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Is the Eichenholtz classification still valid for the diabetic Charcot foot?

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Summary

In his 1966 monograph "Charcot joints", Sidney N. Eichenholtz (1909–2000) described "three well defined stages … in the course and development of a Charcot joint", based on plain X-rays of 68 patients. Since then, medical imaging has advanced very much: computed tomography and magnetic resonance imaging (MRI) scans exceed plain X-ray by far in detecting foot fractures and other injuries. The earliest, nondeforming, X-ray-negative inflammatory stage of the acute Charcot joint of the diabetic foot can be visualised only by use of MRI. This stage, which Eichenholtz evidently failed to recognise, will heal without significant arthropathy, if treated in time. By contrast, the stages considered by Eichenholtz inevitably result in major arthropathy and foot deformity. Hence, superseding the Eichenholtz classification is overdue. We propose an MRI-based classification comprising two severity grades (0 and 1, according to absence/presence of cortical fractures) and two stages (active/inactive, according to presence/absence of skeletal inflammation).

Key words: *diabetes mellitus; osteoarthropathy; neuropathy; joint; Charcot; arthropathy; neuroarthropathy; insensitivity to pain; bone bruise; bone marrow oedema; MRI; history*

Introduction

In 1966, Sidney N. Eichenholtz, M.A., M.D., F.A.C.S., assistant clinical professor of orthopaedic surgery, Cornell University School of Medicine, attending orthopaedic surgeon at the Bronx Veterans Administration Hospital, the Hospital for Special Surgery, the New York Hospital, and director of orthopaedic surgery at the Yonkers Professional Hospital, New York, published a monograph called "Charcot joints" [1].

The monograph displays a collection of X-rays of 68 cases in cross-sectional manner; follow-up studies are lacking. Patients were aged between 41 and 70 years on average. Their Charcot joints (94 in total) were due to syphilis (n = 34), diabetes mellitus (n = 12), alcoholism (n = 4), syringomyelia (n = 3) and leprosy (n = 1), amongst others. The knee (n = 32), foot and toes (n = 31), ankle (n = 13) and hip (n = 7) were most often affected. Chief complaints when first seen were the following: painless swelling (n = 28), pain and swelling (n = 24), instability (n = 17), ulceration (n = 14), numbness (n = 11), weakness (n = 6). Eichenholtz used the term "Charcot joint" to "designate the progressive destructive changes involving joints of patients with or without neurologic disorders provided those changes follow the pathologic sequence to be described" [1]. Mixing with other joint disorders, especially with osteomyelitis, was carefully avoided.

The Eichenholtz stages

This sequence, as Eichenholtz saw it, is stated in two passages of the book (pages 7–8 and page 217), which are quoted here:

"Evolution of a Charcot joint
"To the interested observer, privileged to follow the changes in a neuropathic joint by means of serial roentgenograms, a logical and usually predictable sequence of changes can be detected. No other pathological entity demonstrates the same course of events which are believed to be pathognomonic of Charcot joints. For purposes of classification these changes have been divided into three stages during which various gross pathological findings described previously can be elicited.

"Stage of development
"Roentgenograms of the early formative stage of a Charcot joint will show some evidence of debris formation usually beginning at the articular margins (…..). Synovial biopsy at this point will demonstrate microscopic evidence of the debris embedded within the synovium and pathognomonic of the disease (…..). This will be followed by fragmentation of the subchondral bone and attached articular cartilage (.….). As this process is repeated further disruption and capsular distention results in subluxation or dislocation.

"Stage of coalescence
"This is characterized by absorption of much or all of the fine debris. Most of the larger fragments fuse together and then adhere to and coalesce with the adjacent bones (.….). This process together with the loss of vascularity resulting from the previous disorganization and fragmentation

produces the characteristic sclerosis of the bone ends of a Charcot joint.

"Stage of reconstruction
"The bone ends and major fragments become rounded; re-vascularization produces a diminution in the degree of sclerosis. As more viable bone is reconstituted some attempt at reformation of joint architecture becomes apparent (.....)." [1].

On page 217, Eichenholtz summarised his description of the natural course of a Charcot joint as follows:

"Three well defined stages are described in the course and development of a Charcot joint:
"I Stage of Development
"debris, fragmentation, disruption, dislocation.
"II Stage of Coalescence
sclerosis, absorption of fine debris, fusion of most large fragments.
"III Stage of Reconstruction and Reconstitution
"lessened sclerosis, rounding of major fragment, some attempts at reformation of joint architecture.
"In some patients the process may repeat itself several times; in others, it may literally 'grind to a halt' before completion of the initial series of changes. No explanation is offered for these differences other than the assertion that they represent an inherent part of the disease. It is hoped that an accurate appraisal of the stage of development may be helpful in the prognosis of the disease and the determination of the optimal time for arthrodesing surgery."[1]

Evidently, the Eichenholtz stages are identical to the three physiological phases of fracture healing: inflammation, repair and remodelling underlying the Charcot arthropathy [2]. The stages do not relate to neuropathy, which does not differ between the stages or change during the course of the arthropathy. Presumably, Eichenholtz had in mind a kind of degenerative joint disease like osteoarthritis of the hip with its three severity grades. He did not consider, however, that the destructive Charcot process could come to a halt by appropriate intervention, for example by stopping mechanical usage.

