to indicate the illness (or the syndrome) that several reports and reviews7 have well described in the past.

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References

Response:

What's in a name?

Balduini and colleagues characterized the platelets with GATA1 mutation Arg216Gln, which leads to a subtle beta thalassemic phenotype plus large, agranular platelets, a condition designated “XLTT.”1 In their letter, these authors now propose that our phenotype plus large, agranular platelets, a condition designated XLTT by Balduini et al or the distinctions drawn between GATA1 Arg216Gln mutation and autosomal GPS (which lacks thalassemia features). However, we have a different view of this specific naming controversy and a different philosophical outlook about “lumping” versus “splitting” in the characterization of these platelet disorders.

The question is fundamentally one of nosology (how medical syndromes get their names), a subject with a rich history. We believe this Arg216Gln mutation disorder could be classified in any of the following ways: (1) as a member of the broad spectrum of congenital GATA1 disorders, which presently includes dyserythropoiesis, transient myeloproliferative disease of trisomy 21, porphyria, and macrothrombocytopenia with granule defects; (2) as a unique kind of GPS, inherited in X-linked fashion, with platelets indistinguishable by experts from autosomal GPS (at the light microscope and ultrastructure level); or (3) as its own unique syndrome, “XLTT.” Each classification teaches us something different; none is more “wrong” or “right” than the others. Although we chose the second option, we endorse all 3.

There are biologic and practical reasons not to discard the idea of X-linked GPS, despite the critique of Balduini et al. Biologically, because GATA1 is a master regulator in megakaryopoiesis, it is likely that the autosomal GPS gene(s) (when discovered) will prove to be downstream targets of GATA1. In this hypothetical pathway, it seems to us unreasonable to consider giving different mutations different disease names. This is true of any genetically heterogeneous disorder (for example, the Fanconi anemia pathway, with more than a dozen members, including the BRCA2 gene). We need look no further than thalassemias for evidence of nonconfusion because the name XLT1 itself causes no confusion with thalassemias linked to the globin genes on chromosomes 11 and 16. Practically, some of the distinctions between XLTT and autosomal GPS are out of reach of clinical hematologists, whereas GATA1 sequencing for large, agranular platelets is easy to obtain. Globin-chain ratios are infrequently assessed in any clinical setting. Marrow evaluation for emperipolesis is not standard in our platelet function evaluations. Several percent of the world’s population has a thalassemia trait, so the coincidental appearance of microcytosis with absent alpha granules does not necessarily spell XLTT. Thus, we stand by the name X-linked GPS with a nod of gratitude to the prior work of Balduini et al, and we predict that some fraction of males with sporadic or familial GPS will prove to have GATA1 mutations.

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Reference
Response: What's in a name?

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