Original Article

Chronic Myelogenous Leukemia in Eastern Pennsylvania: An Assessment of Registry Reporting

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Abstract: Background: Chronic myelogenous leukemia (CML) has been reportable to the Pennsylvania Cancer Registry (PCR) since the 1980s, but the completeness of reporting is unknown. This study assessed CML reporting in eastern Pennsylvania where a cluster of another myeloproliferative neoplasm was previously identified. Methods: Cases were identified from 2 sources: 1) PCR case reports for residents of Carbon, Luzerne, or Schuylkill County with International Classification of Diseases for Oncology, Third Edition (ICD-O-3) codes 9875 (CML, BCR-ABL+), 9863 (CML, NOS), and 9860 (myeloid leukemia) and date of diagnosis 2001–2009, and 2) review of billing records at hematology practices. Participants were interviewed and their medical records were reviewed by board-certified hematologists. Results: PCR reports included 99 cases coded 9875 or 9863 and 9 cases coded 9860; 2 additional cases were identified by review of billing records. Of the 110 identified cases, 93 were mailed consent forms, 23 consented, and 12 medical records were reviewed. Hematologists confirmed 11 of 12 reviewed cases as CML cases; all 11 confirmed cases were BCR/ABL positive, but only 1 was coded as positive (code 9875). Conclusions: Very few unreported CML cases were identified, suggesting relatively complete reporting to the PCR. Cases reviewed were accurately diagnosed, but ICD-0-3 coding often did not reflect BCR-ABL-positive tests. Cancer registry abstracters should look for these test results and code accordingly.

Key words: *chronic myelogenous leukemia, disease notification, environmental, exposure, international classification of diseases codes, risk factors*

Introduction

Chronic myelogenous leukemia (CML) is a myeloproliferative neoplasm (MPN) characterized by unrestricted malignant proliferation of myeloid cells in the bone marrow. It is caused by an acquired genetic defect, a balanced translocation of chromosomes 9 and 22, which is characterized by the Philadelphia chromosome (shortened chromosome number 22) and the fusion of the ABL1 gene on chromosome 9 with the BCR gene on chromosome 22.[1] The BCR-ABL protein associated with the BCR-ABL fusion gene has enhanced tyrosine kinase activity that leads to increased bone marrow production of hematopoietic cells.[1]

CML accounts for 15% of leukemias in the United States, with an annual reported rate of CML of 1.6 to 2.0 per 100,000 and approximately 5,000 new cases per year.[2,3] Recent studies, however, suggest that the incidence may be underestimated.[4,5]

Since the 1980s, hospitals in Pennsylvania have been required by law to report all new cases of CML to the Pennsylvania Cancer Registry (PCR). Outpatient clinics and practices have been required to report since 2001. From 2001 through 2008, a statewide average of 177 CML cases per year were reported to the PCR (PA Department of Health, unpublished data). Previous to this investigation, evaluation of CML reporting to the PCR had not been conducted. The objectives of this study were to assess the completeness and accuracy of CML reporting and coding in a tri-county area of Eastern Pennsylvania. This investigation was conducted as part of a larger investigation of MPNs in an area with a known cluster of polycythemia vera and concern about environmental hazards.[6]

Methods

The methodology for the larger investigation is described elsewhere.[6] For the CML portion of the study, investigators received the names and addresses of all residents of Carbon, Luzerne, or Schuylkill County who were reported to the PCR with International Classification of Diseases for Oncology, Third Edition (ICD-O-3) codes 9875 (chronic myelogenous leukemia, BCR/ABL+), 9863 (chronic myelogenous leukemia, not otherwise specified) and 9860 (myeloid leukemia, not otherwise specified) with date of diagnosis from 2001 through 2009 or unknown. In general, cases are reported to the PCR by certified tumor registrars (CTRs) or health information management (HIM) staff in hospitals; doctors' offices and other nonhospital facilities report by faxing medical records which are then abstracted by PCR staff.

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This study was supported by a contract from the Agency for Toxic Substances and Disease Registry to the Pennsylvania Department of Health, #200-2009-32213. The findings and conclusions in this report are those of the authors and do not necessarily represent the official views or positions of the Centers for Disease Control and Prevention/Agency for Toxic Substances and Disease Registry or the Department of Health and Human Services.

PCR staff attempted to identify nonreported CML cases from outpatient facilities by requesting a billing report on all patients with a final International Classification of Diseases, Ninth Revision, Clinical Modification (ICD-9-CM) code of 205.1 at hematology/oncology practices in the tri-county and surrounding areas. PCR staff then matched persons identified by the billing report with the PCR database. For cases listed on the billing report but not in the PCR, medical records were faxed to the PCR; they were reviewed and abstracted by PCR staff.

Current contact information for CML cases was accessed using standard commercial and noncommercial tracing services. Cases were mailed packets of information which included a description of the study and a consent form. For deceased cases, the next of kin listed on the death certificate was mailed a packet. Repeated attempts, both by phone and by mail, were made to contact cases or next of kin who did not respond.

All cases or next of kin were asked to consent to an interview and to a review of the medical records pertaining to their leukemia diagnosis. Medical records were requested from named hospitals or physicians' offices, reviewed for relevance and completeness, arranged in chronologic order, and sent to an expert panel. Each case was reviewed by 3 of the 4 panel members, all of whom were board-certified hematologists. Cases were classified as confirmed cases if the patient met the 2008 WHO criteria for the accelerated or blast phase or the study criteria for chronic phase (BCR/ABL+ and WBC>50,000) or if all of the reviewing panel members determined the case was "definitely" or "probably" CML according to conventional hematology practice standards at the time of diagnosis.

