

The Bone Biopsy Procedure and Diagnosis of Predialysis Renal Osteodystrophy

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Abstract

In end stage renal failure (ESRF) when patients require chronic maintenance dialysis, nearly all of them have abnormal bone histology named renal osteodystrophy (ROD). Because metabolic bone disease can produce fractures, bone pain, and deformities late in the course of the disease, prevention and early treatment are essential. To date, bone biopsy is the most powerful and informative diagnostic tool to provide precise information on the type and severity of renal osteodystrophy, and on the presence and amount of aluminum and strontium deposited in the bone. Although considered as an invasive procedure, bone biopsy has been proven to be safe and free from major complications, but the operator's experience and skill is important in further minimizing of morbidity. Alternatives to the bone biopsy continue to be searched for, but the non-invasive bone markers have not been proven to hold sufficient diagnostic performance related to the bone turnover, mineralization process and bone cell abnormality. Hence, transiliac bone biopsy remains the golden standard for the diagnosis of renal osteodystrophy.

When renal disease develops, mineral and vitamin D homeostasis is disrupted, resulting in diverse manifestations in bone cells and structure as well as the rate of bone turnover. In end stage renal failure (ESRF) when patients require chronic maintenance dialysis, nearly all of them have abnormal bone histology named renal osteodystrophy (ROD) [1]. During the last years, concomitantly with the introduction of new treatment strategies the spectrum of ROD has been changed considerably [2]. Whereas until a decade ago most patients presented with secondary hyperparathyroidism (HPTH) [3], adynamic bone (ABD) [4] has become the most common lesion over the last years. Whilst during the last years the issue of ROD has been studied thoroughly in the dialysis population, much less is known about the spectrum and predisposing factors determining the development of a particular type of ROD in ESRF patients not yet in dialysis. Because this metabolic bone disease can produce fractures, bone pain, and deformities late in the course of the disease, prevention and early treatment are essential. To date, bone biopsy is the most powerful and informative diagnostic tool to provide important information on precisely the type of renal osteodystrophy affecting patients, the degree of severity of the lesions, and the presence and amount of aluminum and strontium deposition in bone [5, 6]. Bone biopsy is not only useful in clinical settings but also in research to assess the effects of therapies on bone [7]. Although considered as an invasive procedure, the bone biopsy has been proven as safe and free from major complications besides pain, hematoma or wound infections, but the operator's experience and skill is important in minimizing morbidity [8]. Alternatives to the bone biopsy continue to be pursued, but the non-invasive bone markers have not been proven to hold sufficient diagnostic performance related to the bone turnover, mineralization process and bone cell abnormality. At present however, the transiliac bone bi-

opsy remains golden standard in the diagnosis of renal osteodystrophy.

The first prerequisite for an informative bone biopsy is proper *in vivo* labeling with antibiotics from the tetracycline family because of their spontaneous fluorescence and binding to actively forming bone surfaces. The first label is administered for 2 days followed by an 8-15 day free interval. During the 2-4 days after the free interval, the patient takes a second course of antibiotics. Bone biopsy is then performed 4-6 days after the last administration of tetracycline. Using two labels with different colors assures accurate assessment of the mineralization rate. For patients with impaired renal function, dosages of tetracycline hydrochloride and Declomycin® are usually 500 mg and 300 mg b.i.d., respectively.

Most bone biopsies are performed under local anesthesia. The transiliac bone biopsy site is 2 cm posterior and 2 cm inferior to the anterior iliac spine. Iliac crest biopsies result in cores with a single cortical surface, while transiliac biopsies yields cores with two cortical surfaces [9]. The specimen is cut in two cylinders. The largest part is used for histological examination on 5 µm Goldner stained undecalcified, methylmethacrylate embedded bone sections. Unstained sections (7 µm) were used for the evaluation of tetracycline labels by fluorescence microscopy. The second part is weighed directly after sampling and used for bulk analysis by means of electrothermal atomic absorption [10].

Our bone biopsy study in an unselected group of 84 ESRF patients revealed 62% of predialysis population to have abnormal bone histology in the absence of aluminum and strontium [1]. ABD was found the most prevalent bone lesion observed in 23% and HPTH (mild form) was diagnosed in only 9% of the patients. The distribution of ROD in our study differs considerably from the ROD spectra reported previously in non-dialysed renal failure patients, al-

lowing tailored specific therapeutic measures for each ROD entity.

As a part of multicentric, prospective, double bone biopsy study (baseline and after a year of treatment) we compared the effect of lanthanum carbonate (LC) and calcium carbonate (CC) on the evolution of renal osteodystrophy in dialysis patients [7]. At the baseline biopsy 65% of the patients showed histomorphometric characteristic for mixed bone lesion and there was no patient diagnosed to have normal bone, which might be partially explained by different type

of classification used for this evaluation. However, LC treated dialysis patients showed almost no evolution towards low bone turnover over a 1 year while CC treatment promoted development of ABD in half of the patients.

