CASE REPORT

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A Case of Hairy Cell Leukaemia Associated with Miliary Tuberculosis

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Abstract

A case of disseminated tuberculosis presented with fever, cough, and severe anaemia. Patient was initially diagnosed to have miliary tuberculosis based on radiological findings and bone marrow examination. Miliary tuberculosis is not a rare presentation of tuberculosis in India. Haematological malignancies and miliary tuberculosis may have many common presenting clinical symptoms, which may lead to masking of the underlying haematological malignancy. We hereby report a case of miliary tuberculosis which was later diagnosed to be a case of hairy cell leukaemia also.

Keywords: Anaemia, cladribine, pancytopenia, splenomegaly, tuberculosis, vemurafenib.

Introduction

Hairy cell leukaemia (HCL) was reported in 1958 by Bouroncle and colleagues as an indolent malignancy associated with pancytopenia and splenomegaly that accounted for 2% of all leukaemias[1]. Hairy cell leukaemia is primarily a disease of middle-aged men. The age of the patients reported has ranged from the 20's to the 80's, but the average age is in the low 50's. The male: female ratio is approximately 4:1[2]. HCL, typically results in reduction in the production of normal red blood cells, platelets, mature granulocytes and monocytes. The increased production of malignant cells, along with a reduction in these mature elements, results in a variety of systemic consequences, including splenomegaly, anaemia, bleeding, and an increased risk of infection[2].

Miliary tuberculosis (TB) is a potentially fatal form of tuberculosis caused by the spread of *Mycobacterium tuberculosis* bacilli. Miliary TB can arise as a result of progressive primary infection or via reactivation of a latent focus with subsequent spread via the blood stream. Since its first description by John Jacob Manget in 1700, it is estimated that miliary tuberculosis accounts for 2% of all cases of tuberculosis in immunocompetent individuals and up to 20% of all extrapulmonary tuberculosis cases[3]. The clinical presentation of miliary tuberculosis is variable, the most common extrapulmonary sites include the lymphatic system, bones and joints, liver, central nervous system (CNS), and adrenal glands. Disseminated TB can give rise to striking haematological changes, so much so that a primary blood disorder is mistakenly diagnosed. The reported haematological abnormalities include anaemia, leucocytopenia, and pancytopenia. Various theories put forward to explain the haematological manifestations of TB include abnormal splenic function and direct invasion of bone marrow[4].

Case report

A 38-year-old male patient, resident of Uttar Pradesh, India, presented to us on 16th of March, 2021, with a history of fever of 2 months duration. Fever was associated with dry cough, breathing difficulty, night sweats, generalised weakness, and loss of appetite. Patient was also complaining of diffuse vague abdominal pain associated with fullness. He initially developed generalised body ache with fatigue, followed by fever and loss of appetite, which made him to lose 5 - 6 kgs of weight over a period of two months. He also complained of shortness of breath on walking a few hundred yards – which was quite unusual for him. Fever was of moderate grade (101° F - 102° F) and intermittent in nature. Patient was pyrexial on admission and was running a temperature of 101.4° F with BP of 100/80 mm of Hg, respiratory rate of 24 per minute and pulse rate of 116 per minute. Patient was fully conscious with GCS 15/15. On general examination, the patient appeared pale, slightly icteric and also was noted to have skin bruises; but there was no obvious lymphadenopathy. Patient was found to have koilonychia. Cardiovascular and neurological examination was unremarkable. On chest auscultation, bilateral coarse bi-basal rales were heard, but breath sounds were not diminished. On abdominal examination, abdomen was distended; on palpation, liver was palpable three fingers below the right costal margin, but spleen was significantly enlarged and palpable with the splenic edge extending more than 8 cm below the left costal margin, which was also confirmed with a dull note on percussion. On imaging,

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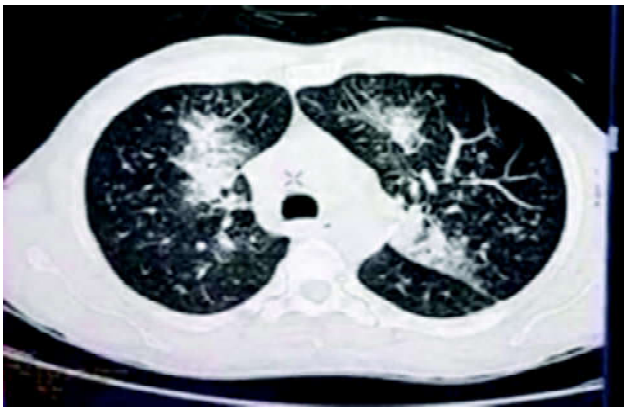