Contemporaries' appraisal of Eichenholtz's monograph

The monograph was met with little enthusiasm, according to book reviews and citations soon after publication [e.g. 3–6]. For example, the *Journal of Bone and Joint Surgery* (Br) critic remarked: "This book is largely devoted to a series of excellent illustrations of Charcot disease affecting almost all the joints of the skeleton. Methods of treatment and arthrodesis are discussed, but there is little fresh information." [3] Another anonymous critic wrote in *Diabetes*, the journal of the American Diabetes Association, "Actually, the volume is more of an atlas than a text since, of the 200-odd pages, only 10 per cent are devoted to superficial discussions of the various aspects of Charcot neuroarthropathy, whereas the other 90 per cent consist of photographs of X rays and pathological material depicting various joint involvements, their progression etc., with appropriate descriptive material." The critic expressed some disappointment "from the diabetologist's point of view", that only 12 cases of the total series were diabetic patients [4]. Jack Edeiken deplored in *Radiology* "There are 73 figures which are poor in quality, and some are repeated. The photographs hardly do justice to the author's remarkable experience."[5] Johnson, in his most careful review on "neuropathic fractures and joint injuries" concluded "Almost all texts, including the recent book on the subject by Eichenholtz, deal primarily with the well-established Charcot joint and make no mention of the early stages of the condition." [6] The Eichenholtz stages did not receive much attention from the medical profession in the 1970s [7–9].

Eichenholtz's achievement

The historical achievement of Eichenholtz was, undoubtedly, his staging scheme because it opened a perspective for a "possible rational timing of therapy", as one of the critics mentioned [4]. The scheme pointed to similarities between the Charcot evolution and the characteristic course of fracture healing. It had some shortcomings, though. The clinical evolution was not considered, nor was the impact of repetitive load-bearing on disease activity in the early phase of the condition. Longitudinal data were not analysed. X-ray was becoming obsolete for staging the Charcot joint when Classen et al., in 1976, showed that bone scintigraphy of the feet could display "areas of potential or future joint involvement months before they become manifest" on X-ray [9]. Nevertheless, Eichenholtz's criteria are still being used for diagnosing Charcot foot in the United States of America [10].
In 1984, Edmonds and Watkins first reported follow-up data showing that immobilising and offloading the very early, X-ray-negative, inflammatory stage of the Charcot foot prevented major deformities [11]. Shibata et al. in 1990 labelled this stage as "stage 0", in addition to Eichenholtz's stages I–III [12]. The X-ray-negative scintigraphic abnormalities later were identified as reactive, inflammatory bone marrow oedema on magnetic resonance imaging (MRI) [13–18], and were shown to resolve by stopping mechanical usage of the foot [19–23].
To date, four small observational series with 74 cases altogether independently reported longitudinal data on this very early "stage 0" acute Charcot foot [20–23]. They demonstrated that treatment by offloading and immobilisation for 6 to 15 months on average stopped the disease activity and, in fact, healed it and prevented major foot deformities [20–23]. By contrast, withholding this treatment in ambulating patients with X-ray-negative acute Charcot foot inevitably resulted in deforming arthropathy with fractures [21, 24–26]. These data underscore the necessity to diagnose and treat the acute Charcot foot as early as possible.

Why should the Eichenholtz stages be abandoned rather than extended?

1. They do not represent the symptoms of Charcot arthropathy. In fact, they have been often mixed with the clinical diagnosis, to which they have no clear

relationship; this mistake on the part of the medical profession proved deleterious for the outcome, for example of the Charcot foot.

