Title

Incidence of Constitutional Chromosomal Abnormalities in a Community Hematology-Oncology Clinic

Journal

Proceedings of the UCLA Department of Medicine, 19(1)

Authors

Keung, Yi-Kong
Hu, Eddie Hong-Long

Publication Date

2015-02-02

CLINICAL COMMENTARY

Incidence of Constitutional Chromosomal Abnormalities in a Community Hematology-Oncology Clinic

Yi-Kong Keung, M.D., FACP, and Eddie Hong-Long Hu, M.D., FACP

Abstract

To investigate the constitutional chromosomal abnormalities in a more community-like setting, we conduct a pilot study of the incidence of constitutional chromosomal abnormalities in our clinic. A total of 274 bone marrow examinations were performed between January 2010 and June 2011. Out of 199 conventional karyotypes obtained, three patients (1.7%) with constitutional chromosomal abnormalities were found: two had pericentric inversion of chromosome 9, inv(9)(p12q13), and one had pericentric inversion of chromosome 2, inv(2)(p11.2q13). The incidence is similar to the incidence as reported in the current literature.

Introduction

Constitutional chromosomal abnormalities in apparently normal individuals have been studied in the general population. Constitutional pericentric inversion of chromosome 9 [inv(9)] occurs in approximately 0.8–2% of the normal population[1,2] and is generally regarded as a normal variant, as is constitutional pericentric inversion of chromosome 2 [inv(2)].[3] However, these constitutional abnormalities may not be entirely benign as they have been associated with infertility, recurrent spontaneous abortion, as well as with myeloid leukemia.[4,5] Inv(9) has also been associated with delayed engraftment after autologous and allogeneic transplantation from donors with inv(9), though this remains controversial.[6-8] To investigate the incidence of constitutional chromosomal abnormalities in a community setting, we conducted a pilot study of the incidence of constitutional chromosomal abnormalities in our clinic.

Patients and Methods

Between January 2010 and June 2011, 248 patients underwent bone marrow examination for various hematological indications at our clinic. Of these patients, 181 underwent cytogenetic analysis. We reviewed the clinical charts. The median age was 68.6 (range 20.5-89.5). Fifty-three percent were male and 47% female.

Results

A total of 274 bone marrow examinations were performed. Of the 274 bone marrow examinations, 199 conventional karyotypes were obtained. Three patients were found with constitutional chromosomal abnormalities: two had pericentric inversion of chromosome 9, inv(9)(p12q13), and one had pericentric inversion of chromosome 2, inv(2)(p11.2q13).

Case 1

A 47-year-old Japanese male with cryptococcal meningitis was referred for evaluation of suspected non-HIV CD4 lymphocytopenia.[9,10] At diagnosis, his absolute CD3 count was 13/μL, CD4 count 3/μL, and CD8 count of 4/μL. Subsequent workup showed normal immunoglobulin levels, negative HIV by serology and by PCR, and negative for HTLV-I/II antibody. Bone marrow examination showed no evidence of lymphoma with 46,XY,inv(9)(p12q13)$_c$ [20]. A year later, his WBC 4,900/μL, hemoglobin 14.3g/dL, and platelet 231,000/μL, neutrophils 84%, and lymphocytes 7%; the absolute CD3 was 251/μL, CD4 34/μL, and CD8 184/μL.

Case 2

A 66-year-old female with hypertension and hyperlipidemia presented with asymptomatic leukocytopenia since 2005. Physical examination is unremarkable. Initial work-up showed normal serum protein electrophoresis, negative HIV serology, negative antinuclear antibody, and hepatitis serology. By 2011, WBC was 3,100/μL, hemoglobin 12.2g/dL, and platelet 289,000/μL. With persistent leukocytopenia, she underwent bone marrow examination, which showed normal morphological findings with 46,XX,inv(9) (p12q13)$_c$[20].

Case 3

A 69-year-old male with history of hypertension and gastroesophageal reflux disorder presented with asymptomatic lymphocytosis, WBC 17,800/μL, Hgb 13.5 g/dL, platelet 227,000/μL, with neutrophils 27%, lymphocytes 68%, and monocytes 4%. Physical examination showed no significant lymphadenopathy or hepatosplenomegaly. Bone marrow examination and the flow cytometry showed majority of CD19+ and CD20+ B-lymphocytes with co-expression of CD5 and CD23, diagnostic of chronic lymphocytic leukemia. The chromosomal analysis of the bone marrow showed

49,XY,inv(2)(p11.2q13),+12,+18,+19[2]/46,XY, inv(2)(p11.2q13)$_c$[18].