Fig. 1: *HRCT chest.*

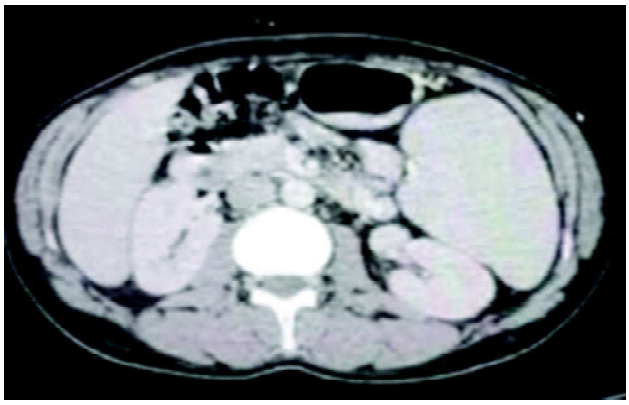

Fig. 2: *CE-CT abdomen.*

HRCT lung (in Fig. 1), showed multiple pretracheal, prevascular and carinal lymph nodes and also consolidation changes with miliary pattern, which are suggestive of thoracic tuberculosis. Abdominal CECT (Fig. 2) showed features suggestive of abdominal tuberculosis with splenomegaly with involvement of abdominal lymph nodes and ileal loops. Bone marrow aspiration/biopsy initially done at our hospital revealed pancytopenia with marked lymphocytosis and plasmacytosis and granulomatous inflammation (possibility of TB cannot be ruled-out). Lab parameters revealed ESR of 130, GBP (Table I) showed pancytopenia with macrocytic normochromic RBCs with lymphocytosis. Reticulocyte count was 0.30%, and his Vit B12 levels were in normal range, i.e., 391 pg/ml. Iron studies – Ferritin: 262 ng/ml, TIBC: 262 ug/dl, iron: 10 ug/dl. In consideration with the presenting clinical symptoms and bone marrow biopsy findings, along with the haematological and radiological reports, we diagnosed it as a disseminated tuberculosis with involvement of the bone marrow. Patient was initiated on anti-tuberculous therapy with low dose prednisone 20 mg OD in view of his bone marrow involvement. He was also transfused with 2 units of PRBC. The haematological abnormalities were only slightly reverted with a four-week course of anti-tuberculous treatment and low dose steroids. Patient remained apyrexial and haemodynamically stable at the end of the fourth week; hence his prednisone dose was tapered. However, in view of the COVID second surge, he was discharged on request with ATT medications prescribed on 19th April, 2021.

The patient was again reviewed in mid-May. We noticed that, his clinical condition was deteriorating further with recurrent episodes of fever. Unresponsive clinical condition with ongoing pancytopenia, even after six weeks of ATT, alerted us to contemplate a possibility of haematological malignancy. Hence, the patient was promptly referred to a haematologist for a repeat bone marrow aspiration/biopsy

Table I:

Inv.		16 March	18 March	19 March	20 March	21 March	24 March	25 March	28 March
CBC	Hb.	3.8	3.8	4		4.3	5	5.9	5.7
	TLC	0.48	0.36	0.37		0.26	0.43	0.52	0.3
	N/L	29/66	33/64	22/76		23/73	25/65	29/69	38/53
	RBC	1.16	1.07	1.29		1.45	1.63	1.95	1.38
	PCV	12.5	11.7	12.6		13.5	15.7	18.3	13.6
	MCV	107.8	109.3	97.7		95.2	96.3	93.8	98.6
	MCH	32.8	32.7	31		29.7	30.7	30.3	31.2
	MCHC	40.4	29.9	31.7		31.2	31.8	32.2	31.6
	PC	60	50	60		77	70	75	70
	ESR		150						
	ANC								
GBP			Pancytopenia: macrocytic normochromic RBCs, lymphocytosis						

and further expert opinion. He was reviewed by a haematologist and a repeat bone marrow aspiration/biopsy was done. The final impression of the repeat biopsy was hairy cell leukaemia and he was further advised to undergo Flow cytometery immuno-phenotyping and BRAF V600 Emutation testing. Comprehensive CLPD immuno-phenotype flow cytometry (25/5/21) concluded hairy cell leukaemia.

Discussion

Our patient was non-diabetic with no background co-morbidities. He was also screened for viral infections (HIV, Hepatitis B and Hepatitis C), which was found to be negative. Clinical manifestations of miliary TB are most likely to be subacute or chronic, the median duration of illness prior to clinical presentation was two months.The question of non-response to the primary treatment is clearly important and the alternative diagnosis should be reviewed with promptness. Hairy cell leukaemia (HCL), a rare and slow-progressive B-cell lymphoproliferative disease, enhances predisposition to infectious complications, especially to disseminated mycobacterial infections[6]. Most patients with HCL present with symptoms related to splenomegaly or cytopenias, (e.g., anaemia, thrombocytopenia, neutropenia, monocytopenia), including weakness and fatigue, infections of variable severity, and/or haemorrhagic findings such as gingival bleeding, ecchymoses, epistaxis[7]. Splenomegaly is frequently massive and may be the most prominent physical finding, mild hepatomegaly may be found in one-fifth of the patients. The most striking laboratory finding in about two-thirds of the patients with HCL is a moderate pancytopenia finding rarely present in patients with CLL[2] HCL is initially suspected in patients presenting with pancytopenia , splenomegaly without lymphadenopathy. Evaluation requires a bone marrow trephine biopsy and aspirate in conjunction with immunophenotyping and flow cytometry. Therapy is indicated only when the patient develops symptoms, significant cytopenias or symptomatic splenomegaly. Purine analogs, i.e., cladribine is the preferred initial treatment for most patients with symptomatic HCL and normal renal function[5]. Haematologist suggested chemotherapy with cladribine, a purine nucleoside analog. Our patient received five doses of cladribine (0.14 mg/kg = 8.5 mg), from 5/6/2021 to 10/6/21. He was reviewed in our OPD recently. Currently he remains apyrexial and his general condition is stable.

The BRAF inhibitor Vemurafenib is an investigational therapy for hairy cell leukaemia (HCL) with *BRAF* mutation[5]. In conclusion, hairy cell leukaemia, a predisposing clinical condition for disseminated tuberculosis.

Conclusion

In conclusion, our case elucidates that physicians must maintain a high index of suspicion when an immunocompetent or healthy young patient presents with a history of pancytopenia and prolonged fever. It is important to evaluate both the positive and negative symptoms at the same time when determining the treatment response.

Early diagnosis and timely referral of patients to a specialist is critical in preventing complications that can arise due to delayed treatment. Physician's awareness of symptoms and patient-physician communication is paramount to unravel the underlying unknown diagnosis that is contributing to the presenting primary infection.

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