International Journal of Medical and Health Research
www.medicalsciencejournal.com
ISSN: 2454-9142
Received: 02-03-2021, Accepted: 20-03-2021, Published: 15-04-2021
Volume 7, Issue 4, 2021, Page No. 19-21

Significance of flower cells in the early diagnosis of adult T-Cell leukemia

Srikumar Chakravarthi[1], Karthikesh Jayakumar[2], Barani Karikalan[3]

[1] Faculty of Medicine, Mahsa University, Selangor, Malaysia

[2] Department of Pathology, KSR Institute of Dental Sciences and Research, Trichengode, Tamil Nadu, India

[3] Department of Pathology, Perdana University - Royal College of Surgeons in Ireland, Selangor, Malaysia

Abstract

Adult T-cell leukaemia (ATL) is a mature T cell malignancy that is peculiar in its pathogenesis due to its association with the human T-cell lymphotropic virus, HTLV-I infection. The common manifestation of ATL is as leukaemia in 75% of cases and as pure lymphoma in the rest. The disease outcome of ATL is poor since treatment response is generally poor or partial and short lived in most patients. ATL, almost always occurs in adults with average age affected being the mid-60s with no gender Predilection. Presence of atypical T lymphoid cells known as the flower cells is pathognomonic of the disease. Other diagnostic tests such as bone marrow examination and lymph node histology are indistinguishable from other peripheral T cell lymphomas. Immunophenotyping is often inconclusive and non-specific. Molecular testing for HTLV-1 is available only in selected research institutions and hence remains inaccessible to many. The above said difficulties lead to difficulty in identifying ATL cases. We present a case of ATL with a brief literature review, emphasizing the importance of recognising flower cells in peripheral blood smear.

Keywords: adult t-cell leukaemia, atypical lymphoid cells, flower cells

Introduction

Adult T-cell leukaemia (ATL) is a mature T cell malignancy. ATL is peculiar in its pathogenesis since it is associated with the human T-cell lymphotropic virus, HTLV-I infection. HTLV-I is found in cells from almost all ATL cases, with extremely rare exceptions [1]. ATL and HTLV-I are frequent in Japan, the Caribbean areas, and some areas of South Africa and America, and in people who have migrated from these areas to other countries [2].The common manifestation of ATL is as leukaemia in 75% of cases and as pure lymphoma in the rest [3]. Among the lymphoma forms, extra-nodal ATLs confined to the central nervous system and gut have been reported. The disease outcome of ATL is poor since treatment response is generally poor or partial and short lived in most patients [4, 5, 6].

Case report

A 67 year old male patient who is on regular treatment and follow up for diabetes mellitus was found to be clinically anemic. Full blood count done showed hemoglobin to be 11g. His white blood cell count was 276000 and platelet count was 68000. His peripheral blood picture showed normocytic normochromic red blood cells and increased white blood cells. Abnormal flower shaped white blood cells were noticed throughout the peripheral smear [Fig1, Fig2, Fig3]. A preliminary diagnosis of adult T cell leukemia was made and the patient was referred to a higher center for confirmation of diagnosis and further management.

