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Short Communication

Myeloid/lymphoid neoplasms with eosinophilia and rearrangement of PDGFRA, PDGFRB, or FGFR1, or with PCM1-JAK2: Overview 2019

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Abstract

Review on the group of myeloid/lymphoid neoplasms with eosinophilia and rearrangement of PDGFRA, PDGFRB, or FGFR1, or with PCM1-JAK2 defined by the WHO 2016.

Keywords
eosinophilia; PDGFRA; PDGFRB; FGFR1, PCM1/JAK2

Clinics and pathology

Disease

Eosinophilia is defined as a peripheral blood eosinophil count > $0.5x10^9$/L, with > $1.5x10^9$/L of eosinophil count sometimes referred to as hypereosinophlia. Eosinophilia is a common clinical phenotype associated with various conditions including allergies, infections, medications, autoimmune disorders and malignancies. Although malignancy-related eosinophilia is rare, it is an important clinical sign of these tumors, which require early diagnosis and clinical intervention. Figure 1 summaries the initial workup of patients with eosinophilia.

Phenotype/cell stem origin

WHO 2016 defines a group of myeloid/lymphoid neoplasms with eosinophilia and rearrangement of PDGFRA, PDGFRB, or FGFR1, or with PCM1 / JAK2 as:

Disease

(1) Myeloid/lymphoid neoplasms with PDGFRA rearrangement
(2) Myeloid/lymphoid neoplasms with PDGFRB rearrangement
(3) Myeloid/lymphoid neoplasms with FGFR1 rearrangement
(4) Provisional entity: Myeloid/lymphoid neoplasms with PCM1/JAK2

Treatment

This group of patients can be treated with tyrosine kinase inhibitors. While patients with PDGFRA or PDGFRB rearrangement are highly sensitive to Imatinib, PCM1-JAK2 patients had varying responses to JAK2 inhibitor Ruxolitinib, which can induce complete remission, although the duration is often limited. FGFR1 inhibitors have not been very successful in treating tumors with FGFR1 rearrangement. PKC412 was effective in a patient with progressive myeloproliferative disorder with (8;13) (Chen et al., 2004); however, subsequent studies with the FGFR1 inhibitor ponatinib were less successful. Novel FGFR1 inhibitors are currently being tested in clinical trials for solid tumors with FGFR1 activation. Recently a new FGFR family kinase inhibitor INCB054828 induced complete resolution of eosinophilia as well as complete hematologic, cytogenetic and molecular remission in a patient with FGFR1 rearranged MPN (Verstovsek et al., 2018).

Genetics

The fusion partner genes for PDGFRA, PDGFRB, or FGFR1 have been steadily accumulating and are updated below in Tables.