2. They do not cover the whole spectrum of the Charcot foot. Eichenholtz meant to describe the entire evolution of the condition. However, his staging scheme excludes the very early, X-ray-negative, acute stage of inflammatory bone marrow oedema (and bone bruises from trabecular microfractures), which is visible only on MRI. Why not label this acute stage as "Eichenholtz stage 0" [12, 20–23, 26, 27]? Neither the acute nor the healed stage "0" would fit Eichenholtz's original scheme. Healed stage "0" cannot be addressed as Eichenholtz stage III, which is characterised by severe foot deformities. Stage III, in fact, represents bone remodelling of healed Eichenholtz stage I (with its devastating joint destruction, after transition through stage II, *vide infra*). Stage "0", however, if treated optimally, will heal without major foot joint deformities, with or without persisting minor skeletal pathologies (e.g. subchondral cysts/sclerosis [20, 28]; see table 4). Thus, stage "0" cannot be represented within a modified Eichenholtz-scheme.
3. Conventional X-ray is inappropriate for diagnosing acute skeletal pathologies of the foot. Computed tomography (CT) and MRI scans reveal that most cortical foot fractures remain undetected by plain X-ray (see table 1) [29–31]. Moreover, bone marrow oedema and bone bruising can only be shown by use of MRI. Hence, an X-ray based staging scheme of the Charcot foot must necessarily be incomplete, inaccurate and imprecise.

MRI should replace X-ray for diagnosing and monitoring the Charcot foot

As reactive skeletal inflammation is the first symptom of acute Charcot foot, MRI rather than X-ray is the modality of choice to detect this condition. Skeletal inflammation of whatever aetiology corresponds to so-called bone marrow oedema on MRI [32]. Hence, X-ray-negative stress injuries (from overuse or sprain [29–31, 33]) as well as X-ray-positive fractures [34] can be visualised by use of MRI because of the inflammatory reaction they induce (table 2) [32, 34–36]. True oedema of the bone marrow – increased interstitial fluid induced by posttraumatic release of cytokines like tumour necrosis factor-alpha (TNF-α), interleukins, prostaglandin-E2 and leukotrienes – "is minor in most conditions so labelled on the MRI findings" [32]. The so-called bone marrow oedema seen on MRI corresponds to inflammatory cell invasion, and vascular and connective tissue proliferation [32]. It matches the histopathological findings of the Charcot foot, showing features of secondary (trabecular) bone healing [1, 35, 37–41]. Oedematous bone resembles "wet zwieback", as a surgeon would say. The time course of bone marrow oedema after a bone trauma has to be considered: it becomes visible only about 3 hours after the inciting event, expands over the next 1 to 2 months, and regresses during the following 3 to 10 months (depending on the extent of the bone injury and the treatment efficacy) [34, 42, 43].

Bone marrow oedema appears hypointense on T1–weighted images, hyperintense on proton density weighted (PDW) / fat suppressed, T2–weighted / fat suppressed and short T1 inversion recovery (STIR) images, and enhanced on T1–weighted images after injection of gadolinium contrast. However, STIR images are sufficient, and contrast media is not required in most cases of Charcot foot [34, 44]. CT scans may be helpful to fully explore the extent of bone lesions once the inflammation has healed and the bone has become remineralised [45].

Proposal for a new classification of the Charcot foot, based on MRI

An acute Charcot foot has to be considered in every patient with a swollen foot that is insensitive to pain on punctate stimulation with 512 mN pinprick stimulator [21]. Bone marrow oedema on MRI definitely establishes the diagnosis. A healed Charcot foot has to be considered in every patient with a nonswollen, pain-insensitive foot (on punctate stimulation with 512 mN pinprick stimulator) and a recent history of bone marrow oedema.

Four distinct clinicopathological categories of the Charcot foot can be discerned, comprising two stages and two grades. Active stage (stage A, acute) and inactive stage (stage B, becalmed, healed) are differentiated by presence/absence of skeletal inflammation (e.g. bone marrow oedema on MRI). The two grades are differentiated by the presence/absence of cortical fractures. Grade 1 is characterised by one or more present or past cortical fractures

Table 1: Skeletal pathology in patients with acute sprain, as shown by X-ray and simultaneous computed tomography (CT) and magnetic resonance imaging (MRI) scan [29].

Patients, n = 75	X-ray	CT	MRI
Metatarsal fractures (n)	48	86	85
Tarsal fractures (n)	24	74	100
Marrow oedema of – Metatarsal bones (n)	–	–	18
– Tarsal bones (n)	–	–	9

Table 2: Grading of bone stress injury, according to MRI findings. Adapted from Kiuru et al. [16, 17].

Grade I Endosteal marrow oedema (X-ray negative)
Grade II Periosteal bone oedema and endostal oedema (X-ray negative)
Grade III Muscle oedema, periosteal oedema and endosteal marrow oedema (X-ray negative)
Grade IV Fracture line (X-ray positive)
Grade V Callus in cortical bone (X-ray positive)