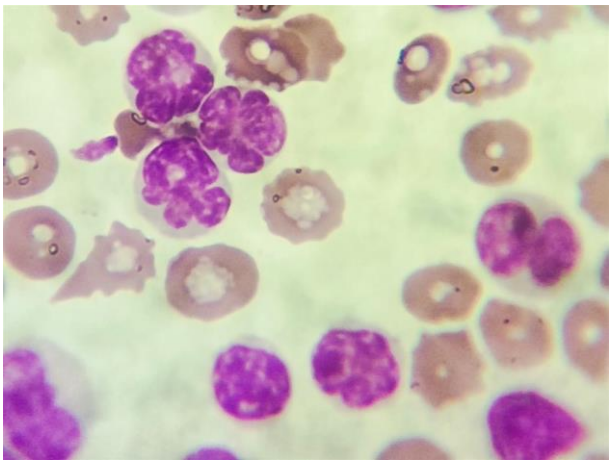

Fig 1

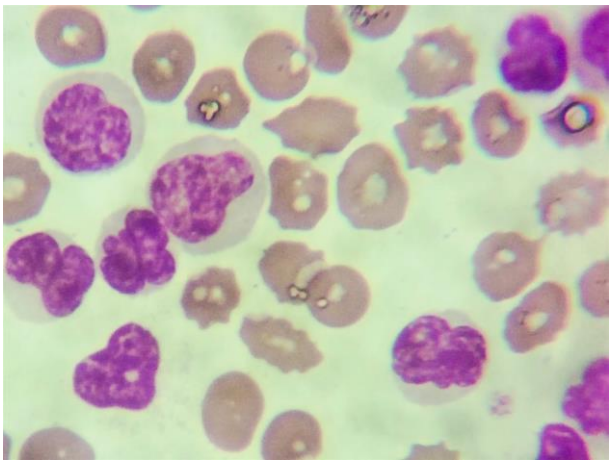

Fig 2

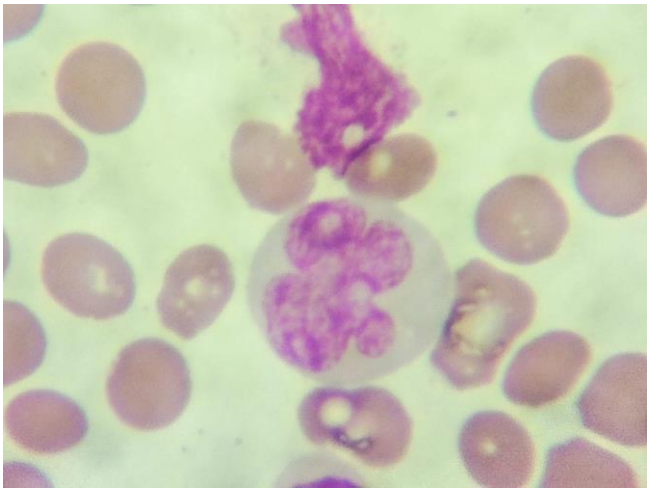

Fig 3

Discussion

ATL, almost always occurs in adults and is very rare in children. Very few cases in childhood have been previously reported [8]. The average age affected is the mid-60s with no gender prevalence. Occasionally, Familial ATLs have been recorded in Japan, England and USA [9, 10] which raises the possibility of genetic predisposition. Clinical classification of ATL includes the following four types: acute, chronic, lymphomatous, primary cutaneous tumoral or smoldering [3, 10]. The most frequently found type of clinical presentation is that of acute, which is about 65% of cases. This form of ATL presents itself with various systemic signs and symptoms, organomegaly, specifically lymphadenopathy, and leukaemia. The chronic form generally presents as lymphocytosis over months or a few years, skin lesions, no organomegaly or mild lymph node involvement, and normal to slightly elevated lactate dehydrogenase. Smouldering ATL is generally asymptomatic or may present as skin rashes with normal white blood cell count, no lymphocytosis and <3% atypical lymphoid cells. Less than one third of patients have lymphoma with no leukemia component. Chronic and smouldering ATL progressing to acute form is frequently reported with hemophagocytic syndrome as the initial sign of disease transformation [11].

Blood pictures show a variable range of anaemia and thrombocytopenia. Eosinophilia and neutrophilia may be seen. In leukemic types, the white blood cell count is elevated with atypical lymphocytes in the peripheral blood that are pleomorphic, with the major population of cells being medium sized lymphocytes showing chromatin condensation and a polylobulated or convoluted nucleus, invisible nucleolus, named as a “flower cell”. Occasionally, immunoblast-like cells or blasts exhibiting prominent nucleolus and diffuse chromatin may be noticed in the circulation. In the pure lymphoma forms and smouldering types of ATL, the blood picture is normal [12].

Bone marrow studies may show proliferation of lymphoid cells with morphology similar to those seen in the blood. The trephine biopsy of bone marrow may show a variable amount of atypical lymphoid cells depending on the degree of involvement. Even in the leukaemic types of ATL, the presence of atypical lymphoid cells may be very less or patchy. The extent of atypical lymphoid cell proliferation may range from interstitial to diffuse. Some cases may present with features of hypercalcaemia owing to action of increased osteoclasts that result in bone resorption. ATL has similar lymph node morphology as of other T cell neoplasms [13, 14].

The immuno phenotypic profile of the ATL lymphoid cell is the same as that of a mature activated T cell. The cells are usually CD2 and CD5 positive and are often CD7 negative. The cells may show weak or negative expressions of CD3 and T-cell receptors (TCR)-β in the cell membrane, but show cytoplasmic expression. Most commonly expressed immunophenotyping is that of a positive expression for CD4 and negative expression for CD8, but exceptions where both the markers are expressed together have been recorded and also have been found to have a poor clinical outcome [15]. The most distinctive immunophenotypic feature is the positivity for CD 25 owing to the presence of interleukin-2 (IL-2) receptors in the neoplastic cells. This feature is distinctive but not specific to ATL since it is also found in other T-cell neoplasms like prolymphocytic T cell leukaemia and Sezary syndrome in a lower density. Molecular test for HTLV-I is not generally needed for ATL disease confirmation in cases with typical clinical presentation and have a HTLV-I positivity in serological testing. But, if patients show HTLV-I negativity in serological testing and are strongly suspected to have ATL, molecular testing for HTLV-I is essential in the pure lymphoma types to differentiate them from other T-cell malignancies, and, also to differentiate smouldering ATL patients from a healthy carrier of the virus [12, 16].

The clinical outcome of ATL is generally poor, with average survival being less than a year, for both acute types and lymphoma types. The projected four year outcome is expected to be about five percent for both the types. Smouldering and chronic ATL tend to be slightly better, having a projected four year outcome of 62% and 26.9% respectively [17]. Age, clinical types, performance status, raised LDH levels, increased β2-microglobulin, elevated serum CD25, raised serum neuron-specific enolase, increased proliferative rate and signs of hypercalcaemia are the major factors influencing patient prognosis [18, 19]. In chronic ATL, the proliferative rate of the atypical cells estimated by Ki-67 expression, LDH and albumin levels seem to differentiate subtypes with unfavourable and favourable outcome [20]. Currently, the preferred drug regimen is IFN-α/ZDV, a formula that has been reported to a positive effect on the outcome of most ATL cases [21].