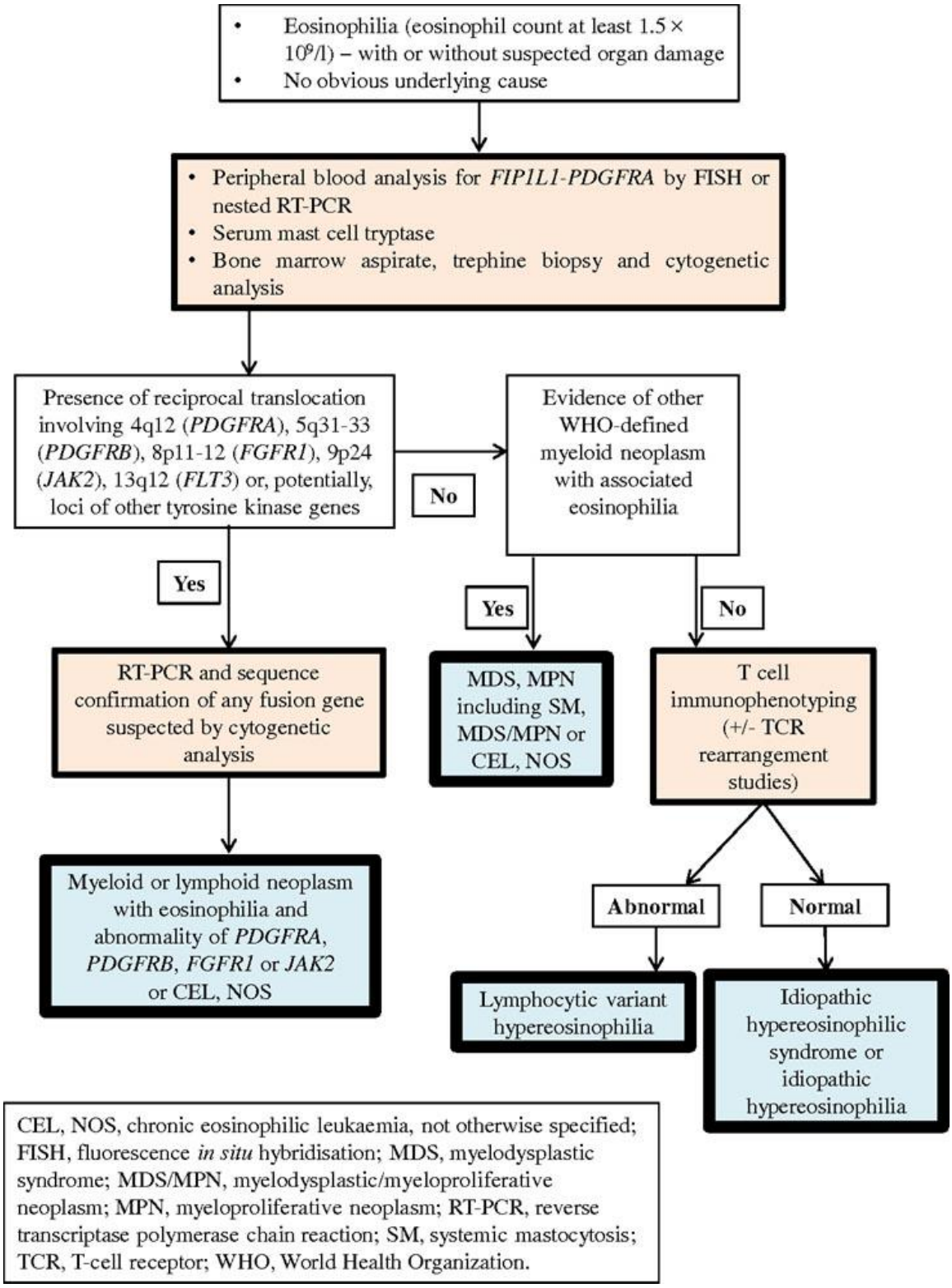

Figure 1. Testing algorithm for possible haematological neoplasms with clonal eosinophilia. Courtesy of the British Committee for Standards in Haematology

Gene name	Rearrangements	Detection methods				Ref (PMID)
		Karyotype	FISH	RT-PCR	NGS	
BCR	t(4;22)(q12;q11.2)	Yes	Yes	Yes	Yes	15034867
CDK5RAP2	ins(9;4)(q33;q12q25)	Yes	Yes	Yes	Yes	16845659
ETV6	t(4;12)(q12;p13)	Yes	Yes	Yes	Yes	17555450
FIP1L1	del(4)(q12q12)	No	Yes	Yes	Yes	12660384
FOXP1	t(3;4)(p13;q12)	Yes	Yes	Yes	Yes	26319757
KIF5B	t(4;10)(q12;p11)	Yes	Yes	Yes	Yes	16498388
STRN	t(2;4)(p24;q12)	Yes	Yes	Yes	Yes	17555450
TNKS2	t(4;10)(q12;q23.3)	Yes	Yes	Yes	Yes	25658984

Table 1: PDGFRA fusion partners, chromosome locations, detection methods and references

