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Referrals for suspected hematologic malignancy: A survey of primary care physicians

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Little is known about referrals from primary care providers (PCPs) for suspected hematologic malignancies, including their clinical triggers and frequency. A random sample of 190 Massachusetts PCPs were presented with a vignette concerning a patient with a new finding of moderate anemia, asked how they would respond, and then asked what they would do if the patient returned with persistent anemia plus one additional sign or symptom. We also asked about referral behaviors for suspected hematologic malignancies during the prior year. A total of 134 (70.5%) PCPs responded. At first anemia presentation, only 3.8% reported referring to hematology. The development of a second sign or symptom yielded higher referral rates: pancytopenia = 88.7%, leukopenia = 63.9%, thrombocytopenia = 63.9%, lymphadenopathy = 42.9%, leukocytosis = 37.6%, night sweats = 25.6%, and weight loss = 23.3%. The median yearly number (interquartile range) of patients PCPs reported suspecting of having hematologic malignancy was 5 (3, 10), and the median formally referred was 5 (3, 10). We conclude that anemia plus signs and symptoms suggestive of myelodysplasia or leukemia (compared with those suggestive of lymphoma) are more likely to prompt hematology referral. In addition, given their rarity, the number of yearly referrals suggests a satisfactory level of PCP surveillance.

The primary care physician (PCP) is frequently the first point of contact for patients with cancer and thus serves a vital role in detecting symptoms, making diagnoses, and facilitating initiation of treatment. There is an extensive literature regarding PCP referrals for solid tumors, especially for malignancies such as breast and gastrointestinal cancer where there are abundant evidence-based screening guidelines [1–4]. In contrast, little is known about referrals for suspected hematologic malignancies [5], such as the frequency of such referrals, their clinical triggers, the factors that influence the choice of hematologist, and the quality of information exchanged. In the case of chronic hematologic malignances such as myelodysplasia, multiple myeloma, follicular lymphoma, and chronic lymphocytic leukemia, PCPs may have a lack of knowledge of so-called "alarm symptoms," and sparse experience with relevant diagnostic workups [6,7]. As even chronic blood cancers can be lethal and are increasingly treatable [8–11], prompt and efficient referral by PCPs for suspected hematologic malignancies is likely to improve care.

We aimed to survey a broad sample of PCPs as to their referral practices for suspected hematologic malignancies. We first sought to evaluate their approach to anemia (both singly and in combination with subsequent clinical findings), as anemia is a common first presenting sign for hematologic cancers. We then aimed to characterize how often PCPs suspect hematologic malignancy, the frequency and type of resulting consultation, the factors that affect their choice of hematologist, and the quality of information exchanged upon referral. Finally, we were also interested in how PCPs perceive their own ability to diagnose and treat these disorders, how often referrals have been completed when patients are seen in follow-up, and ultimately, how PCPs view the quality of the referral system within which they operate.

A total of 134 (70.5%) of 190 eligible Massachusetts PCPs completed surveys; 37 opted out either by postcard or when contacted by telephone, and the remaining 19 never responded. Most respondents were male (58.7%) and identified as internists (67.7%). PCPs were approximately evenly-distributed with respect to academic affiliation, with 21.1% reporting no affiliation with an academic center and 17.3% reporting being full-time faculty. The median reported patient panel size during the prior 12 months was 1,800 patients, and the median percentage of patients $\geq$ 65 years was 30.0% (Supporting Information Table 1).

Clinical actions for isolated anemia are shown in Table I; clinical actions for persistent anemia and one additional sign or symptom are shown in Table II. Of note, among patients most likely to be referred to a hematologist (those with pancytopenia, thrombocytopenia, or leukopenia), PCPs reported recommending low levels of 2-week follow-up in addition to the referral (10.6%, 16.7%, and 15.6%).

TABLE I. PCPs' First Reported Clinical Action when Patient Presents with New-Onset Anemia (Hg = 80% of Normal)[a]

PCP action	% Reporting
Iron studies	93.2
Differential	85.7
B12/folate	85.0
Stool guaiac	69.2
Reticulocyte count	66.2
2-week follow-up	30.8
Colonoscopy	26.3
SPEP	17.3
Depends on age	12.0
EGD	8.3
Refer to hematologist	3.8
Obtain imaging	1.5

[a]Respondents could choose more than one action.

Among all respondents, the median number (IQR) of patients in the prior 12 months suspected of having a hematologic malignancy was 5 (3, 10); of those suspected patients, the number formally referred to a specialist was 5 (3, 10), and the median number to receive curbside consultation was 0 (0, 0). PCP characteristics associated with higher levels of suspicion of hematologic malignancies are reported in Table III. Accounting for panel size, PCPs with stronger academic affiliation reported being more suspicious of hematologic malignancy than other physicians, while PCPs with a higher proportion of patients in managed care as well as those who were more recent graduates reported suspecting fewer patients of having hematologic malignancy. Table III also details PCP characteristics associated with curbside consultation and formal referrals, adjusting for the number of patients suspected to have hematologic malignancy.

