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CASE SERIES

Subcortical bone marrow and deep marrow differences: A comparison in a series of 5 cases

Samir B. Kahwash[1,2]

[1]Department of Pathology and Laboratory Medicine, Nationwide Children's Hospital, Columbus, Ohio, United States; [2]Department of Pathology, Ohio State University College of Medicine, Columbus, Ohio, United States

Abstract

This manuscript documents examples of bone marrow cores where subcortical spaces are significantly different in comparison with deep core spaces. The differences include significantly higher or lower cellularity in addition to discrepant involvement by malignant processes. While this phenomenon is generally familiar to practicing pathologists, it is not adequately illustrated in the medical literature. Publication of such illustrated examples may help generate more interest in this phenomenon as well as emphasise the constant need for adequate marrow specimens to avoid diagnostic pitfalls.

Keywords: Bone marrow, cellularity, posttransplant, subcortical

INTRODUCTION

The astonishing advances at the molecular and genetic levels in the last few years have enabled performance of extensive studies and conducting panels of ancillary tests utilising smaller specimens and fewer cells. These advancements may have inadvertently contributed to creating a false sense of security that may result in clinicians exerting less effort and obtaining smaller tissue samples resulting – at times- in insufficient specimens and hence less informative morphologic reports. In paediatric haematopathology, this may include overlooking the importance of obtaining a core biopsy, after aspirating the marrow, or more commonly, obtaining a smaller than adequate core biopsy. Reporting definitive data on a suboptimal specimen without highlighting specimen inadequacy context risks misinterpretation and/or out-of-context conclusions.

On the other hand, calling a specimen inadequate can be at times perceived as subjective, especially considering that adequacy can be a relative term or case dependent and that morphologic inadequacy of one component of the specimen can often be mitigated using other components or remedied by ancillary studies.

An accurate description of specimen adequacy is a very important component of a pathology report. This is especially true regarding bone marrow core, but with an added peculiarity: The subcortical marrow is not only insufficient but can also be misleading. While this fact is well-known among practicing haematopathologists, it may not be widely known outside the field of haematopathology. Furthermore, a pathologist who cites specimen inadequacy due to a subcortical only marrow space has limited number of illustrated literature and studies to reference. The purpose of this report is to further highlight the peculiarity of subcortical marrow - defined here as the one or two marrow spaces closest to bone cortex- and share illustrated cases where the subcortical marrow has been grossly misrepresentative or misleading:

Case 1: A10-year-old boy, status post kidney transplant who was found to have abdominal masses suspicious for post-transplant lymphoproliferative disorder. The marrow sample showed no evidence of posttransplant lymphoproliferative disorder (PTLD), and the core biopsy showed significantly lower cellularity of subcortical spaces compared to the rest of marrow (Figure 1A and B).

Case 2: A 5-year-old girl with a new diagnosis of neuroblastoma (NBL) had a staging bone

**Address for correspondence:* Samir B. Kahwash, M.D.; Department of Pathology and Laboratory Medicine, Nationwide Children's Hospital, Columbus, OH, United State of America. Tel: 614-722-5427. Fax: 614-722-5308. Email: *samir.kahwash@nationwidechildrens.org*

