

TITLE PAGE

Chronic fibrosing osteomyelitis **of the jaws**: An important cause of recalcitrant facial pain. A clinicopathologic study of 331 cases in 227 patients

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ABSTRACT

Objective. A retrospective and followup analysis of 331 cases of **Chronic Fibrosing Osteomyelitis of the Jaws (CFOJ)** in 227 patients.

Study Design. Demographic, clinical, surgical and microscopic characteristics were tabulated for all patients. A followup mail survey was used to determine degree of symptom relief experienced since surgery.

Results. The female/male ratio approached 7/1 with a mean age of 53 years. The most common sites were the mandibular posterior followed by the maxillary posterior regions. Consistent clinical findings included intractable jaw pain mimicking odontogenic origin but unresponsive to usual therapies, minimal or undetectable radiographic abnormalities on plain films but dramatic radiolucencies detected on **Cone Beam Computerized Tomography**, and large cavities either empty or filled with blood mixed with lipid globules encountered at surgery. The most common histomorphologic findings were vital lamellar bone, prominent resting and reversal lines, microshards and splaying of trabeculae, rounded trabeculae, marrow fibrosis and pools of erythrocytes and lipid globules, often together. Moderate to complete relief of symptoms for periods up to 108 months post-surgery were reported by 83% of the 70 patients who returned the survey.

Conclusions. Based upon this study, CFOJ is a unique entity with consistent clinicopathologic features. Its features suggest a pathogenesis based on bone marrow ischemia. CFOJ can be treated on a rational basis with a justifiable expectation of success and probably cure.

Chronic Fibrosing Osteomyelitis **of the Jaws**: An Important Cause of Recalcitrant Oral Facial
Pain

A Clinicopathologic Study of 331 Cases in 227 Patients

Background

Chronic fibrosing osteomyelitis of the jaws (CFO) is the most recent name for a painful condition which may affect one or more segments of the jaws.¹ Similar (perhaps in some cases identical) conditions have been previously reported and studied under a variety of names, including Ischemic Osteonecrosis,² Bone Marrow Edema Syndrome,³ Neuralgia Inducing Cavitational Osteonecrosis (NICO),^{4,5} Ratner Bone Cavity,⁶ and Alveolar Cavitational Osteopathosis⁷. Because of its atypical pain pattern, the frequent lack of or unclear findings on routine ~~plane~~ **plain (periapical or panoramic)** radiographs and the fact that the pain often mimics dental-related pain, this condition often goes unrecognized by health care providers. Consequently these patients suffer not only needless or inappropriate therapy, but continued pain and the resultant depression and other psychological difficulties that can accompany chronic undiagnosed and inadequately treated pain¹. **Moreover, in view of the many factors associated with its occurrence specifically in the jaws as described above and below, we believe and suggest that this condition would be more appropriately termed chronic fibrosing osteomyelitis of the jaws (CFOJ) and will so refer to it in this report.**

Between the years 2007 and 2013 over 600 specimens of CFOJ were received by the Indiana University School of Dentistry Oral Pathology biopsy service (IUSDOP) **from all contributors,**

including over 300 from one large private endodontic practice (EP) in central Indiana. Because the EP has been committed to attending to these patients and developing specific clinical diagnostic and therapeutic protocols, it has now developed into, in essence, a referral center for patients with suspected CFOJ. At the same time, the experience gained by IUSDOP in studying these cases has aided in clarifying the essential histomorphologic features of this condition. Working in partnership, then, the EP and IUSDOP have identified clear clinicopathologic correlations, allowing consistent and reliable diagnosis of CFOJ.

The aims of the current study were to a) perform a detailed retrospective analysis of the demographic, clinical, surgical and histomorphologic features of the existing CFOJ cases, b) survey the corresponding patients from the EP who were reachable and willing to respond in order to gain a better understanding of the natural history and long-term response to therapy, and c) glean from this information some understanding of the pathogenesis of this condition.

Methods and Materials

Clinical Protocol

IRB. This protocol was reviewed and approved by the Indiana University Institutional Review Board (re #IRB000000228) (Study #1404722078) in compliance with the Helsinki Declaration. Each subject signed a detailed informed consent form.

The entire cohort of 331 cases from 227 patients was selected from patients treated by the EP and diagnosed by IUSDOP between 2007 and 2013 and, upon thorough review whose clinical, surgical and microscopic features, met the essential criteria used in this study.

Demographics

The demographic data was recorded for each patient (Table I), including gender, age and site(s) of lesion(s)

History. For each patient a complete medical and dental history was taken, with special note of hospitalizations, procedures, trauma and medications. A history of present illness was elicited, including location, onset, and duration of symptoms and awareness of any agents or events associated with the onset or recurrence of symptoms. Previous dental procedures, including their dates and outcomes, present or on-going medications, both prescription and over the counter (including supplements), were noted, as well as a history of any physical therapy or chiropractic manipulation.

