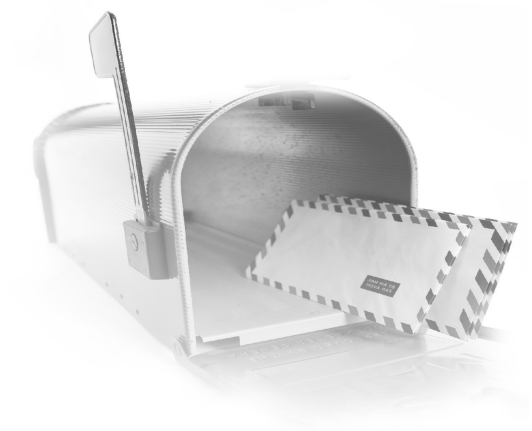

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Letters to the Editor

Incidental abdominal computed tomography findings in patients newly diagnosed with Philadelphia-negative myeloproliferative neoplasm

TO THE EDITOR: Philadelphia chromosome-negative myeloproliferative neoplasms (Ph$^-$ MPNs) include essential thrombocythemia (ET), polycythemia vera (PV), prefibrotic/early primary myelofibrosis (pre-PMF), and overt primary myelofibrosis (PMF). These clonal hematologic disorders are characterized by increased blood cell counts, thrombotic or hemorrhagic vascular events [1], and myelofibrotic or leukemic transformation [2, 3].

Because current standard guidelines do not recommend abdominal computed tomography (CT) for the initial evaluation of patients with Ph$^-$ MPN, abdominal CT is not routinely performed at the time of MPN diagnosis [4], and is only performed in patients with relevant symptoms or signs [5]. However, abdominal CT scans performed at the time of diagnosis of Ph$^-$ MPN may provide useful clinical information. For instance, splanchnic thrombosis is often asymptomatic and may be detected in MPN patients at the time of diagnosis [6]. As previously reported, abdominal CT detects volumetric splenomegaly in all pre-PMF patients and in only 50% of ET patients at diagnosis [7]. PV patients with volumetric splenomegaly at diagnosis had a poorer prognosis than those without; however, the prognosis is better than that of patients with palpable splenomegaly [8]. In addition, abdominal CT performed at the time of MPN diagnosis revealed asymptomatic splenic infarction [9] and abdominal aortic calcification, indicative of a poor prognosis (submitted for publication). Several cancers are more common in Ph$^-$ MPN patients than in the general population [2, 10]. The cumulative incidence of malignancies tends to increase immediately after MPN diagnosis [2], suggesting the possibility of pre-existing malignancies at diagnosis. Because malignancies are more common in the abdominal and pelvic cavities, abdominal CT performed at the time of MPN diagnosis may detect such malignancies. Besides the information on the spleen or abdominal aortic calcification that has already been reported in Ph$^-$ MPN patients, this study retrospectively analyzed the incidental findings of abdominal CT scans performed at the time of MPN diagnosis.

Patients who were diagnosed with ET, PV, pre-PMF, or PMF and who had undergone abdominal CT at the time of diagnosis (between January 2002 and December 2021) at Chungnam National University Hospital, Daejeon, Korea, were enrolled. The medical records of the enrolled patients were reviewed. We did not record the presence of volumetric splenomegaly, splenic infarction, abdominal aortic calcification, or prostate abnormalities. Before 2016, abdominal CT was performed in selected patients with relevant symptoms or signs to identify splenomegaly and confirm the diagnosis. Subsequently, abdominal CT was routinely performed for the initial evaluation of patients at the time of MPN diagnosis. For patients diagnosed with ET before 2017, the diagnosis was revised on the basis of the 2016 World Health Organization diagnostic criteria [11]. During the study period, 365 patients (150 with ET, 48 with pre-PMF, 136 with PV, and 31 with PMF) were newly diagnosed with Ph$^-$ MPN. Of these patients, we enrolled 219 (60.0%), including 94 with ET (median age, 62 yr; range, 18–90 yr), 24 with pre-PMF (median age, 67.5 yr; range, 31–88 yr), 80 with PV (median age, 64.5 yr; range, 18–66 yr), and 21 with PMF (median age, 64.5 yr; range, 18–90 yr). The patients were followed-up for a median of 3.4 years (range, 0.1–20.2 yr).