Data were entered into the REDCap data management system[7] and exported into SAS for analysis. The study was approved by the institutional review boards at the University of Pittsburgh and the Pennsylvania Department of Health and conducted from May 2011 through November 2012.

Results

For tri-county residents, the PCR received 88 CML case reports with year of diagnosis from 2001 through 2009 and 11 CML case reports with no date of diagnosis specified but submitted during the same time period. Of these 99 cases, 18 (18%) were coded as 9875 (CML, BCR-ABL+) or both 9875 and 9863 (CML, NOS); 81 (82%) were coded only as 9863. An additional 9 cases with code 9860 (myeloid leukemia, NOS) were reported. Review of billing information at hematologist/oncologist offices by PCR staff led to the identification of 2 additional CML cases.

Of the 110 cases identified, 93 (85%) were successfully traced and were mailed consent forms. Of these 93 cases located, 23 (25%) consented, 4 (4 %) refused, 1 (1%) was unable to consent, and 65 (70%) did not respond despite repeated attempts to contact them by phone and mail. Medical records were obtained for 12 (52%) of the 23 who consented. Of the 11 not obtained, facilities were unable to find them (n = 2), unwilling to send them (n = 3), or required proof of executorship (n = 6). The expert panel of hematologists confirmed 11 (92%) of the 12 cases reviewed as CML cases; 9 were labeled as "definitely CML" by all 3 reviewers and 2 were labeled as "definitely CML" or "probably CML" by all 3. The case not confirmed as CML had been reported as 9860 (myeloid leukemia, not otherwise specified) and was negative for the BCR-ABL mutation. All 11 confirmed cases were BCR-ABL+ according to their medical records, but only 1 case (8%) was coded as 9875 (CML, BCR-ABL+) in the PCR.

Discussion

To our knowledge, this is one of the few studies of CML reporting in the United States. Our findings suggest that completeness of CML reporting to the PCR in the tri-county area was high, given that review of billing information in outpatient settings revealed that only 2 additional cases may have been missed. These 2 patients did not respond to our request to participate in the study and thus were not assessed by our expert panel, so their true case status is unknown.

A previous study indicated possible underreporting of CML to the Surveillance, Epidemiology, and End Results (SEER) Program of the National Cancer Institute by as much as 70%, possibly because of a change in reporting requirements or because outpatient cases were missed.[4] A recent comparison of claims data to registry data from outpatient clinics suggested that leukemia in general was underreported during the first year after diagnosis, but after allowing for time lags only about 4% of leukemia cases were missed.[5] We found very little evidence of underreporting of CML to the PCR from hematology practices in the tri-county area.

In the tri-county area, the accuracy of PCR reporting was much higher for CML than for the other MPNs as determined by the larger study,[6] with almost all reported CML cases confirmed by the expert panel. The diagnosis of CML is relatively straightforward because of the availability of genetic testing for the Philadelphia chromosome and the BCR-ABL fusion gene, which has been standard practice for many years, whereas the diagnoses of other MPNs involves use of a newer genetic test and more complex diagnostic criteria.

Although almost all CML cases reported were confirmed as CML, the specific codes assigned to cases were not accurate: all of the 11 cases we confirmed were BCR-ABL positive, which means that all 11 should have been coded as 9875. Instead, most were coded as 9863. Statewide in 2001 through 2008, more than 3 times as many cases of CML coded as 9863 were reported to the PCR than cases coded as 9875 (Pennsylvania Department of Health, unpublished data). Because testing for the Philadelphia chromosome or the BCR-ABL fusion gene is normally part of the diagnostic tests for patients with suspected CML, cancer registry abstracters should look for these results and code accordingly.

This investigation was limited by its low response rate (25%), which may have been partly due to "study fatigue" among residents of the tri-county area, the site of many studies of MPNs following the report of a suspected cluster

of PV cases in 2005.[8,9] We were only able to evaluate a small percentage of cases for accurate diagnoses and coding. The study may also have been limited by the scope of additional case-finding efforts at hematology practices; review of billing records was confined to practices within the tri-county and nearby areas.

Conclusion

In summary, our findings suggest that reporting of CML to the PCR is relatively complete, given that only 2 additional cases were identified by the billing record review at outpatient clinics. The subset of reported CML cases we reviewed were accurately diagnosed, reflecting use of BCR-ABL genetic tests, but inaccurately coded, reflecting inattention by coders to BCR-ABL test results.

Acknowledgments

We thank Wendy Aldinger, Robin Otto, and staff at the PA Cancer Registry for providing information from the PCR and for their review of billing records at hematology practices. We are also indebted to David Marchetto and James Logue at the Pennsylvania Department of Health for their facilitation of the study. We are grateful to Anthony Rizzardi of Hazelton General Hospital and the Pennsylvania Department of Health clinics in Wilkes Barre and Pottsville for sharing their clinic space with study interviewers. We appreciate the work of Dr. Emmanuel Besa as an expert panelist. We thank Brittany Eckberg for entering data and compiling copies of medical records for review. Finally, we thank the late Paul Roda for his assistance with this study as an expert panelist, advisor, and editor, and for his career-long work toward better detection and treatment of myeloproliferative disorders.

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