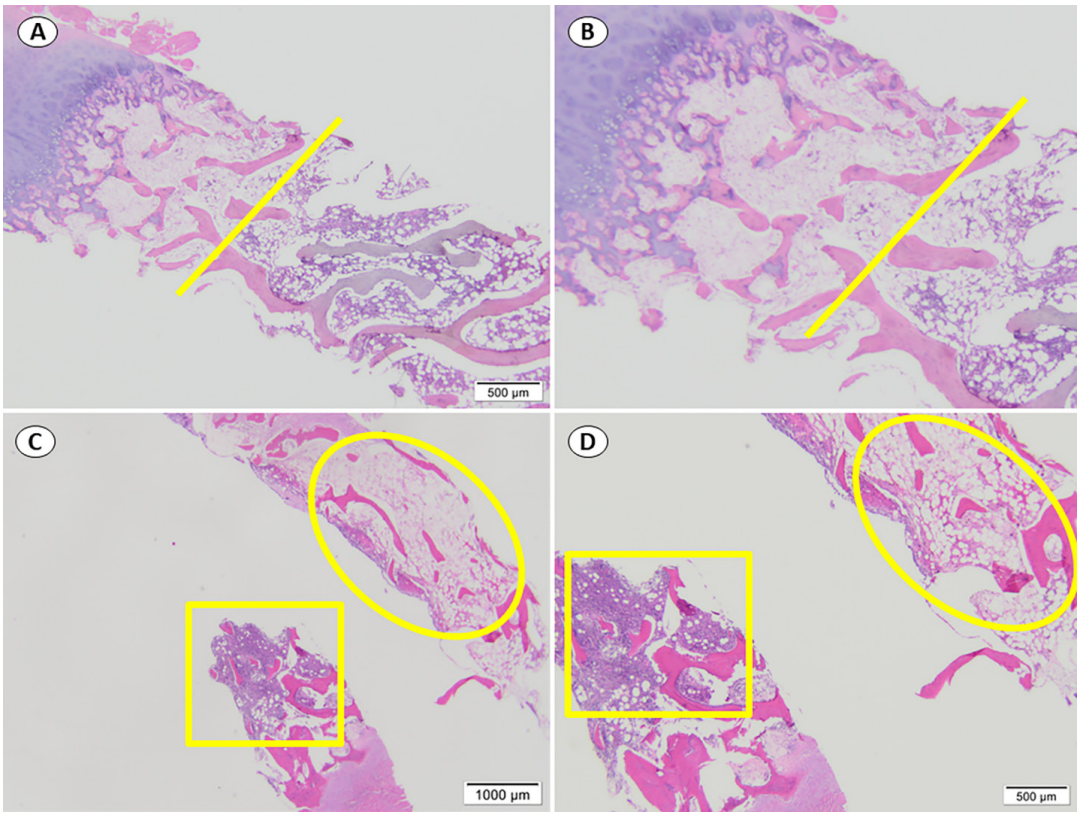

Figure 1: An example of subcortical marrow space showing significantly lower cellularity compared to deep marrow (A&B) and a case where subcortical marrow shows significantly higher cellularity (C&D).

marrow evaluation. The marrow was negative for metastasis, but the subcortical spaces showed significantly higher cellularity (Figure 1C and D).

Case 3: A one-year-old girl who was being worked up for anaemia was found to have thrombocytopenia and circulating peripheral blasts. Bone marrow core biopsy showed extensive marrow fibrosis admixed with megakaryoblasts. Cytogenetic and molecular genetic studies showed t(1,22). She met diagnostic criteria for acute megakaryoblastic leukaemia (AMKL). The core biopsy was significant for extensive marrow involvement by leukaemia, sparing the subcortical marrow (Figure 2A-D).

Case 4: A 3-year-old boy presented with cervical lymphadenopathy and biopsy was diagnostic for anaplastic large cell lymphoma (ALCL). The patient was treated but relapsed a year later. Bone marrow examination at relapse showed extensive marrow involvement by ALCL sparing the subcortical marrow (Figure 3).

Case 5: A 28-year-old man had an enlarged cervical lymph node that biopsy showed metastatic desmoplastic small round cell tumour (DSRCT) and RT-PCR confirmed the presence of t(11;22) (p13, q12) characteristic of DSRCT. Bilateral bone marrow sampling showed extensive metastases to bone marrow that spared the subcortical marrow space (Figure 4).

DISCUSSION

A search of the literature in PubMed for "subcortical marrow" yields no pertinent publications. A review of six published articles and one book chapter that discussed normal bone marrow morphology and/or marrow cellularity (references 1,2,3,4,5,6,7) shows that only one of them (reference 2) had a mention of subcortical marrow, describing it as hypocellular. The latter is not always true. While subcortical marrow hypocellularity is common, marrow cores with higher cellularity than deep core are not infrequent in the paediatric population (including one case example featured in this manuscript). More importantly, cases showing other important