The most frequent findings were renal cysts (N=67, 30.6%), followed by hepatic cysts (N=38, 17.4%), gallstones (N=26, 11.9%), fatty liver (N=12, 5.5%), hepatic hemangioma (N=10, 4.6%), and duodenal diverticulum (N=9, 4.1%). The proportion of patients with these findings did not differ according to the MPN subtype. Hepatic calcification was more frequent in PMF patients (4 of 21; 19.0%) than in those with other MPN subtypes ($P<0.001$) (Table 1). However, its clinical implications remain unclear. Owing to the non-inclusion of healthy individuals as controls, we could not ascertain whether these findings are more prevalent in Ph$^-$ MPN patients than in the general population. However, these lesions are frequently detected in the general population, and their prevalence does not appear to differ

Table 1. Incidental findings of abdominal computed tomography.

	Total (N=219)	ET (N=94)	pre-PMF (N=24)	PV (N=80)	PMF (N=21)	*P*
Splanchnic thrombosis						
Arterial	1 (0.5)	0 (0.0)	0 (0.0)	1 (1.3)	0 (0.0)	0.734
Venous	2 (0.9)	1 (1.1)	0 (0.0)	1(1.3)	0 (0.0)	0.752
Gastrointestinal tract						
Duodenal diverticulum	9 (4.1)	6 (6.4)	1 (4.8)	2 (2.5)	0 (0.0)	0.422
Colonic diverticulum	4 (1.8)	2 (2.1)	0 (0.0)	2 (2.5)	0 (0.0)	0.780
Liver						
Cyst	38 (17.4)	17 (18.1)	5 (20.8)	12 (15.0)	4 (19.0)	0.899
Calcification	8 (3.7)	3 (3.2)	0 (0.0)	1 (1.3)	4 (19.0)	<0.001
Hemangioma	10 (4.6)	8 (8.5)	1 (4.2)	1 (1.3)	0 (0.0)	0.094
Fatty liver	12 (5.5)	6 (6.4)	0 (0.0)	6 (7.5)	0 (0.0)	0.366
Gallbladder						
Gallstone	26 (11.9)	12 (12.8)	1 (4.2)	11 (13.8)	2 (9.5)	0.612
Wall thickening	2 (0.9)	2 (2.1)	0 (0.0)	0 (0.0)	0 (0.0)	0.443
Pancreas						
Cyst	2 (0.9)	2 (2.1)	0 (0.0)	0 (0.0)	0 (0.0)	0.443
Spleen						
Nodule	2 (0.9)	2 (2.1)	0 (0.0)	0 (0.0)	0 (0.0)	0.443
Kidney						
Cyst	67 (30.6)	27 (28.7)	7 (29.2)	28 (30.6)	5 (23.8)	0.714
Stone	2 (0.9)	2 (2.1)	0 (0.0)	0 (0.0)	0 (0.0)	0.443
Ovary						
Cyst	4/103 (3.9)	3/49 (6.1)	0/13 (0.0)	1/35 (2.9)	0/6 (0.0)	0.580
Lymphadenopathy	2 (0.9)	2 (2.1)	0 (0.0)	0 (0.0)	0 (0.0)	0.443
Tumors						
Adrenal tumor	4 (1.8)	3 (3.2)	0 (0.0)	1 (1.3)	0 (0.0)	0.580
Benign renal tumor	1 (0.5)	1 (1.1)	0 (0.0)	0 (0.0)	0 (0.0)	0.721
Renal cell carcinoma	2 (0.9)	1 (1.1)	0 (0.0)	1 (1.3)	0 (0.0)	0.910
Colon cancer	1 (0.5)	1 (1.1)	0 (0.0)	0 (0.0)	0 (0.0)	0.721
Ovarian tumor	4/103 (3.9)	1/49 (2.0)	0/13 (0.0)	3/35 (8.6)	0/6 (0.0)	0.425
Uterine myoma	5/103 (4.9)	2/49 (4.1)	0/13 (0.0)	3/35 (8.6)	0/6 (0.0)	0.608
Non-splanchnic thrombosis						
Arterial	1 (0.5)	1 (1.1)	0 (0.0)	0 (0.0)	0 (0.0)	0.721
Venous	2 (0.9)	0 (0.0)	0 (0.0)	2 (2.5)	0 (0.0)	0.320
Aortic calcification	149 (68.0)	59 (62.8)	17 (70.8)	57 (71.3)	16 (76.2)	0.511

Values are presented as number (%).
Abbreviations: ET, essential thrombocythemia; PMF, overt primary myelofibrosis; pre-PMF, prefibrotic/early primary myelofibrosis; PV, polycythemia vera.

from that in our study patients [12-15]. Logistic regression analysis was performed to identify risk factors for incidental findings. Older age (>60 yr) was the only independent risk factor for renal cysts (Table 2). No independent risk factors were detected for the other findings (data not shown). Incidental CT findings did not affect the likelihood of thrombosis or overall survival (data not shown). Therefore, these lesions appeared to be incidental.

