Granulocyte Stimulating Factors’ effect on Bone Marrow Hyperplasia and MRI Interpretation.

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Learning Objectives

- Review the incidence of granulocyte colony stimulating factor (G-CSF) induced bone marrow stimulation and yellow/red reconversion resulting in metastasis mimicking lesions on MRI.
- Briefly investigate how similar bone marrow lesions appear on FDG PET imaging.
- Explore the recommended MRI techniques utilised to differentiate bone marrow metastasis from stimulation or reconversion.

Background

The administration of G-CSF in cancer treatment is a common practice used to counter chemotherapy induced neutropenia or to facilitate mobilisation of stem cells for autografting. Despite its obvious benefits, G-CSF utilisation can also create a diagnostic dilemma as the resulting bone marrow stimulation or yellow to red marrow reconversion can mimic diffuse infiltrative metastasis on MRI\(^2,3\). The reasoning behind such a quandary is that any increase in marrow cellularity, regardless of aetiology, will ultimately increase the water to fat ratio, in turn altering MRI signal intensity\(^3\).

This review will examine the current literature describing the incidence of G-CSF induced bone marrow changes mimicking metastasis and the current MR techniques utilised to sidestep this predicament.

Imaging Findings OR Procedure Details

Hartman (2004)\(^2\) examined 25 individuals with soft tissue sarcomas or primary bone tumours who received G-CSF as a part of their treatment and found 40% showed marrow reconversion, of which 70% mimicked diffuse marrow infiltrating tumour and the other 30% mimicked focal metastases. Of the above all had a shorten signal on T1 weighted imaging and 90% had T2 signal prolongation (Figure 1).
Altehoefer (2001) performed a series of lumbar MRIs over several months on 12 healthy stem cell donors who received short term G-CSF for stem cell mobilisation. Approximately 14 days after G-CSF administration imaging revealed a significant decrease in bone marrow signal (12% mean) on T1 weighted imaging and an increase in signal (59% mean) on out-of-phase GE sequences in all patients (Figure 2). The benefit of this study was that the effect was attributable to G-CSF alone and it offers a time course by which to predict benign increased bone marrow cellularity following G-CSF administration. Figure 2 demonstrates one of the MRI series, clearly illustrating signal intensity changes consistent with bone marrow hyperplasia.

These bone marrow changes on T1 weighted images were also reflected in studies performed on patients receiving G-CSF for glycogen storage disease type Ib (to prevent neutropenia), breast cancer (G-CSF supported chemotherapy) and children with musculoskeletal malignancies (G-CSF supported chemotherapy). The latter two studies noted the similarity of the marrow changes to metastasis, acknowledging the diagnostic difficulty this creates.

Several reports and case studies have described a similar diagnostic dilemma with marrow stimulation on PET imaging. Mabuchi (2012) and Nakamoto (2010) presented case studies observing focal intense homogenous uptake of F-18-fluorodeoxyglucose (FDG) following G-CSF therapy (Figure 3). The homogenous uptake was useful for suggesting benign lesions, however both noted the potential diagnostic difficulty inherent in these lesions.

Although the accuracy of MRI when differentiating between neoplastic and benign infiltrate appears to be good, it is also non-specific.

One of the primary features of hyperplasia that distinguishes it from neoplasia is the presence of fat in hyperplasia that is rare in cancerous lesions. Fat suppression with T1 weighted imaging can help identify this. Although any lesion not composed of fat on a T1 weighted image should be treated as suspicious, sources tend to agree that an out-of-phase signal decrease of >20% should be the threshold for differentiation between benign and malignant marrow abnormalities. Disler (1997) found that in-phase/out-of-phase imaging achieved 100% sensitivity and 94-100% specificity in differentiating benign from metastatic lesions in bone marrow.

Images for this section:
Fig. 2: Altehoefer (2001) - Image shows the T1, T2 and GE MRI series performed on a healthy stem-cell donor administered G-CSF. The first image is the baseline MRI, the second was obtained the day of G-CSF administration, the third was at 2 weeks and the fourth was at 6 weeks post administration. a) The T1 weighted series shows distinct loss of signal intensity in the third image before normalising, b) The T2 weighted series displays a fluctuating course with an initial decrease in intensity followed by an increase before normalising, c) The out-of-phase GE series displays the most striking result with an obvious increase in signal intensity by the third image before returning to baseline.

Fig. 1: Hartman (2004) displays an example of focal signal changes in bone marrow consistent with yellow to red reconversion.
Fig. 3: Hanrahan (2010) displays a sagittal FDG PET image of bone marrow stimulation.
Conclusion

The incidence of bone marrow hyperplasia following administration of G-CSF occurs commonly in patients and the progression to marrow reconversion is significant.

In-phase / out-of-phase imaging is often used to assess fatty infiltrate that is present in marrow hyperplasia but rare in metastasis\textsuperscript{15}. Several studies recommend an out-of-phase decrease of signal >20% as a useful threshold for differentiating metastasis from benign hyperplasia\textsuperscript{12,16,20}. However it should be noted that this process is not perfect and occasionally a bone marrow biopsy is required\textsuperscript{15}.

It is also important to acknowledge that MRI is not the only imaging modality prone to misinterpretation of bone marrow in this situation. PET imaging in particular can also misinterpret metastasis mimicking lesions following the use of G-CSF and current literature recommends caution interpreting PET imaging following administration of G-CSF for this very reason\textsuperscript{16,20}.

Personal Information

References