Discussion

It is generally believed that constitutional pericentric inversion of chromosome 9, chromosome 2, and other chromosomes are benign and of no clinical significance, although they have been implicated with infertility, recurrent spontaneous abortion, and myeloid leukemia.[4,5] If it is true, the incidence of the constitutional chromosomal abnormalities detected in the bone marrow biopsies in our hematology patients should be similar to the incidence estimated from other populations, such as prenatal amniotic samples. The crude incidence of constitutional chromosomal abnormalities is estimated to be 1.7% in this pilot study, which is similar to the incidence reported in the literature based on prenatal amniotic fluid specimens[1] or adult peripheral blood.[2] The occurrence of constitutional abnormalities in our patients with non-HIV related lymphocytopenia, asymptomatic leukocytopenia, and chronic lymphocytopenia respectively, while intriguing, may just be coincidental. In view of the limited sample size in this pilot study, a larger study is required to confirm our finding.

REFERENCES

1. **Hsu LY, Benn PA, Tannenbaum HL, Perlis TE, Carlson AD**. Chromosomal polymorphisms of 1, 9, 16, and Y in 4 major ethnic groups: a large prenatal study. *Am J Med Genet*. 1987 Jan;26(1):95-101. PubMed PMID: 3812584.
2. **Tawn EJ, Earl R**. The frequencies of constitutional chromosome abnormalities in an apparently normal adult population. *Mutat Res*. 1992 Sep;283(1):69-73. PubMed PMID: 1380666.
3. **Hysert M, Bruyère H, Côté GB, Dawson AJ, Dolling JA, Fetni R, Hrynchak M, Lavoie J, McGowan-Jordan J, Tihy F, Duncan AM**. Prenatal cytogenetic assessment and inv(2)(p11.2q13). *Prenat Diagn*. 2006 Sep;26(9):810-3. PubMed PMID: 16821252.
4. **Daya S**. Issues in the etiology of recurrent spontaneous abortion. *Curr Opin Obstet Gynecol*. 1994 Apr;6(2):153-9. Review. PubMed PMID: 8193255.
5. **Mozziconacci MJ, Sobol H, Philip N, Stoppa AM, Brunel V, Granel B, Blaise D, Sainty D, Birnbaum D, Lafage-Pochitaloff M**. Constitutional balanced pericentric inversions of chromosomes X, 2, and 5 in myeloid malignancies. *Cancer Genet Cytogenet*. 1998 Nov;107(1):28-31. PubMed PMID: 9809030.
6. **Keung YK, Knovich MA, Hurd DD, Pettenati M**. Constitutional pericentric inversion of chromosome 9 and bone marrow transplantation. *Br J Haematol*. 2003 Nov;123(4):748-9. PubMed PMID: 14616986.
7. **Keung YK, Pettenati M, Hurd DD, Powell BL, Buss DH**. Allogenic marrow grafts from unrelated donors with congenital pericentric inversion of chromosome 9. *Br J Haematol*. 2002 Jan;116(1):237-8. PubMed PMID: 11848092.
8. **Lee SG, Park TS, Lim G, Lee KA, Song J, Choi JR**. Constitutional pericentric inversion 9 and hematological disorders: a Korean tertiary institution's experience over eight years. *Ann Clin Lab Sci*. 2010 Summer;40(3):273-7. PubMed PMID: 20689141.
9. **Smith DK, Neal JJ, Holmberg SD**. Unexplained opportunistic infections and CD4+ T-lymphocytopenia without HIV infection. An investigation of cases in the United States. The Centers for Disease Control Idiopathic CD4+ T-lymphocytopenia Task Force. *N Engl J Med*. 1993 Feb 11;328(6):373-9. Review. PubMed PMID: 8093633.
10. **Zonios DI, Falloon J, Bennett JE, Shaw PA, Chaitt D, Baseler MW, Adelsberger JW, Metcalf JA, Polis MA, Kovacs SB, Kovacs JA, Davey RT, Lane HC, Masur H, Sereti I**. Idiopathic CD4+ lymphocytopenia: natural history and prognostic factors. *Blood*. 2008 Jul 15;112(2):287-94. doi: 10.1182/blood-2007-12-127878. Epub 2008 May 2. Erratum in: Blood. 2014 Jul 17;124(3):463. Kovacs, Stephen J [corrected to Kovacs, Stephen B]. PubMed PMID: 18456875; PubMed Central PMCID:PMC2442741.

Submitted February 2, 2015