Of the 219 Ph^- MPN patients enrolled, 3 (1.4%) had splanchnic thrombosis, and 2 developed splanchnic vein thrombosis. Abdominal CT was performed in one PV patient because of abdominal distension and pain, which revealed thrombosis of the portal, splenic, and superior mesenteric vein, with marked splenomegaly. Another ET patient developed asymptomatic portal vein thrombosis that was detected on an abdominal CT performed during the initial evaluation. One patient with ET developed an asymptomatic left internal iliac artery thrombosis (Table 1). Of the three patients with splanchnic thrombosis, two were asymptomatic, often leading to a missed diagnosis. If abdominal CT had not been performed at the time of diagnosis, this might have led to erroneous risk stratification and treatment.

Of the 219 Ph^- MPN patients enrolled, 4 (1.8%) had an adrenal adenoma and 1 (0.5%) had a benign renal tumor (angiolipoma). Of the 103 female patients, benign ovarian tumors and uterine myomas were reported in 4 (3.9%) and 5 (4.9%) patients, respectively. Malignant tumors were reported in three patients (1.4%); one patient each with ET

Table 2. Logistic regression analysis of risk factors for renal cyst in patients with myeloproliferative neoplasm (N=219).

	Univariate analysis			Multivariate analysis		
	OR	95% CI	*P*	OR	95% CI	*P*
Age >60 yr	3.23	1.65–6.31	0.001	2.23	1.65–6.31	0.001
Male	1.62	0.90–2.91	0.107	-	-	-
Volumetric splenomegaly	0.81	0.43–1.52	0.509	-	-	-
WBC >11.0×10^9/L	0.90	0.50–1.60	0.713	-	-	-
Monocyte >1.0×10^9/L	1.29	0.60–2.79	0.518	-	-	-
Platelet >1,000×10^9/L	0.71	0.33–1.50	0.369	-	-	-
LDH >1.5×UNL	1.29	0.71–2.35	0.398	-	-	-
Positive *JAK2*V617F	0.92	0.45–1.95	0.856	-	-	-
ET	0.86	0.48–1.54	0.603	-	-	-
pre-PMF	0.93	0.37–2.35	0.872	-	-	-
PV	1.38	0.77–2.49	0.284	-	-	-
PMF	0.69	0.24–1.96	0.480	-	-	-
Hypertension	1.98	1.11–3.56	0.022	1.26	0.71–2.57	0.353
Diabetes mellitus	1.24	0.66–2.71	0.424	-	-	-
Chronic kidney disease	1.38	0.61–3.08	0.438	-	-	-
Dyslipidemia	1.96	0.98–3.92	0.058	-	-	-
Smoking	1.07	0.57–2.03	0.832	-	-	-
Hepatic cyst	0.91	0.42–1.96	0.809	-	-	-
AAC	2.49	1.25–4.96	0.009	1.19	0.48–2.98	0.705
Thrombosis[a)]	1.33	0.68–2.57	0.406	-	-	-

[a)]Thrombotic vascular events occurred before or at diagnosis.
Abbreviations: AAC, abdominal aortic calcification; CI, confidence interval; ET, essential thrombocythemia; LDH, lactate dehydrogenase; OR, odds ratio; PMF, overt primary myelofibrosis; pre-PMF, prefibrotic/early primary myelofibrosis; PV, polycythemia vera; UNL, upper normal limit.

and PV had renal cell carcinoma. A case of colon cancer has been reported in a patient with ET. None of the patients were symptomatic (Table 1). All patients had early-stage malignancies and had undergone successful surgical treatment. Such malignancies may not be detected at an early stage if abdominal CT was not performed at the time of diagnosis, which may lead to delayed treatment and a poor prognosis.

Our study had some limitations. First, because of the retrospective study design, we could not enroll all patients who presented to our hospital during the study period. Therefore, the prevalence of incidental findings calculated for the study patients may not be representative of all patients with MPNs. Second, because MPNs are relatively rare hematological disorders, the sample size was relatively smaller. Despite these limitations, we found that a small population of Ph^- MPN patients had asymptomatic splanchnic thrombosis and malignant tumors at the time of MPN diagnosis. As mentioned earlier, we previously reported that volumetric splenomegaly and asymptomatic splenic infarction detected by abdominal CT performed at the time of diagnosis are clinically useful for determining the diagnosis and prognosis [7-9]. The advantages of performing abdominal CT may offset the risks associated with radiation exposure and medical costs. Altogether, these data show that performing abdominal CT during the initial evaluation of newly diagnosed Ph^- MPN patients is reasonable.