When considering to whom to refer, respondents rated specialist reputation (96.2%) as most important, while the possibility of losing a referred patient to a specialist was rated as least important (15.8%; Supporting Information Table 2). Among respondents who did not report "always or usually" writing a formal letter and/or an email (49.6%), 62.5% reported "always or usually" giving a patient test results to take to the specialist meeting (Supporting Information Table 3). Thus, 18.9% of all patients were reportedly sent to hematologic specialists with no documentation (email, letter, or test results given to patient). Finally, 38.4% of respondents reported that patients have not seen the specialist "always, usually or sometimes" at the time of PCP follow-up, although only 2.3% reported that this "always or usually" occurs.

We found that PCPs were highly suspicious of hematologic malignancies, reporting both suspecting and referring a median number of five patients per year out of a median annual patient panel size of 1800. This rate of suspicion and referral (278 per 100,000) greatly exceeds the national incidence rates of malignancies such as non-Hodgkin's lymphoma (19.5 per 100,000)[12] and myelodysplasia (3.5 per 100,000)[13], and even that for all of the hematologic malignancies combined. Our data suggest that even in the absence of national screening guidelines, PCPs are performing an acceptable job in terms of suspecting hematologic malignancy and referring those patients to hematologists.

TABLE II. PCPs' Reported Clinical Actions When Patient Presents with Persistent Anemia (Hg = 80% of Normal) and One Additional Sign or Symptom[a]

Sign/Symptom[b]	Imaging (%)	Hematologist referral (%)	2-Week follow-up (%)
Fever	46.6	8.3	58.7
Leukocytosis	33.1	37.6	51.1
Leukopenia	15.8	63.9	28.6
Lymphadenopathy	67.7	42.9	28.6
Night Sweats	69.2	25.6	37.6
Pancytopenia	9.8	88.7	12.8
Thrombocytopenia	15.0	63.9	32.3
Thrombocytosis	15.0	42.9	48.1
Weight loss	54.1	23.3	43.6
Insistent family	21.1	39.9	57.9
Patient feels unwell	32.3	6.8	77.4

[a]Note: Respondents could choose more than one action.
[b]All row differences were significant at $P \leq 0.01$.

In our two-step anemia vignette, signs and symptoms suggesting myelodysplasia or leukemia most often prompted early referral, while those suggesting lymphoma were generally followed by imaging. This seems clinically reasonable, but still may result in delay of diagnosis and treatment by trained hematologic specialists. Interestingly, we found that an insistent family member could influence hematology referral for persistent anemia more so than night sweats, leukocytosis, or weight loss. We also found that several lower-cost and effective laboratory tests (e.g., reticulocyte count) were relatively underutilized, while over 25% reported obtaining colonoscopy as a first step. Taken together, these findings suggest that utilization of diagnostic anemia protocols may be a way to both improve care and decrease costs.

We found that recent residency graduates suspected fewer hematologic malignancies than other physicians, an observation that may be explained by their lack of clinical experience. Moreover, when younger PCPs did suspect hematologic malignancy, they more often formally referred patients and less often sought curbside consultation. We also found that PCPs with a high number of older adults in their practice suspected fewer hematologic malignancies. This was surprising given that hematologic malignancies are significantly more prevalent in older adults and the gap between so-called "alarm symptoms" and actual cases of malignancy is felt to be smaller in the elderly [6]. This may be explained by the recent finding that even classic signs and symptoms of hematologic malignancy (such as anemia and back pain in multiple myeloma) can be effectively hidden by significant comorbidity [14], which itself is more likely in older adults.

Our respondents reported that approximately one in five hematology referrals are made without any formal documented information exchange. Although our survey did not include every potential way for a PCP to contact a specialist (e.g., phone or shared medical record), these results suggest that there may be a gap in the flow of information between PCPs and hematology specialists. A recent national survey of 4720 PCPs and specialists found that while 69.3% of PCPs reported "always" or "most of the time" sending notification of the reason for referral, only 34.8% of specialists said they "always" or "most of the time" receive such information [15]. The lack of formal referral letters, emails, or even conveyance of test results may result in the specialist failing to obtain essential medical history [16] and may also foster replication of costly tests and procedures [17]. The former issue is especially important in hematologic oncology, as changes in blood counts over time—rather than absolute values at presentation—are often key to understanding potential progression of disease.

We recognize limitations to our work. First, our finding that the referral system for hematologic malignancies functions relatively well may not be completely generalizable to other states, especially ones that lack a large metropolitan region such as Boston (which contains several tertiary-care hospitals). Second, despite our excellent response rate (70.5%) for a physician survey, [18] our overall sample size was limited, which reduced our power to assess some associations in our analyses. Third, our work may have been affected by participation bias, as the PCPs who answered our survey may have also been those physicians most likely to actively suspect hematologic malignancies. Although participation bias is less of a concern when obtaining a high response rate such as ours, as with any cross-sectional survey, our study was also subject to recall bias (e.g., selective mem-

TABLE III. Associations of PCP Characteristics with Number of Patients Suspected of Having Hematologic Malignancy, Curbside Consultation Requested, and Formal Consultation Requested[a]