Pre-operative diagnostic studies and procedures. Routine pulp testing, including thermal, electrical and percussion sensitivity of the teeth was conducted. **This was performed on every tooth in the quadrant involved as well as the opposing quadrant.** Periodontal probing was performed throughout the dentition. Firm palpation of the alveolar process was conducted in all segments, both maxillary and mandibular, in order to test for the acute palpation sensitivity which we have found to be so characteristic of CFOJ lesions. Current periapical radiographs

were either accepted from referrals or were taken (Figure 1). Much more helpfully, Cone Beam Computed Tomography (CBCT) were taken (Figure 2). In some cases, if there was minimum visibility of medullary bone loss on the CBCT, a Technetium 99 (Tech 99) bone scan was procured. Further, a very important part of the presurgical evaluation was intraosseous anesthesia of the suspected area. The technique utilized an X-Tip (Dentsply Maillefer, Johnson City, TN, U.S.A.) trephinator placed into the medullary defect passing through the gingiva and cortex. Then 1.8 cc of 3% mepivacaine was injected into the medullary bone defect. The patient was then released with instructions to challenge the area if any specific triggers (e.g., exercise, chewing, bending down, etc.) were known and to call back the next day with a report on the amount of relief, if any, experienced from the intraosseous anesthesia. **Thus the clinical diagnostic algorithm used was as follows:**

- a) **Patient complains of chronic jaw pain (> 6 months)**
- b) **Frequent common histories: multiple attempts to correct pain in area; e.g., splints, endodontic procedures, extractions, rounds of antibiotics, multiple practitioners, history of dry socket, bad taste in area, all tissues appear clinically normal**
- c) **Rule out odontogenic origin (e.g., pulp pathology, cracked tooth syndrome, periodontal disease)**
- d) **Rule out temporomandibular disease, and Eagle and Ernest syndromes**
- e) **Alveolar process over lesion very palpation tender**
- f) **Often able to eliminate pain completely although temporarily by carefully localized local anesthetic**

Surgical procedure. Following the administration of general anesthesia* profound local anesthesia was added. Then a full-thickness rectangular flap was designed to extend beyond the anticipated margins of the bony lesion and incised. The horizontal component of the incision was made in the gingival sulcus when around teeth, and near the ridge crest in edentulous areas. The osteotomy through the cortical plate was made with a high speed nitrogen drive Hall Drill (Conmed Linvatec, Largo, FL, U.S.A.) using a large round end fissure or round bur. The entry centered initially over the largest part of the defect as seen on the CBCT (Figure 3). The lesion then underwent thorough curettage, **all curettage performed with either straight or right angle curettes. No rotary instrumentation was used except for decortication for access purposes. The defects were curetted in every direction until firm resistance was met, signifying transition from diseased medullary bone to normal bone (working assumption used in all cases). In addition, the cortical plate osteotomy had to be extended in any direction in which it inhibited access to the involved friable mushy bone (Figure 3). The extent of the bony curettage included any medullary space/bone of poor integrity and any excavations which produced hemorrhage with an oily sheen.** and ~~the~~ **T**he tissue removed was prepared to be submitted for routine pathologic examination and ~~for microbiologic culture.~~

Cultures were not routinely taken for two reasons: First, the involved jaw usually showed no clinical signs of infection (redness, swelling, drainage, fever); second, practically all these patients had been on multiple rounds of antibiotics from multiple practitioners before getting to us, to no or only temporary avail. The cavity was then irrigated with hydrogen peroxide and chlorhexidine. Next, the defect was packed with demineralized freeze-dried bone allograft (DFDBA) mixed with plate-rich plasma (PRP) derived from the patient. The graft was then covered with CaSO₄ mixed with platelet poor plasma (PPP) derived from the patient to

preclude connective tissue growing into the surgical defect. Finally, the flap was replaced and sutured.

*Except when the CFOJ finding was unexpected at the time of surgery

Microscopic Review

All cases coded for CFOJ which were submitted to IUSDOP by the EP from 2007 to 2013 were examined histologically. When necessary the tissue was briefly decalcified and all cases were stained with standard hematoxylin and eosin. The cases were assessed for the presence or absence of 19 separate microscopic parameters (Tables II and III).

Followup Survey

A followup paper survey was sent to all patients in the study. This 20 item survey consisted of questions related to the history of the lesion(s) as well as the nature of the signs and symptoms experienced before and since the surgery. **(Please see Supplemental Material.)** Specific attention was paid to the extent of relief of symptoms, if any, from the time of surgery to the time completion of the survey.

Results

Demographic findings (Table I). The records of 227 CFOJ patients were examined and the demographic and clinical data tabulated.

Gender: Of the total of 227 patients 198 (87%) were female and 29 (13%) were male, a female/male ratio of almost 7/1.

