


## Case Report

# A rare case of paraneoplastic cholestasis as the first presentation in a patient with Hodgkin lymphoma

Melina Dissanayake, Aruna Gunapala

National Hospital, Sri Lanka.

**Key words:** Hodgkin, lymphoma, paraneoplastic, cholestasis, idiopathic intra hepatic cholestasis, vanishing bile duct syndrome

Corresponding Author: Melina Dissanayake, E-mail: <m35571@pgim.cmb.ac.lk>  <https://orcid.org/0000-0002-3131-8244>

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## Introduction

Cholestasis in lymphoma is not a rare occurrence, with clinical reviews suggesting an incidence of 3-10% and a 30-70% frequency in autopsy studies [1]. The aetiology of cholestasis in a lymphoma patient can be categorized into tumour related causes and unrelated causes. The tumour related causes are extra hepatic biliary obstruction secondary to lymphadenopathy, intrahepatic infiltration with tumour, paraneoplastic cholestasis (PC), haemolysis and chemotherapy or radiotherapy. The unrelated causes are viral hepatitis, previous underlying liver diseases and conjugation defects. There are two types of PC identified by liver biopsy, idiopathic cholestasis (IC) and vanishing bile duct syndrome (VBDS). Cholestasis in lymphoma is most likely to develop in the follow up period, while cholestasis manifesting as the presenting complaint is rare (4%) [2] especially when it is due to a paraneoplastic phenomenon. Here, we report a rare case of a young woman who presented with cholestatic jaundice and was diagnosed to have Hodgkin's lymphoma (HL) complicated with paraneoplastic cholestasis.

## Case discussion

A 24-year-old female presented to our hospital with a three-month history of jaundice, pruritus, and passage of 'tea coloured' urine, associated with nocturnal pyrexia, malaise, lethargy, loss of appetite and a weight loss of 13kg. She denied passage of clay-coloured stools or altered bowel habits. There was no history of hair loss, oral ulcers, skin rashes or joint pain or swelling. Her past medical history was significant for a newly diagnosed type 2 diabetes mellitus (DM) which was poorly controlled on oral medications. She had a positive family history of type 2 DM in her mother but denied any family history of malignancies, liver diseases or connective tissue diseases. There was no history of intravenous drug abuse, high risk sexual behaviour, blood transfusions or alcohol

consumption. She did not give a history of use of over-the-counter drugs or herbal remedies.

On examination, she had a body mass index of 18 kg/m<sup>2</sup>. She was afebrile and not pale but deeply icteric, with multiple scratch marks over the body. There were no skin rashes, alopecia or oral ulcers. The thyroid gland was not enlarged. There were bilateral, multiple, non-tender, firm anterior and posterior cervical lymph nodes measuring 2x3cm<sup>3</sup> in size, together with bilateral multiple axillary lymph nodes 1x2 cm<sup>3</sup> in size. There were no flapping tremors or bilateral pitting ankle oedema. Her cardiovascular, respiratory and central nervous system examination was unremarkable. On examination of the abdomen, there was no abdominal distension, tenderness, organomegaly or free fluid. Her breast and digital rectal examinations, too, were unremarkable. Laboratory findings were consistent with cholestasis and acute liver failure (Table).

**Table: Summary of investigations**

	On admission	After 3 cycles of chemotherapy
Aspartate aminotransferase (8-33 U/L)	362	213
Alanine aminotransferase (7-56 U/L)	376	135
Gamma glutamyl transferase (0-30 U/L)	90	32
Alkaline phosphatase (44 -147 U/L)	1692	310
Lactate dehydrogenase (140 - 280 U/L)	366	110
Total bilirubin (0.3 - 1.2mg/dL)	24.18	3.64
Direct bilirubin (<0.3 mg/dL)	17.89	2.60
Albumin (3.4 - 5.4 g/dL)	2.9	3.3
PT-INR (10 -12sec/1 -2 sec)	3.6	1.18
Erythrocyte sedimentation rate (<15mm/hr)	132	45

Serological tests for hepatitis A, hepatitis B, hepatitis C, cytomegalovirus and human immunodeficiency virus 1 and 2 were negative. She also tested negative for antinuclear antibodies, anti-mitochondrial antibodies, anti-liver-kidney microsomal antibodies and anti-smooth muscle antibodies. Ultrasound scan (USS) of the abdomen was normal. Chest radiograph revealed a mediastinal mass with bilateral hilar lymphadenopathy. (Figure 01) Contrast enhanced computed tomography of the abdomen and chest confirmed a mediastinal lymph node mass measuring 8 cm x 6.5 cm x 5 cm seen on the left side of the lung involving the para tracheal, subcarinal, subaortic & hilar mediastinal nodes. The liver was mildly enlarged with a smooth outline, there was no intra hepatic or extra hepatic biliary duct obstruction or focal liver lesions. Cervical lymph node biopsy confirmed the diagnosis of nodular sclerosing HL. Positron emission tomography demonstrated hyper- metabolic, prominent and enlarged lymph nodes in the cervical, axillary, mediastinal, mesenteric and splenic hilar groups. The liver appeared normal and the intra and extra hepatic bile ducts were within normal limits. (Figure 02)

