5 Haraway JR, George PM. Use of fully denaturing HPLC for UGT1A1 genotyping in Gilbert syndrome. *Clin Chem* 2005;51:2183–5.
- 6 Sherlock S, Dooley J. Jaundice. In: *Diseases of the liver and biliary system*. 11th edn. London: Blackwell, 2002:214–17.
- 7 Fevery J. Bilirubin in clinical practice: a review. *Liver Int* 2008;28:592–605.
- 8 de Morais SM, Uetrecht JP, Wells PG. Decreased glucuronidation and increased bioactivation of acetaminophen in Gilbert's syndrome. *Gastroenterology* 1992;102:577.

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