Age: The age range was 38-90 years. The mean age for all 227 patients was 53 years; however there was notable difference between genders: for females the mean age was 54 years, while for males it was 45 years.

Site: For purposes of clarity and simplicity the sites were mapped according to jaw sextants corresponding to tooth numbers: Sextant #1 upper right (tooth areas 1-5); sextant #2 upper anterior (tooth areas 6-11); sextant #3 upper left (tooth areas 12-16); sextant #4 lower left (tooth areas 17-21); sextant #5 (tooth areas 22-27); and sextant #6 (tooth areas 28-32). The frequency of sites involved in descending order in terms of % of patients was as follows: sextant 4: 78 (34%); sextant 6: 70 (31%); sextant 1: 60 (26%); sextant 3: 57 (25%); sextant 2: 35 (15%); and sextant 5: 5 (2%). **(Site distribution is also presented as a partial skull diagram in the**

Supplemental Material. The percentages total more than 100% due to multiple site involvement in some patients. Specifically, 38 patients (17%) had two sextant involvement, 6 patients (3%) had three sextant involvement, and 11 patients (5%) had more than 3 sextant involvement. In addition, in 143 patients (63%) the lesion was recurrent in the same site.

Clinical findings. Patients returned to the office seven to ten days post-surgically for assessment of their course of healing and the effect of medications, and for suture removal and tissue

inspection. Post-operative symptoms varied from complete disappearance of symptoms to one case of worsening of the patient's original complaints. Oral antibiotics were continued for two more weeks and recommendations for oral analgesics were added as needed. The sutures were removed and tissues inspected. Almost universally, the soft tissue overlying the operated areas appeared to be in an advanced state of healing compared to those observed for similarly wounded surgical areas.⁸

Radiographic findings: The radiographic appearance of CFOJ is quite variable and very difficult to identify with intraoral periapical or panoramic images. CBCT is a much better modality for identifying areas affected by CFOJ, but even this method cannot detect all lesions. For example, in conjunction with the current study, in a subset of 20 biopsy-proven CFOJ cases, only 80% were identified with CBCT. The radiographic appearance of maxillofacial bone affected by CFOJ can range from normal appearing bone to a well-defined radiolucency. The most common radiographic finding associated with CFOJ is a diffuse radiolucency with homogenous trabecular bone, not unlike osteopenia. However, while osteopenia is more generalized, the diffuse radiolucency associated with CFOJ is regional. Moreover, ~~the diffuse radiolucency seen in the maxillary CFO usually extends between~~ **the diffuse radiolucencies seen in the maxillary CFOJ cases usually extend between** the roots of teeth, whereas true osteopenia seems to be confined to the supporting bone rather than the alveolar bone. The most common sites for this appearance of CFOJ are the areas of missing mandibular third molars and around the roots of maxillary premolars and molars. The remnants of lamina dura are often present in the areas of missing third molars. Finally, when the CFOJ occurs in relation to an extraction site, the radiographic appearance of the CFOJ must be correlated with the history of extraction. When

this is done ~~often the extraction site is multiple years old while the radiographic appears like it is only multiple months~~ **it is often the case that an extraction site which is in fact multiple years old appears radiographically as if it were only several months old.**

Surgical findings: The most typical findings were as follows. The cortical plate was usually intact, but often covered a very large underlying cavity in the bone. The medullary bone appeared to drain a sanguineous exudate which had droplets of lipid floating on the surface (so-called “chicken broth” appearance) (Figure 4). **It is our hypothesis that these globules represent the coalescence of the lipid released from degeneration of lipocytes resulting from infarction of the marrow, and appearing in the form of lipid globules microscopically. This is one of the findings identified most consistently in our cases (see microscopic findings and discussion).** Often there were abnormally large spaces in the medullary bone and/or the trabeculae were friable, having a “mushy” character. In addition, soft tissue of a fibrillary and/or fatty nature was often encountered.

Pathologic findings: After a review of all the biopsy specimens of CFOJ from the EP, a total of 331 biopsy cases were accepted. (Many patients had more than one specimen removed either simultaneously or sequentially.) The histopathologic findings and the percentage of cases showing each are shown in Tables II (findings in bone) and III (findings in bone marrow and soft tissue). Table IV tabulates the chief histopathology features (those findings present in 80% or more of the cases examined).

In 99% of the cases the bone was vital, as reflected by the presence of osteocytes within the lacunae. Also in 99% of the cases the bone was lamellar, although 41% also included some woven bone (only 1% showed woven bone only) (Figure 5). 98% showed resting and reversal (cement) lines (Figures 5 and 6). Another very common finding was the presence of narrow microshards of bone lying free and unattached to a bone trabecula (Figures 5, 7, 9-11). Almost equally as common (95%) and often in close proximity to groups of microshards was a delamination or splaying effect (Figure 5,7, 9-11) at one or more edges of bony trabeculae. Also common (90%), and in our experience rarely seen in other bone disease in the jaws, was the presence of trabeculae with distinctly rounded external contours (Figures 5 and 6).