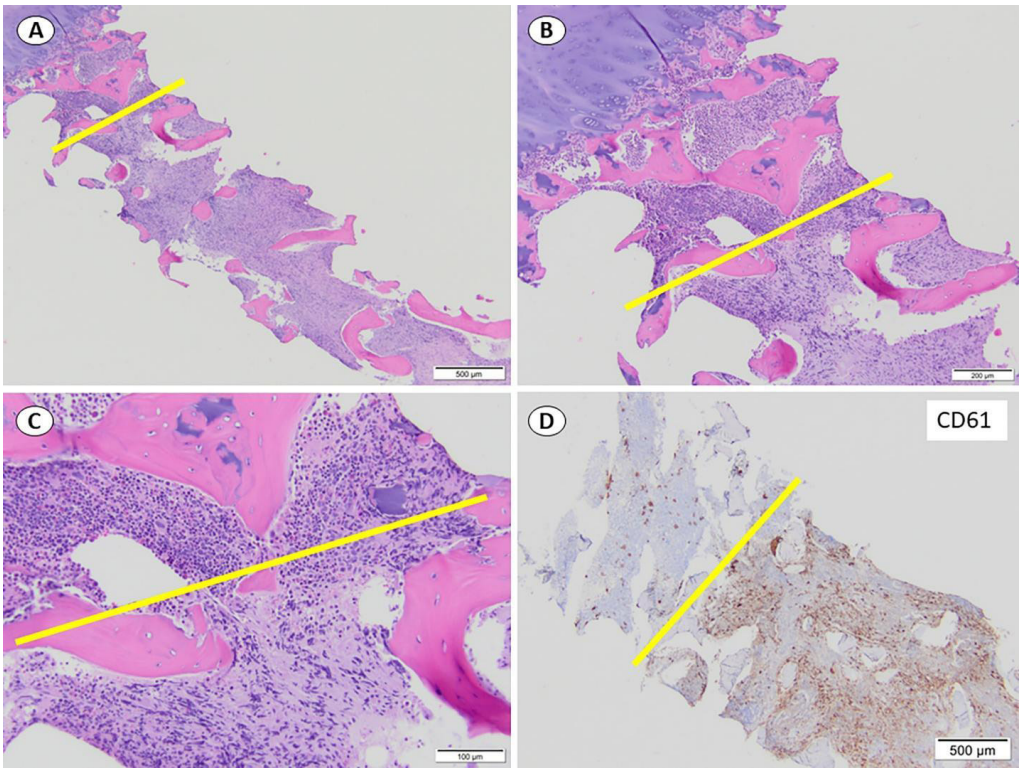

Figure 2: An example of subcortical marrow space showing minimal changes while the deep core marrow spaces show extensive involvement by acute megakaryocytic leukemia (A, B, C&D).