Gene name	Rearrangements	Detection methods				Ref (PMID)
		Karyotype	FISH	RT-PCR	NGS	
AGGF1	add(5)	Yes	Yes	Yes	Yes	28552906; 29284681
ATF7IP	t(5;12)(q33;p13)	Yes	Yes	Yes	Yes	24628626
BIN2	t(5;12)(q32;q13)	Yes	Yes	Yes	Yes	20085582
CAPRIN1	t(5;11)(q33;p13)	Yes	Yes	Yes	Yes	17296564
CCDC6	t(5;10)(q33;q21)	Yes	Yes	Yes	Yes	10910073
CCDC88C	t(5;14)(q33;q32)	Yes	Yes	Yes	Yes	15496975; 24772479
CEP85L	t(5;6)(q33-34;q23)	Yes	Yes	Yes	Yes	21938754
CPSF6	t(5;12)(q33;q15)	Yes	Yes	Yes	Yes	26355392
DIAPH1	t(5;5)(q31.3;q32)	No	Yes	Yes	Yes	28751768
DOCK2	del(5)	No	Yes	Yes	Yes	28552906
DTD1	t(5;20)(q33;p11)	Yes	Yes	Yes	Yes	24772479
EBF1	del(5)(q32q33)	No	Yes	Yes	Yes	23835704
ERC1	t(5;12)(q33;p13)	Yes	Yes	Yes	Yes	17690697
ETV6	t(5;12)(q33;p13)	Yes	Yes	Yes	Yes	8168137
GCC2	t(2;5)(q37;q31)	Yes	Yes	Yes	Yes	30697976
GIT2	t(5;12)(q33;q24)	Yes	Yes	Yes	Yes	17296564
GOLGA4	t(3;5)(p22;q31)	Yes	Yes	Yes	Yes	20085582
GOLGB1	t(3;5)(q13;q32)	Yes	Yes	Yes	Yes	26355392
HIP1	t(5;7)(q33;q11)	No	Yes	Yes	Yes	9616134
KANK1	t(5;9)(q32;p24)	Yes	Yes	Yes	Yes	20164854
MPRIP	t(5;17)(q32;p11)	Yes	Yes	Yes	Yes	26355392
MYO18A	t(5;17)(q32;q11)	Yes	Yes	Yes	Yes	28261327
NDE1	t(5;16)(q32;p13)	Yes	Yes	Yes	Yes	17301821
NIN	t(5;14)(q33;q24)	Yes	Yes	Yes	Yes	15087377
NUMA1	t(5;11) (q32;q13.4)	Yes	Yes	Yes	Yes	28449810
PCM1	ins(8;5)(p23;q33q35)	Yes	Yes	Yes	Yes	29169164
PRKG2	t(4;5)(q21;q33)	Yes	Yes	Yes	Yes	18262053
RABEP1	t(5;17)(q33;p13)	Yes	Yes	Yes	Yes	11588050
SART3	t(5;12)(q32;q23)	Yes	Yes	Yes	Yes	20107158
SATB1	t(3;5)(p24;q32)	Yes	Yes	Yes	Yes	28552906
SPECC1	t(5;17)(q33;p11.2)	Yes	Yes	Yes	Yes	15087372
SPTBN1	t(2;5)(p21;q33)	Yes	Yes	Yes	Yes	18262053
TBL1XR1	(3;5)(q26;q32)	Yes	Yes	Yes	Yes	28509585
TNIP1	t(5;5)(q32;q33)	No	Yes	Yes	Yes	28408464

TP53BP1	t(5;15)(q33;q22)	Yes	Yes	Yes	Yes	15492236
TPM3	t(1;5)(q21;q32)	Yes	Yes	Yes	Yes	16838028
TRIP11	t(5;14)(q33;q32)	Yes	Yes	Yes	Yes	9373237
TSC1	t(5;9)(q32;q34)	Yes	Yes	Yes	Yes	29384404
WDR48	t(1;3;5)(p36;p21;q33)	Yes	Yes	Yes	Yes	20085582
ZMYND8	t(5;20)(q32;q13)	Yes	Yes	Yes	Yes	28408464

Table 2: PDGFRB fusion partners, chromosome locations, detection methods and references

Gene name	Rearrangements	Detection methods				Ref (PMID)
		Karyotype	FISH	RT-PCR	NGS	
BCR	t(8;22)(p11;q11)	Yes	Yes	Yes	Yes	11746971; 11739186
CNTRL	t(8;9)(p12;q33)	Yes	Yes	Yes	Yes	10688839
CPSF6	t(8;12)(p11;q15)	Yes	Yes	Yes	Yes	18205209
CUX1	t(7;8)(q22;p11)	Yes	Yes	Yes	Yes	21330321
FGFR1OP	t(6;8)(q27;p11)	Yes	Yes	Yes	Yes	9949182
FGFR1OP2	t(8;12)(p12;p11); ins(12;8)(p11;p12p22)	Yes	Yes	Yes	Yes	15034873
ERVK-6	t(8;19)(p12;q13)	Yes	Yes	Yes	Yes	12393597

Table 3: FGFR1 fusion partners, chromosome locations, detection methods and references

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