Without doubt the three most common changes seen in the bone marrow were the presence of fibrosis (Figures 6) (usually delicate) in the bone marrow (96%), pools of free erythrocytes (Figures 6-11) (93%) and the presence of clear lipid-like vacuoles (Figures 6,8 and 11) (80%) suspended within these pools of erythrocytes. Also of note, 86% of the cases contained fatty marrow, 34% hematopoietic marrow, 29% both and 5% neither. Less common microscopic findings included inflammation (40%), prominent blood vessels (40%), granulation tissue (34%), nerves (34%), scar (12%), lining epithelium (6%), bacteria (2%) and foreign body (1%).

Followup Survey Findings: A total of ~~239~~ **227** surveys were mailed and 80 were returned for a response rate of ~~33.5~~ **35%**, **Of these 80 surveys returned, 10 were excluded from the results due to incomplete or lack of pain relief information. Thus a total of 70 cases form the basis of the followup results which** are displayed in the graph in Figure 12, expressed as level of pain relief (complete, moderate, minimal or none) vs time elapsed since surgery (in months). Of

these, 32 (46%) patients experienced complete relief, 26 (37%) moderate relief, 3 (4%) minimal relief and 9 (13%) no relief. Thus 56 (83%) of the patients answering this part of the survey experienced complete or moderate relief of pain. Moreover, examination of the graph in Figure 12 reveals that the degree of pain relief was not related to the time elapsed since surgery. In other words, it appears that any given patient either experienced pain relief or did not, regardless of the time elapsed since surgery. Thus the degree of pain relief did not appear to be a function of time. **This conclusion was further supported using the Mantel-Haenszel chi-square test. Specifically, the data as presented in the bar graph were tested for a time trend, and tested again with the times collapsed into two-year intervals instead of one. Neither analysis showed a significant trend over time (p=0.28 using individual years and p=0.23 using the collapsed intervals. Finally, as displayed in the Results Respondents column of TABLE I, the demographic data of the survey respondents compare very favorably with those of the entire cohort of 227 patients. There is a small difference in average ages, but the female to male ratio was very similar as was the distribution of the lesions amongst the various sextants and the percentage that had recurrent lesions at the same site. This suggests that the respondents were quite representative of the entire cohort.**

Discussion

General comments

The current study comprises the largest number of lesions and patients with CFOJ yet reported in which all the cases were clinically evaluated, treated and diagnosed by the same small group

of clinicians and pathologists. As indicated above, CFOJ of the jaws, or similar lesions, have been reported by numerous authors and given a variety of names. However, since these studies have been carried out in a variety of ways and involved lesions, patients and reports from a variety of clinicians and surgeons, we cannot be certain that they all represent the same condition we are reporting in this study. Nevertheless, we believe they have enough similarity that they can serve as useful comparisons and contrasts with those reported here. It is not our purpose in this paper to present a comprehensive history of all aspects of CFOJ, but rather to report our findings and compare them as legitimately as possible to those of major previous reports. For an exhaustive, complete and very scholarly review of all aspects of this topic we would refer the reader to the paper by Bouquot and McMahon.²

Demographic findings

Our demographic findings agree to a remarkable degree with those reported in the few other large studies reported.^{5,11,12} Particularly notable are the marked female gender predilection, the tendency for these lesions to occur in middle-aged to older adults and the high percentage which occur in the posterior quadrants or sextants of the jaws.

Clinical and radiographic findings

It is an unfortunate hallmark of CFOJ that the lesions are very difficult to find on intraoral radiographs used routinely in dentistry. They are somewhat more visible on panoramic images, and Roberts has suggested using a stereoscopic technique in viewing them to give 3-D illusion (personal communication). This problem is due to the large amount of medullary trabecular bone that must be missing in order to be radiographically detectable for the clinician. Bender

and Seltzer reported this phenomenon in the 1960's^{9,10}. One of the endodontists in the EP was called by the hospital to come and review the several "hot spots" found on the Tech 99 bone scan which had been ordered by an osteopathic physician for his patient to help diagnose her facial pain. Less than coincidentally, these areas of uptake were all in regions where she was having chronic pain of non-odontogenic origin. From that fortuitous finding, all of our suspected CFOJ cases were scanned using Tech 99 from that time forward until CT scans became readily available to dentistry. Bouquot et al.¹¹ found a high degree of correlation between positive Technetium 99 scans and the histopathologic findings of NICO (CFO) similar to what we report in the current cases of CFOJ.