PCP characteristics	Adjusted odds ratio for number of patients for whom hematologic malignancy suspected[b]	Adjusted odds ratio for number of patients for whom curbside requested[c]	Adjusted odds ratio for number of patients for whom formal referral requested[d]
Stronger academic affiliation ($\geq$3 vs. $<$3)	1.91 [1.74–2.10]	1.04 [0.66–1.52]	0.35 [0.25–0.50]
High number elderly patients (top quartile vs. lower quartiles)	0.95 [0.84–1.07]	1.12 [0.70–1.80]	0.28 [0.18–0.44]
High number managed care patients (above median vs. below)	0.46 [0.41–0.51]	3.71 [2.37–5.81]	0.33 [0.22–0.50]
More recent residency completion (1996 or later vs. before 1996)	0.73 [0.66–0.81]	0.34 [0.22–0.52]	7.68 [5.03–11.73]
Primarily internal medicine vs. other	0.55 [0.50–0.61]	0.66 [0.41–1.05]	0.29 [0.21–0.42]

[a]From binomial logistic regression, adjusting for all other variables in the table as well as gender and race/ethnicity (white vs. other).
[a]Odds ratio for (# Suspected)/(Total # Patients in Panel) with [95% Confidence Interval].
[c]Odds ratio for (# Curbside/# Suspected) with [95% Confidence Interval].
[d]Odds ratio for (# Formal/# Suspected) with [95% Confidence Interval].

ory of referral behaviors), information bias (e.g., knowledge gap of patient panel demographics, digit preference bias), and social desirability bias (e.g., disinclination to report aberrant referral behaviors).

In summary, we found that anemia plus signs and symptoms suggesting of myelodysplasia or leukemia (compared with those suggestive of lymphoma) are more likely to prompt early hematology referral, and that overall, there was an adequate level of suspicion for hematologic malignancy among PCPs. We also found a high level of formal referrals rather than curbside consultation, and PCPs reported that most referrals were completed upon follow-up. We thus conclude that despite the absence of specific guidelines for screening and surveillance, the overall referral system for suspected hematologic malignancies functions relatively well.

Methods

Details of our survey method have been described previously [19]. Briefly, the names of all Massachusetts PCPs were obtained from the American Medical Association in March of 2010; 375 of these were randomly selected for inclusion in the survey. We then searched the Massachusetts Board of Registration in Medicine online directory to verify that the physicians (1) were currently in practice in Massachusetts; (2) graduated from medical school in 2005 or earlier; (3) had a listed specialty or were board-certified in internal medicine, general medicine, family medicine or geriatrics; and (4) had no nonprimary care subspecialty listed. The final precontact eligible sample consisted of 250 physicians. Of these, 60 reported upon contact that they did not engage in primary care and were reclassified as ineligible. The final eligible sample thus included 190 PCPs.

Survey questions were devised utilizing established standards for survey development [20,21]. Pilot testing and cognitive debriefing with three PCPs and two hematologists allowed for iterative revision in addition to assessment of face validity, content validity, and response burden. The 34-item questionnaire included questions about PCPs "Professional Background" and sections entitled "Signs and Symptoms," "Flow of Referral Information," "Deciding to Refer and Choosing a Specialist," and "Final Questions About You" (sociodemographic questions about the respondent, adapted from the Consumer Assessment of Healthcare Providers and Systems (CAHPS) 3.0 Survey "demographic" domain) [22]. The study was approved by the Dana-Farber/Harvard Cancer Center Office for Human Research Studies.

Recruitment was by FedEx® courier services, with follow-up telephone contact; all PCPs who completed the survey received a $100 VISA gift card. For the vignette questions, initial anemia workup actions were analyzed descriptively; significant differences in the second stage (anemia plus one additional sign or symptom) were identified using Wald chi-square statistics obtained from logistic regression models. We next assessed the number of suspected hematologic malignancies, formal referrals, and curbside consultations in the entire cohort reported for the prior year, calculating the median number and interquartile range (IQR) for each variable. We did not adjust for panel size, as we were aiming to report median suspicion and referral burden among the total responding physician population for each item, a number we felt was most important from a resource utilization perspective.

Next, using multivariable binomial regression analysis, we assessed PCP characteristics associated with higher numbers of suspected hematologic malignancies, this time taking into account the size of each PCP's patient panel. Finally, we analyzed responses to questions about choice of specialist and flow of referral information. Likert scale responses were dichotomized, and bivariate associations of these answers with PCP variables were assessed utilizing Fisher's exact test. Variables significant on univariate analysis ($P < 0.05$) were entered into multivariable models using backwards elimination. Analyses were conducted with the SAS statistical package (SAS 9.2, SAS Institute, Cary, NC).

Acknowledgments

The findings and conclusions are those of the authors and do not necessarily represent the position of the Centers for Disease Control (CDC).

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Additional Supporting Information may be found in the online version of this article.
Conflict of interest: Nothing to report.
Published online 12 March 2012 in Wiley Online Library (wileyonlinelibrary.com).
DOI: 10.1002/ajh.23172

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