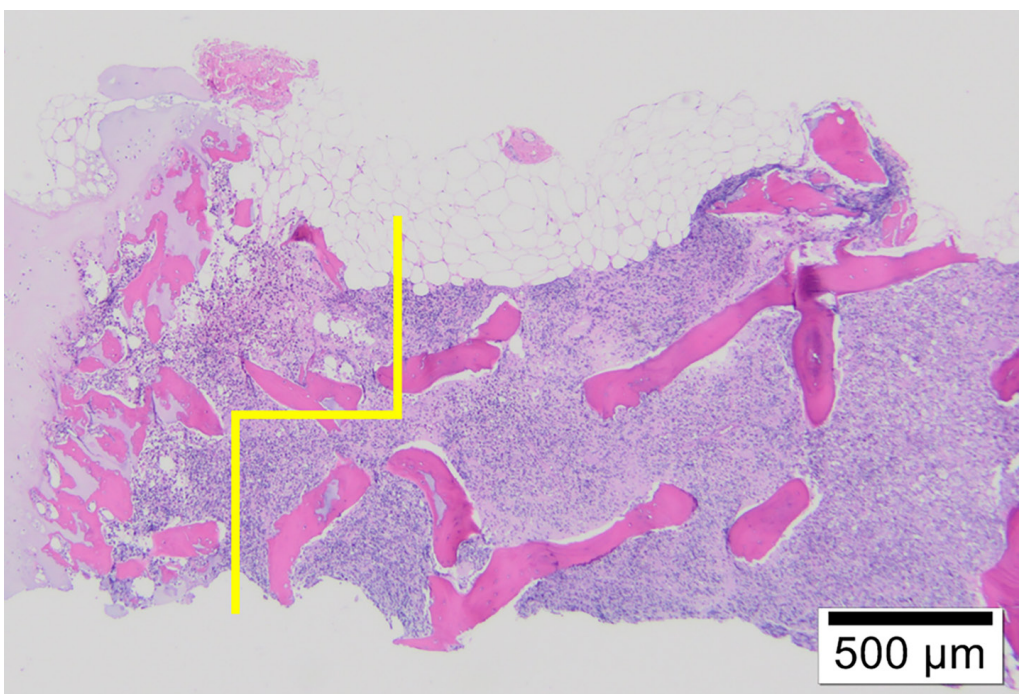

Figure 3: An example of subcortical marrow space showing no involvement with anaplastic large cell lymphoma while the deep marrow shows extensive involvement.

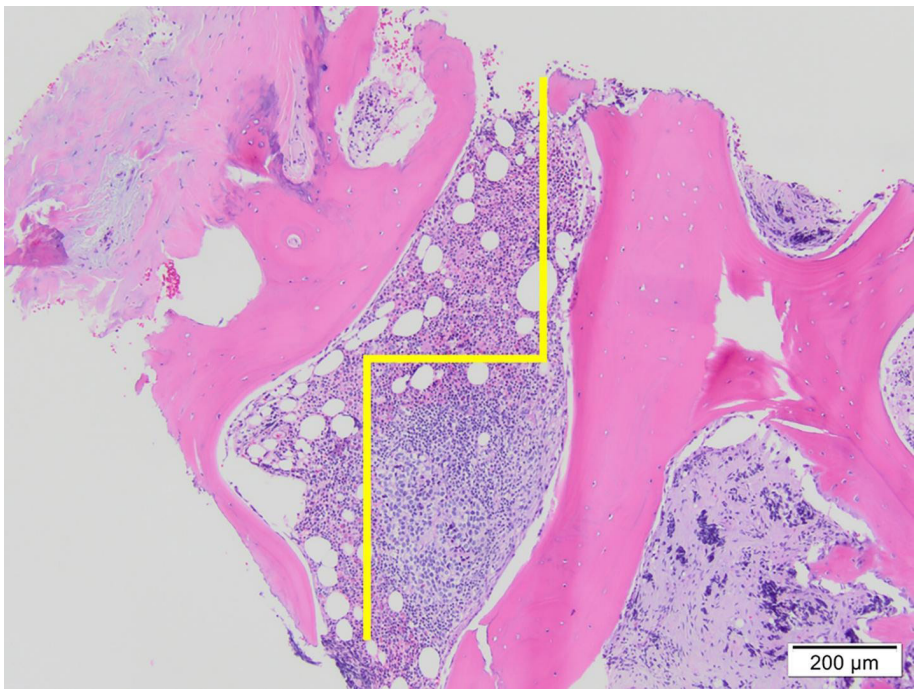

Figure 4: An example of subcortical marrow space showing minimal changes while the deep core marrow spaces show extensive involvement by desmoplastic small round cell tumour.

discordant findings between subcortical and deep marrow spaces can be more consequential.

Although the cases illustrated here are randomly - and not methodically - selected, they suggest that the best description of subcortical marrow space peculiarity is to label it as "different" or not necessarily representative: The cellularity may be lower or higher and other findings – including involvement by hematopoietic or nonhematopoietic metastatic tumour- can be discordant. The causes of discordance are not clear, but they may be related to a difference in blood supply.

CONCLUSIONS

Subcortical marrow is different, and often shows higher or lower cellularity in comparison with deep core and at times other discrepant findings. While the occurrence of significant discordance can be noted by case examples as in this manuscript, the prevalence of such discordance can only be learned by conducting systemic reviews. Until a systemic review is performed, it is important to emphasize the potential of discordance in reporting all cases where the core biopsies contain only subcortical marrow spaces.

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