As indicated in the Results section, the radiographic appearance of CFOJ is quite variable and very difficult to identify with intraoral periapical or panoramic images. CBCT is a much better modality for identifying areas affected by CFOJ but is not able to identify all lesions. It is not uncommon that a CFOJ which is virtually undetectable on intraoral/panoramic radiographic images will be very clearly delineated with CBCT. Accordingly, the radiographic findings, or lack thereof, must be interpreted in the context of the entirety of the clinicopathologic picture.

Finally, it must be acknowledged that underlying bone disease such as generalized osteopenia, osteoporosis, other specific metabolic bone diseases as well as antiresorptive medication could certainly affect the radiographic appearance of the bone in these patients and lesions. However, as these factors were not routinely recorded in the records of these patients the present study does not allow us to make any conclusions in that regard.

Surgical findings

Prior to our use of the surgical technique described in Methods and Materials – Operative Procedure, the lesions were packed with antibiotic-saturated resorbable collagen sponges based on the assumption that the lesions were primarily low grade infections. This technique was used for several years with relatively good success resulting in complete or substantial relief of pain. Unfortunately, there were still 30-40% of the patients who would return in a few months or years with recurrent pain in the same area. This clinical experience agreed with the recurrence rate found by Bouquot and others¹². After clinical and radiographic findings suggested incomplete healing of the original lesion, the site would be re-surgerized using the same technique. Usually the lesion would be much smaller than the original, and the tissues removed were more fibrous. There was almost always a scar band exiting through the center of the original osteotomy (“fibrous healing defect”). We found that reentries into the medullary bone were necessary anywhere from two to four times before these patients no longer had recurrent symptoms.

Microscopic findings

As indicated above, the chief histopathologic features (present in 80% or more) we identified in our 331 lesions were as follows: predominantly vital bone, lamellar architecture, prominent resting and reversal (cement) lines, microshards, splaying, rounded trabeculae, marrow fibrosis, pools of erythrocytes and lipid globules. Many, although not all, of these features have been described by others.¹¹⁻¹⁵ On the other hand some of the features that have been described in other large series, such as plasmostasis and necrotic bone, were not features we recognized in our

cases. Still others, such as “microcracking,” we interpreted as similar to what we describe as delamination or splaying effect.

In assessing our microscopic findings we asked ourselves two principal questions: 1) How are the chief histopathologic features observed in these specimen consistent with the clinical and surgical findings? And 2) What might these findings imply regarding the pathogenesis of CFOJ?

In assessing the first issue, we must remember that the specimens submitted to us consist of poor quality bone remaining in the lesion together with mostly curettings from the walls of the bony crypts which have been created by this process. The vitality (as indicated by the presence of osteocytes within the lacunae) and predominantly lamellar nature of the bone are consistent with bone which in vivo is still connected to its blood supply and which has been present for long enough that, even in the face of remodeling, is mature (predominantly lamellar). **While there was some necrotic bone identified, it is our interpretation that the vital bone represents the curettings from the walls of the cavity and that most of the necrotic bone resulting from the marrow infarct has already been resorbed.** The rounded trabeculae that are often seen are consistent with some slow resorption but stiff resistance by the bone to the process. The frequent resting and reversal (cement) lines are indicative of a long-standing process of slow remodeling seen in chronic low-grade inflammatory disease of bone. The delamination or splaying effect at the edges of some of the bony trabeculae, especially in combination with the presence of microshards in the neighborhood, suggests that **when the splaying extends the entire length of the trabecula the latter will fragment into microshards.** ~~the former process leads to the latter results in this particular condition.~~ The common presence of variably sized clear vacuoles

suggesting lipid suggests that they result from necrosis of marrow lipocytes resulting in breakage of their walls, releasing the lipid. The almost universal presence of numerous free erythrocytes suggests hemorrhage, perhaps secondary to thrombosis of tiny vessels supplying the marrow, simultaneously infarcting the marrow and spilling erythrocytes into the cavity surrounding the now released globules of lipid. This same phenomenon may very well account for the consistent surgical finding of a cavity containing blood which is surfaced by an “oily sheen” (or “chicken-broth” appearance mentioned above). Finally, the frequent presence of nerve fibers and bundles suggests that they may persist after the bone marrow is infarcted, leaving them vulnerable to damage and perhaps having something to do with the pain.