(full cortical breaks), while grade 0 is characterised by absence of full cortical breaks (table 3). Cortical breaks mark the quantitative distinction in severity between nondeforming and deforming damage; deformation is decisive for the outcome. Inflammation marks the distinction in quality between active and inactive disease process, which is decisive for the choice of treatment [46]. The categories differ from each other clinically, and in terms of histopathology and medical imaging (table 4). In the active stages, venous interleukin-6 (IL-6) and TNF-α are elevated, and more so in grade 1 cases [47]; both inflammation markers respond to offloading treatment, and are normal in the inactive stages of either grade [47]. Local inflammation promotes bone loss [35, 48, 49]. Hence, grade 1, but not grade 0, active cases display inflammatory local osteoporosis [50, 51], which is reversed by offloading treatment [50, 51]. Grade 1 may take longer to heal than grade 0 [21, 42]. Once healed, grade 1 cases are more deformed and lack more foot function than grade 0 cases. Consequently, inactive grade 1 cases need bespoke footwear to ensure nontraumatic ambulation, whereas for inactive grade 0 cases, off-the-shelf footwear may suffice [21]. The prognosis of grade 1 cases is worst; the risk of foot ulceration, and subsequent amputation and death, is substantially increased owing to devastating foot deformity [2, 25, 52].

Of course, these four categories apply irrespective of the trigger mechanism of the Charcot foot, which can be any kind of damage inducing localised bone inflammation (e.g., sprain, overuse, surgical trauma, secondary infection, gout attack, activated osteoarthritis, Lyme arthritis) in a person with pain-insensate feet.

Conclusion

As a result of advances in medical imaging technology, the X-ray-based Eichenholtz stages of the evolution of the diabetic Charcot foot have become obsolete. MRI is more sensitive than X-ray to detect acute skeletal injuries and, hence, MRI-based categories are more appropriate to describe the evolution of the Charcot foot than X-ray-based categories. Early MRI improves detection and management and, hence, the prognosis of acute Charcot foot and other skeletal affections like rheumatoid arthritis [53].

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Table 3: Categories of Charcot's arthropathy of the foot (Charcot foot), based on magnetic resonance imaging (MRI).

Stage	**Severity grade**	
	Low severity = grade 0 (without cortical fracture)	High severity = grade 1 (with cortical fracture)
Active arthropathy (acute stage)	Mild inflammation / soft tissue oedema No skeletal deformity X-ray: normal MRI: abnormal (bone marrow oedema, microfractures, bone bruise)	Severe inflammation / soft tissue oedema Severe skeletal deformity X-ray: abnormal (macrofractures) MRI: abnormal (bone marrow oedema, bone bruise, macrofractures)
Inactive arthropathy (becalmed stage)	No inflammation No skeletal deformity X-ray: normal MRI: no significant bone marrow oedema	No inflammation Severe skeletal deformity X-ray: abnormal (past macrofractures) MRI: no significant bone marrow oedema

Table 4: Clinicopathological and CT/MRI features of the proposed categories of the Charcot foot.

	Clinical symptoms	**CT and MRI features** [1]	**Histopathology** [2]
Active stage, grade 0	Mild inflammation (swelling, warmth, pain [?], increased by unprotected walking); no gross deformity	Obligatory: diffuse BMO and STO (Kiuru Grade I–III), no cortical disruption. Facultative: subchondral trabecular microfractures (bone bruise); ligament damage	Lamellar bone with active surface. Remodelling of trabeculae associated with microfractures. Marrow space replaced by loose spindle cells.
Active stage, grade 1	Severe inflammation (swelling, warmth, pain [?], increased by unprotected walking); gross deformity, increased by unprotected walking	Obligatory: fracture(s) with cortical disruption, BMO and STO (Kiuru grade IV). Facultative: osteoarthritis, cysts, cartilage damage, osteochondrosis, joint effusion, fluid collection, bone erosion/necrosis, bone lysis, debris, bone destruction, joint luxation/subluxation, ligament damage, tenosynovitis, bone dislocation.	Increased vascularity of the marrow space, active remodelling of woven bone. Compatible with response to (impaction) fracture. Osteonecrosis. Thickened synovium, fragmented cartilage and subchondral bone, invasion of inflammatory cells and vascular elements
Inactive stage, grade 0	No inflammation, no gross deformity.	No abnormal imaging, or minimal residual BMO; subchondral sclerosis, bone cysts, osteoarthrosis, ligament damage	Sclerosis of bone characterised by broad lamellar trabeculae with collagenous replacement and a low vascularity of the marrow space
Inactive stage, grade 1	No inflammation; persistent gross deformity, ankylosis	Residual BMO, cortical callus (Kiuru grade IV); joint effusion, subchondral cysts, joint destruction, joint dislocation, fibrosis, osteophyte formation, bone remodelling, cartilage damage, ligament damage, bone sclerosis, ankylosis, pseudoarthrosis	Woven bone, immature and structurally disorganised, fibrosis

BMO = bone marrow oedema; STO = soft tissue oedema
[1] From [16, 17, 20, 27, 28, 45] and own observations (unpublished)
[2] Adapted from [1, 37, 38]
Kiuru grades: see table 2

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