To the editor:

**Misleading information about ALIP and VEGF in myelodysplasia**

The study by Bellamy et al has numerous critical limitations. First, the authors incorrectly assume that abnormal localization of immature precursors (ALIPs) can be identified in the bone marrow clot section, which has no bony trabeculae. It should be pointed out that ALIPs are collections of immature myeloid precursors in the central, inter trabecular region of the bone marrow trephine biopsy section. Moreover, this is a feature of microarchitecture disorganization in the bone marrow biopsy sections in myelodysplastic syndromes (MDSs), which also show disorganized erythroid and megakaryocytic precursors in the trabecular region. In a normal human bone marrow biopsy, myeloid precursors are near the trabecular region, and erythroid and megakaryocytic precursors are in the inter trabecular region. This physiologic cell distribution may be reversed in the bone marrow biopsy of cases with MDS. The data presented by Bellamy et al show only myeloid and monocytoid blasts in a clot section without bony trabeculae, which is typical of blasts seen in a bone marrow aspirate. Moreover, it is reported that most myeloid blasts and myeloid leukemia cell lines express vascular endothelial growth factors (VEGFs) and their receptors. This simply indicates that, like acute myeloid leukemia blasts, immature myeloid cells in MDS do express VEGF and this is not specific to displaced/ectopic blasts or ALIP.

Second, the authors show absence of VEGF in a healthy human bone marrow clot section, but their data highlight only the absence of VEGF in mature myeloid cells (neutrophils). Like normal bone marrow, Figure 4 in Bellamy et al clearly demonstrates absence of VEGF in all mature myeloid cells in cases with MDS. Therefore, we do not know whether healthy human bone marrow blasts differ from “dislocated myeloid precursors” (Bellamy et al), and they do not have autocrine or paracrine promotion by VEGF.

Third, their data show that cases with refractory anemia (RA, or low-risk MDS) were 100% (8 of 8) positive for VEGF, and only 72% (16 of 22) of cases with refractory anemia with excess of blasts (RAEB) and RAEB in transformation (RAEBt) show positivity for VEGF. According to our experience and that of others, only 30% of cases with RA show presence of ALIP and more than 95% of cases with RAEB/RAEBt (high-risk MDS) do have ALIP in their bone marrow biopsies. Bellamy et al do not clarify how many RA and RAEB/RAEBt cases were with ALIP and without ALIP, why RAEB/RAEBt cases with ALIP do not demonstrate positivity for VEGF, and what is the explanation for VEGF positivity in RA cases without ALIP.

Fourth, the authors do not mention anything about the international prognostic scoring system (IPSS) in MDS. This scoring system is used by most physicians to make a therapeutic decision in cases with MDS. It will be interesting to know about any correlation between VEGF expression and IPSS risk categories.

Finally, most investigators will agree that lymph-node fine-needle aspirates do not give enough information about lymph node architecture. Likewise, bone marrow clot sections are not suitable to start assuming about architectural disorganization in MDS. To get the full picture about ALIP in MDS and the autocrine or paracrine promotion by VEGF or other growth factors, authors should justify their conclusions on the basis of bone marrow biopsy examinations.

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**References**


Response:

**Expression of VEGF in myelodysplasia**

Dr Mangi interprets our data as indicating that the means by which we diagnose ALIP was based solely on findings derived from bone marrow clot sections. The definition of ALIP as originally proposed by Tricot et al resides upon resolving the spatial relationship between myeloblast clusters to bone trabeculae within trephine biopsies, as we described in “Discussion.” Indeed, we stress that the displacement of myeloid precursor clusters from their paratrabecular locale represents an adverse
To the editor:

Pseudo Pelger-Huët anomaly in myelodysplastic syndrome: hyposegmented or apoptotic neutrophil?

Huët first observed an abnormal hyposegmented neutrophil granulocyte in 1928, and a year later Pelger reported an additional case. Such a cell later became known as Pelger-Huët anomaly. In 1932 Huët pointed out its hereditary and systemic character. The Pelger-Huët anomaly is a familial anomaly that is transmitted as a Mendelian dominant trait but that is unaccompanied by any other abnormalities such as pseudo Pelger-Huët anomaly. The morphologic characteristic seen in pseudo Pelger-Huët anomaly is similar to Pelger-Huët anomaly. The acquired pseudo Pelger-Huët anomaly has been associated with pathologic conditions including myelodysplastic syndromes (MDS).

MDS are a closely related group of bone marrow disorders seen in elderly populations characterized by peripheral cytopenias and dysplastic hematopoiesis. But dysplastic hematopoiesis is a feature not confined only to MDS; this feature is also seen during the administration of certain drugs and in megaloblastic anemia. On the other hand, some abnormalities such as pseudo Pelger-Huët anomaly and micromegakaryocytes are considered to be highly characteristic and highly prognostic of MDS. One or the other of these abnormalities occurs in a high percentage of MDS patients.
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