The second question we tried to answer was “What might the chief histopathologic features imply regarding the pathogenesis of CFOJ?” Three points are worthy of mention here. *First*, many, though not all, of the histopathologic features typically observed in the CFOJ are also seen in areas of long bone affected by infarct/ischemia.¹⁶ This leads us to the strong suspicion that CFO is basically a consequence of ischemia of the bone (especially the marrow) of the jaw. This view is shared by others who have studied this topic extensively.^{2,3,5,14,16} The picture has also been interpreted and described as the Bone Marrow Edema syndrome³, which is considered a mild form of ischemic osteonecrosis. *Second*, since the jaw, especially the mandible, even under normal circumstances has a very modest blood supply, any one or perhaps a combination of many different events or pre-existing conditions which might further restrict its blood supply could push the situation over the tipping point for the bone marrow, triggering infarction and necrosis of the bone marrow. *Third*, possible contributing factors which could accumulate to reach this tipping point might include: genetic predisposition to hypercoagulation (or

hypofibrinolysis), vascular anatomy of bone peculiar to the patient, presence of a history of a preceding dental, periodontal or jaw bone infections (and or trauma), or the excessive use of therapeutic or anesthetic agents with vasoconstricting properties. Bouquot and McMahon have reviewed the various factors which could serve individually or in combination to reach that tipping point of bone marrow infarct.² Glueck and colleagues have reviewed specifically the association of antithrombotic factor deficiencies and hypofibrinolysis with osteonecrosis and Legg-Perthes Disease.^{17,18}

Based upon the preponderance of clinical, radiographic, surgical and histopathologic findings, we believe that the condition we refer to in this report as CFOJ is the same as that which has in many if not most instances previously been reported as NICO.

Accordingly, the sequence of events leading to CFOJ might be as follows: From a variety of possible directions, events come together to cause an infarct of the bone marrow. But perhaps because of the small size of the mandible and maxilla, the periosteal blood vessels continue to supply enough blood and oxygen to maintain the vitality of the bone cortex. The infarct of the marrow causes necrosis of the marrow lipocytes with release of their cytoplasmic lipid which congeals into globules. The thrombosed and damaged vessels that normally supply oxygen to the marrow fall apart, continuously releasing the erythrocytes which are seen microscopically surrounding the lipid globules which resulted from necrosis of the marrow lipocytes.

Survey Findings:

As indicated in the Results section, 83% of the 70 patients who answered that portion of the followup survey reported moderate or complete relief of pain, while only 17% reported minimal or no relief. Furthermore, the degree of pain was not related to the time elapsed since surgery. In other words, in aggregate it appears that the degree of pain relief was not a function of time. A given patient either experienced significant relief or did not. This observation is certainly consistent with the proposed pathogenesis of CFOJ being one in which any number of factors combine to reach a tipping point at which the ischemic osteonecrosis is precipitated. It may be that those patients who did not respond to the standard therapy described above were so predisposed to ischemic osteonecrosis that they defied the therapy that had worked for most of the other patients.

Summary

Based upon this large series of cases, all diagnosed, managed and followed by the same small group of clinicians and pathologists, several conclusions can be made: First, CFOJ is in fact a real and unique entity which can usually be diagnosed clinically and microscopically with confidence. Second, evidence suggests a pathogenesis based upon ischemia of the bone marrow. Third, CFOJ can be treated on a rational basis. And fourth, properly diagnosed and appropriately treated, there is justifiable expectation of success as measured by relief or significant diminution of symptoms, suggesting healing of the bone.

While much remains to be learned about this unusual condition it is hoped that the results of this study will assist our health care colleagues to recognize the clinicopathologic features, include CFOJ in their clinical differential diagnosis and either manage the patients themselves or refer them to practitioners in a better position to do so. With greater recognition, both clinical and pathologic, and with appropriate treatment or referral, these patients then can be removed from the general category of atypical facial pain patients and have a reasonable hope for cure.

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TABLE I DEMOGRAPHIC DATA

FEATURE	RESULTS ALL PTS	**RESULTS RESPONDENTS
GENDER: F/M RATIO	198/29=87%/13% = 6.7/1	58/7=89%/11%=8.3/1
AV AGE OVERALL(YRS)	53	58
AV AGE FEMALES	54	57
AV AGE MALES	45	62
*SEXTANT INVOLVEMENT {N(%)}		
#1	60 (26)	16 (25)
#2	35 (15)	5 (8)
#3	57 (25)	16 (25)
#4	78 (34)	29 (45)
#5	5 (2)	2 (3)
#6	70 (31)	24 (37)
2 SEXTANTS INVOLVED	38 (17)	10 (15)
3 SEXTANTS INVOLVED	6 (3)	1 (2)
OVER 3 SEXTANTS INVOLVED	11 (5)	2 (3)
RECURRENT AT SITE	23 (10)	9 (14)
HISTORY OF PREVIOUS PROCESS/PROCEDURE AT SITE	143 (63)	17 (26)

*Jaw segments divided into 6 sextants

**Based on the 65 of the 70 respondents with complete data

TABLE II HISTOPATHOLOGIC FEATURES: BONE

FEATURE	%
VITALITY (OSTEOCYTES IN LACUNAE)	99
ARCHITECTURE	
LAMELLAR	99
WOVEN	42
BOTH	41
RESTING AND REVERSAL LINES	98
SPLAYING	95
MICROSHARDS	98
ROUNDED TRABECULAE	90