Conclusion

Since molecular tests for HTLV-1 virus detection are available only in very few research institutions, flower cells identified in the peripheral blood smears can prove to be crucial since this is a finding that requires a simple test that allows easy spotting of acute ATL cases.

References

1. Kikuchi M, Jaffe ES, Ralfkiaer E. Adult T-cell leukaemia/lymphoma. In: Jaffe ES, Harris NL, Stein H, Vardiman JW, eds. World Health Organization classification of tumours. Tumours of haematopoietic and lymphoid tissues. Lyon: IARC Press, 2001, 200-203.
2. Matutes E, Catovsky D, Adult T. cell leukaemia lymphoma. In: Whittaker JA, ed. Leukaemia, 3rd edn. Oxford: Blackwell Scientific Publications, 1998, 416-433.

3. Shimomaya M. Diagnostic criteria and clinical subtypes of ATLL. A report from the Lymphoma Study Group (1984–87). Br J Haematol,1991:79:428-437.
4. Hattori T, Asou N, Suzushima H *et al.* Leukaemia of novel gastrointestinal T-lymphocyte population infected with HTLV-I. Lancet,1991:337:76-77.
5. Cabrera M E, Labra S, Ford A *et al.* HTLV-I induced intestinal lymphoma. Leuk Lymphoma,1999:35:637-640.
6. Dungerwalla M, Osuji N, Waldman AD *et al.* Isolated central nervous system involvement in adult T-cell lymphoma/leukaemia. Br J Haematol,2005:130:511-515.
7. Pombo de Oliveira MS, Matutes E, Famadas LC *et al.* Adult T-cell leukaemia/lymphoma in Brazil and its relation to HTLV-I. Lancet,1990:336:987-990.
8. Yamaguchi K, Sung Yul L, Shimizu T. *et al* Concurrence of lymphoma type adult T-cell leukemia in three sisters. Cancer,1985:561:688-1690.
9. Matutes E, Spittle MF, Smith NP *et al.* The first report of familial adult T-cell leukaemia lymphoma in the United Kingdom. Br J Haematol,1995:89:615-619.
10. Bittencourt AL, Vieira MG, Brites CR, Farré L, Barbosa HS. Adult T-cell leukemia/lymphoma (ATL) in Bahia, Brazil: Analysis of prognostic factors in a group of 70 patients. Am J Clin Pathol,2007:128:875-82.
11. Aouba A, Lambotte O, Vasiliu V *et al.* Hemophagocytic syndrome as a presenting sign of transformation of smouldering to acute adult T-cell leukemia/lymphoma: efficacy of anti-retroviral and interferon therapy. Am J Hematol,2004:76:187-189.
12. Matutes E. "Adult T-cell leukaemia/lymphoma." Journal of clinical pathology,2007:60(12):1373-7. doi:10.1136/jcp.2007.052456.
13. Lennert K, Kikuchi M, Sato E *et al* HTLV-positive and -negative T-cell lymphomas. Morphological and immunohistochemical differences between European and HTLV-positive Japanese T-cell lymphomas. Int J Cancer 19853565-72.
14. Ohshima K, Suzumiya J, Sato K *et al* Nodal T-cell lymphoma in an HTLV-1 endemic area: proviral HTLV-1 DNA, histological classification and clinical evaluation. Br J Haematol,1998:101:703-711.
15. Tamura K, Unoki T, Sagawa K.*et al* Clinical features of OKT4+/OKT8+ adult T-cell leukemia. Leuk Res,1985:91:353-1359.
16. Karthikesh Jaya kumar, Sri Kumar Chakravarthi, Barani Karikalan. Pure Red Cell Aplasia of Pregnancy - A Potentially Fatal and Rare Entity. Academic Journal of Cancer Research,2020:13(2):22-24.
17. Shimoyama M. Treatment of patients with adult T-cell leukemia-lymphoma: an overview. In: Takatsuki K, Hinuma Y, Yoshida M, eds. Advances in adult T-cell leukemia and HTLV-I research. Tokyo: Japan Scientific Societies Press,1992:39:43-56.
18. Sadamori N, Mine M, Hakariya S.*et al* Clinical significance of B2-microglobulin in serum of adult T cell leukemia. Leukemia,1995:9:594-597.
19. Nishimura S, Asou N, Suzushima H *et al.* P53 gene mutation and loss of heterozygosity are associated with increased risk of disease progression in adult T cell leukemia. Leukemia,1995:9:598-604.
20. Shirono K, Hattori T, Takatsuki K. A new classification of clinical stages of adult T-cell leukemia based on prognosis of the disease. Leukemia,1994:8:1834-1837.
21. Bazarbachi A, Panelatti G, Ramos JC, Tortevoye P, Otrock Z, Taylor G, A worldwide meta-analysis on the use of zidovudine and interferon-alpha for the treatment of adult T-cell leukemia/ lymphoma. Blood,2007:110:610a-1a.