Ik-Chan Song[1], Jeong Suk Koh[1], Sora Kang[1], Myung-Won Lee[1], Kyung Sook Shin[2], Deog-Yeon Jo[1]
[1]Division of Hematology/Oncology, Department of Internal Medicine, [2]Department of Radiology, Chungnam National University College of Medicine, Daejeon, Korea

Correspondence to: Deog-Yeon Jo
Division of Hematology/Oncology, Department of Internal Medicine, Chungnam National University Hospital, 282 Munhwa-ro, Jung-gu, Daejeon 35015, Korea
E-mail: deogyeon@cnu.ac.kr

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Clinically relevant core genes for hematologic malignancies in clinical NGS panel testing

TO THE EDITOR: Recent advancements in next-generation sequencing (NGS) technologies have enabled comprehensive genomic characterization of hematological malignancies. This has led to the discovery of numerous biomarkers, transforming the diagnosis, risk stratification, and personalized therapeutic intervention for these diseases. With the clinical significance of molecular testing, an increasing number of laboratories offer NGS analysis for hematological malignancies. Although various in-house and commercial panels are available, the target of genomic regions and genes of each panel are different. Therefore, I want to suggest several clinically relevant core genes for hematologic malignancies panels focusing on DNA testing, and, it will be helpful when employing clinically applicable NGS panel testing for hematologic malignancies.

MYELOID MALIGNANCIES PANEL

According to the recently released 5th edition of the World Health Organization Classification of haematolymphoid tumours: myeloid and histiocytic/dendritic neoplasms [1], the myeloid malignancies panel should target genes of newly defined entities: *NPM1* and *CEBPA*, and molecular alterations defining "AML, myelodysplasia-related", such as *ASXL1, BCOR, EZH2, RUNX1, SF3B1, SRSF2, STAG2, U2AF1*, and *ZRSR2* for acute myeloid leukemia. Newly defined entities for myelodysplastic neoplasms (MDS), *SF3B1* and *TP53*, and the diagnostic criteria for BCR-ABL1-negative myeloproliferative neoplasms (MPN), *JAK2, CALR, MPL, CSF3R*, and *KIT*, should also be targeted.

With respect to prognosis, the recently released Molecular International Prognostic Scoring System for myelodysplastic syndromes (IPSS-M) [2] offers a curated list of 31 genes that merit prioritization. Also, certain genes are known to correlate with poor prognosis in *BCR::ABL1*-negative MPN. Moreover, the myeloid malignancy panel requires testing for therapeutic markers, such as *FLT3* mutations (including *FLT3*-ITD) and *IDH1/2* mutations to select targeted drugs for acute myeloid leukemia (AML), and *ABL1* mutations to assess the response to tyrosine kinase inhibitor drugs for chronic myeloid leukemia (CML) [3].

In addition to, the 5th edition of the WHO classification of hematolymphoid tumors recognizes subtypes of myeloid neoplasms associated with germline predisposition to myeloid and histiocytic/dendritic neoplasms [1], and genes for these subtypes should be included in the panel. A comprehensive summary of the genes related to myeloid malignancies and their clinical significance is presented in Table 1.

ACUTE LYMPHOBLASTIC LEUKEMIA PANEL

In the recently released 5th edition of the World Health Organization classification of hematolymphoid tumors: lymphoid neoplasms [4], the category denoted as *BCR::ABL1*-like features have gained acknowledgment for their diverse array of genetic abnormalities, including JAK-STAT alterations, *ABL1* class fusions, and various other mutations. Mutations in *SH2B3, IL7R*, and *JAK1/2/3* have been linked to JAK-STAT alteration [5]. Moreover, the ICC 2022 classification introduced two distinctive entities characterized by hotspot point mutations: *IKZF1* N159Y and *PAX5* P80R [6]. In T-cell lymphoblastic leukemia (T-ALL), *NOTCH1* activating mutations and CDKN2A/B deletions represented pivotal pathogenic genes, collectively detected in 50–60% of cases, and approximately 30% of T-ALL cases exhibiting *NOTCH1* mutations were concomitant with *FBXW7* mis-