TABLE III HISTOPATHOLOGIC FEATURES: MARROW AND SOFT TISSUE

FEATURE	%
FIBROSIS	96
POOLS OF ERYTHROCYTES	93
LIPID GLOBULES	80
INFLAMMATION (CHRONIC)	40
GRANULATION TISSUE	34
PROMINENT BLOOD VESSELS	40
NERVES	34
SCAR	12
FOREIGN BODY	1
LINING EPITHELIUM	6
BACTERIA	2

TABLE IV CHIEF HISTOPATHOLOGIC FEATURES

FEATURE	%
VITALITY OF BONE	99
LAMELLAR ARCHITECTURE	99
RESTING AND REVERSAL LINES	98
MICROSHARDS	98
SPLAYING	95
ROUNDED TRABECULAE	90
MARROW FIBROSIS	96
POOLS OF ERYTHROCYTES	93
LIPID GLOBULES	80

LEGENDS

Figure 1a. **(All radiographs and the clinical photograph displayed in Figures 1, 2 and 3 are from the same patient.)** Preoperative periapical radiograph of a 36 year old female patient experiencing right mandibular aching of several months duration. Pulp testing was inconclusive of any pulpal disease. Both molars were percussion sensitive but neither was greater. Apical periodontal ligament space looked slightly widened on tooth #31.

Figure 1b. Postoperative periapical radiograph. In an effort to relieve her pain, endodontic therapy was performed on both molars. Unfortunately the aching was not improved. Teeth remained percussion tender and alveolar process was very tender to palpation.

Figure 2a. Sagittal reformatted view of right mandible demonstrating sparse medullary trabecular pattern in the #32 edentulous area as well as inferiorly to teeth #29 and #30.

Figure 2b. Axial reformatted view of the mandible demonstrating sparse medullary trabecular pattern in a lengthy zone near the inferior border of the mandible in the second molar region.

Figure 2c. Coronal reformatted view of face in the second molar region demonstrating notable absence of medullary bone lingual and inferior to the endodontically treated second molar (#31) (compared to the appearance of the same region on the left side). The entire canal filling was not captured in this view due to the root curvature.

Figure 3. Clinical photograph of the lengthy osteotomy used to access the large bony defect in the #29-32 area of the right mandible. An additional small osteotomy can be seen to access an extension of the bony defect extending coronally between bicuspid teeth #28 and #29.

Figure 4. Clinical photograph showing the oily fat globules which rise up on the blood which comes out of the bony defect. This is a common finding with CFO lesions and not seen in routine periapical surgeries performed by endodontists.

Figure 5. Histopathology of CFO. Demonstrates vital bone characterized by osteocytes (OC) within lacunae, both lamellar (LB) and woven bone (WB), prominent resting and reversal lines (RRL), rounded trabeculae (RT), splaying (SP) of the edge of a bone trabecula, and nearby microshards (MS) of bone (H&E stain, original magnification x100). *A high-resolution version of this slide for use with the Virtual Microscope is available as eSlide: VM03846.*

Figure 6. Histopathology of CFO. Demonstrates rounded trabeculae (RT) with prominent resting and reversal lines (RRL), fatty bone marrow exhibiting fibrosis (MF), and a pool of extravasated erythrocytes (EE) containing variably-sized lipid globules (LG) (H&E stain, original magnification x100). *A high-resolution version of this slide for use with the Virtual Microscope is available as eSlide: VM03847.*

Figure 7. Histopathology of CFO. Demonstrates complete splaying (SP) of a bony trabecula, numerous neighboring microshards (MS) of bone and extravasated erythrocytes (EE) (H&E stain, original magnification x100). *A high-resolution version of this slide for use with the Virtual Microscope is available as eSlide: VM03846.*

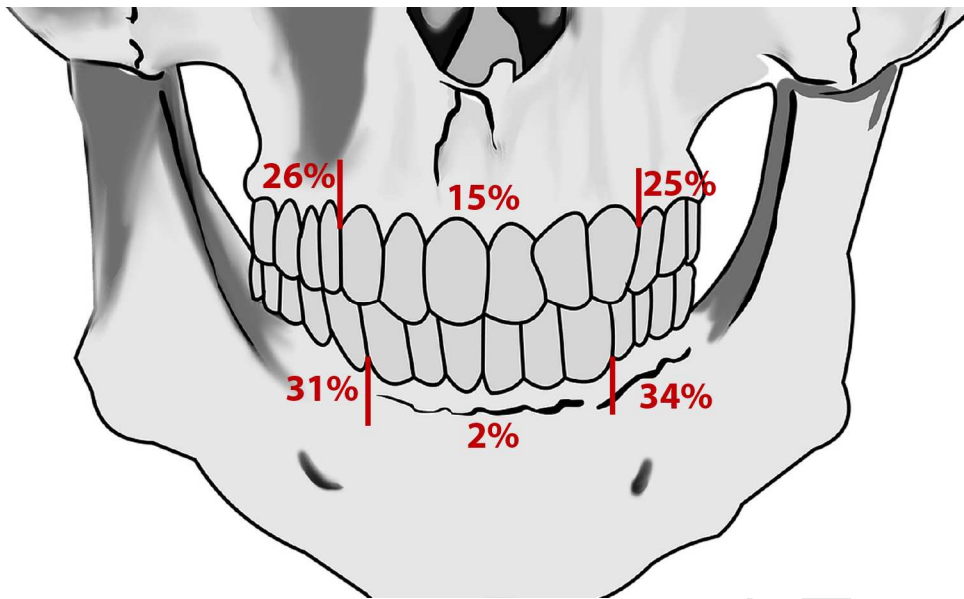
Figure 8. Histopathology of CFO. Demonstrates large pool of extravasated erythrocytes (EE) suspended in which are numerous variably-sized lipid-like globules (LG) (H&E stain, original magnification x100). *A high-resolution version of this slide for use with the Virtual Microscope is available as eSlide: VM03848.*