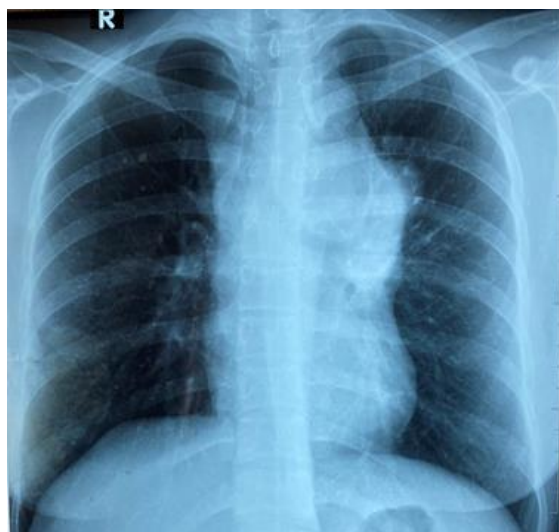


Figure 01: Chest- X-ray PA

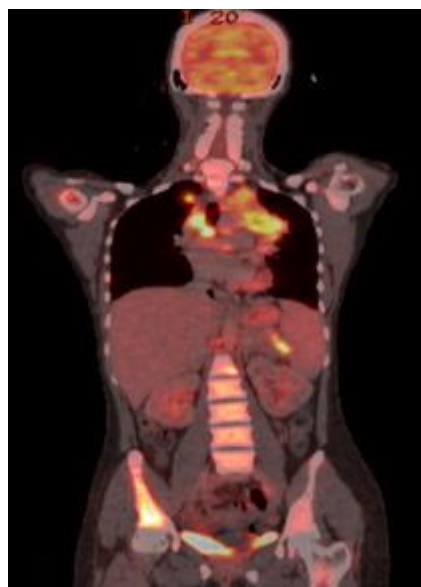


Figure 02: Positron emission tomography scan before treatment

A diagnosis of stage IVB nodular sclerosing HL was made according to the Cotswolds-modified Ann Arbor classification. To further evaluate for biliary obstruction, a magnetic resonance cholangio pancreatogram was performed which did not show any evidence of obstruction in the intrahepatic or extra hepatic bile ducts or in the pancreatic ducts. Although a liver biopsy was planned, to further investigate a possible cause for cholestatic jaundice, the patient and the next of kin refused liver biopsy. Hence, a decision was made to go ahead with chemotherapy, after referring to the oncology team. Six cycles of ABVD regimen [doxorubicin (Adriamycin), bleomycin, vinblastine and dacarbazine] were commenced. Following completion of six cycles, the patient had a marked clinical improvement with resolution of jaundice and pruritus and improvement of the liver profile as shown in Table 01.

## Discussion

This patient, who presented with cholestatic jaundice with underlying HL, raised both diagnostic and a therapeutic challenge. Although jaundice in lymphoma is not rare [1], it is found as the presenting complaint in only 4% of patients with HL [2]. When a HL patient presents with cholestatic jaundice, it is of utmost importance to exclude other causes of liver abnormalities as PC is a diagnosis of exclusion. Multiple investigations did not reveal any anatomical obstruction to bile flow in our patient and there was no direct neoplastic involvement of the liver or nodal compression of bile ducts. Blood investigations ~~too~~ excluded infection with HIV 1 & 2, CMV, EBV and Hepatitis A, B & C as the cause of cholestasis. After a meticulous workup, her manifestation was in concordance with the diagnosis of paraneoplastic cholestasis [3].

The exact pathophysiology of paraneoplastic cholestasis has not yet been clearly described, although it is postulated to be due to release of cholestatic cytokines or due to hormones such as androgens or 17-alkylating oestrogens released from cells [4]. We faced a diagnostic challenge as we were unable to proceed with a liver biopsy to arrive at a histological diagnosis to distinguish between IIC and VBDS [5]. Nevertheless, it is questionable as to whether it would have altered our management plan. Although IIC has a better prognosis compared to VBDS [5], the ultimate management is chemotherapy in both entities [6,7,8].

Other treatment options have been considered in the literature, such as steroids, intravenous immunoglobulins and ursodeoxycholic acid for VBDS, without any solid evidence [9]. Radiotherapy is considered as a second option by Yalcin *et al.* for patients failing chemotherapy for IIC, with complete resolution of jaundice [10]. Our patient was started on chemotherapy following confirmation of the diagnosis of HL and showed marked improvement of her cholestasis after 3 cycles of ABVD, with complete resolution of jaundice.

## Conclusion

PC should be considered as a differential diagnosis in patients presenting with jaundice related to HL, especially in those where no other apparent cause is found. It is a life-threatening complication of HL that can progress to fulminant hepatic failure unless managed with early and appropriate interventions.

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