Our experience of performed more than 150 transiliac bone biopsies showed no evidence of serious complications besides a few patients who experienced moderate pain at the site of bone biopsy. So, we can conclude this method as safe and valuable diagnostic tool in diagnosis of renal osteodystrophy.

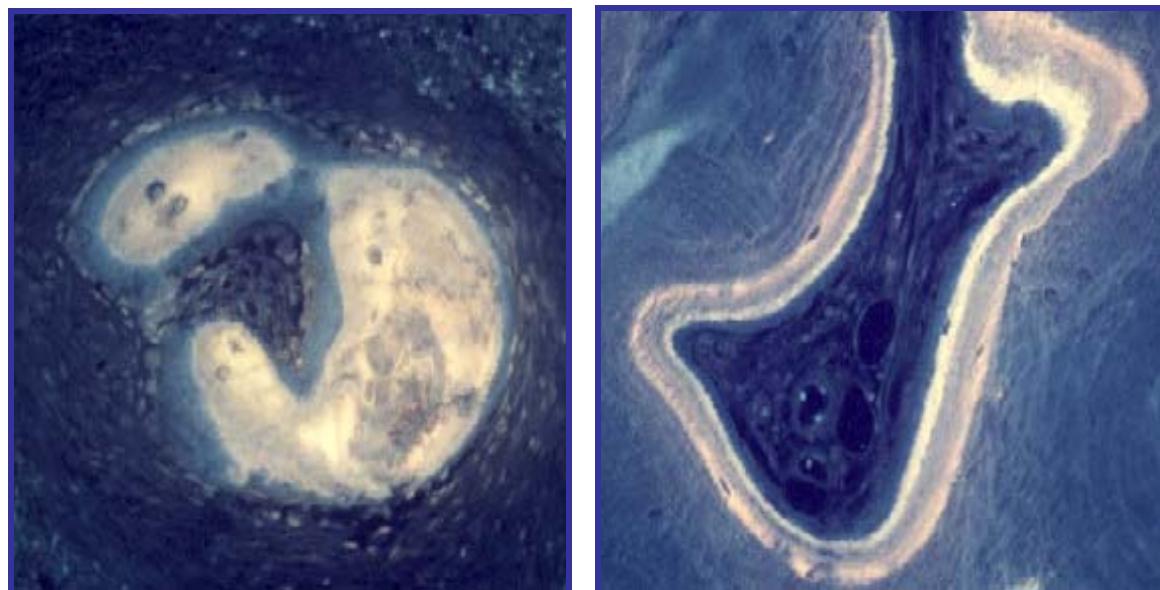


Figure 1. Example of a tetracycline double labelling at the bone-osteoid interface in an undecalcified 7 μm thick section of human trabecular bone. A. The clearly separated labels indicate an intact, active bone mineralization. B. The diffuse labeling is indicative for a disturbed mineralization

Histological classification of ROI)

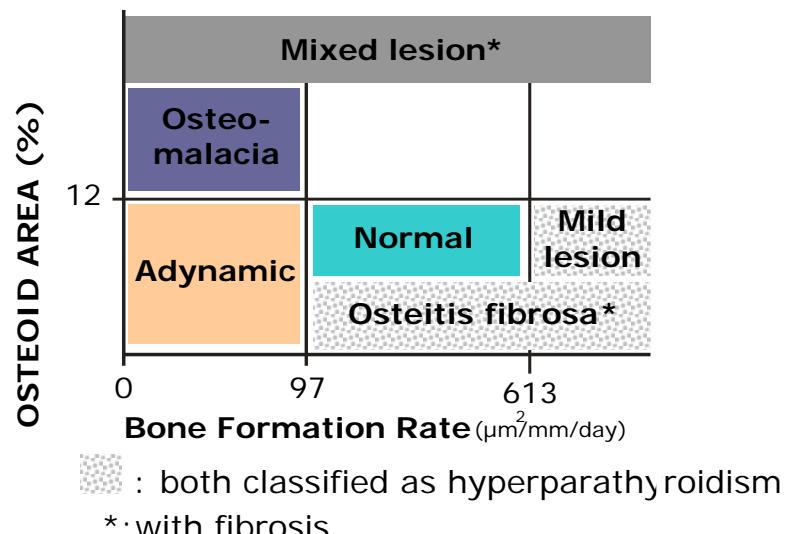


Figure 2. A schematic overview of classification of bone histology

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