Figure 9. Histopathology of CFO. Demonstrates splayed trabecula (SP), microshards (MS) and extravasated erythrocytes (EE) (H&E stain, original magnification x100). *A high-resolution version of this slide for use with the Virtual Microscope is available as eSlide: VM03848.*

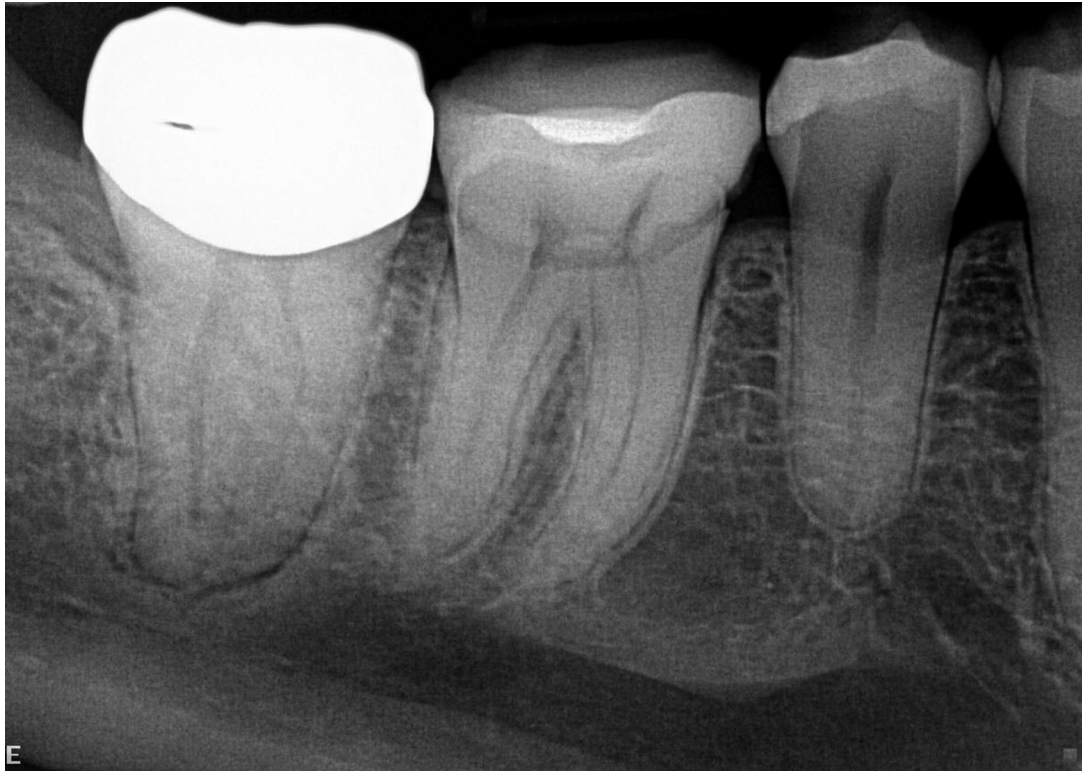
Figure 10. Histopathology of CFO. Demonstrates complete splaying (SP) of a bony trabecula, numerous microshards of bone (MS) and extravasated erythrocytes (EE) (H&E stain, original magnification x100). *A high-resolution version of this slide for use with the Virtual Microscope is available as eSlide: VM03849.*

Figure 11. Histopathology of CFO. Demonstrates splayed trabeculae (SP), microshards (MS), and extravasated (EE) erythrocytes containing lipid globules (LG) (H&E stain, original magnification x100). *A high-resolution version of this slide for use with the Virtual Microscope is available as eSlide: VM03850.*

Figure 12. Graph displaying the followup results in terms of number of patients experiencing complete, moderate, minimal or no relief plotted against number of months elapsed between surgery and completion of the survey.



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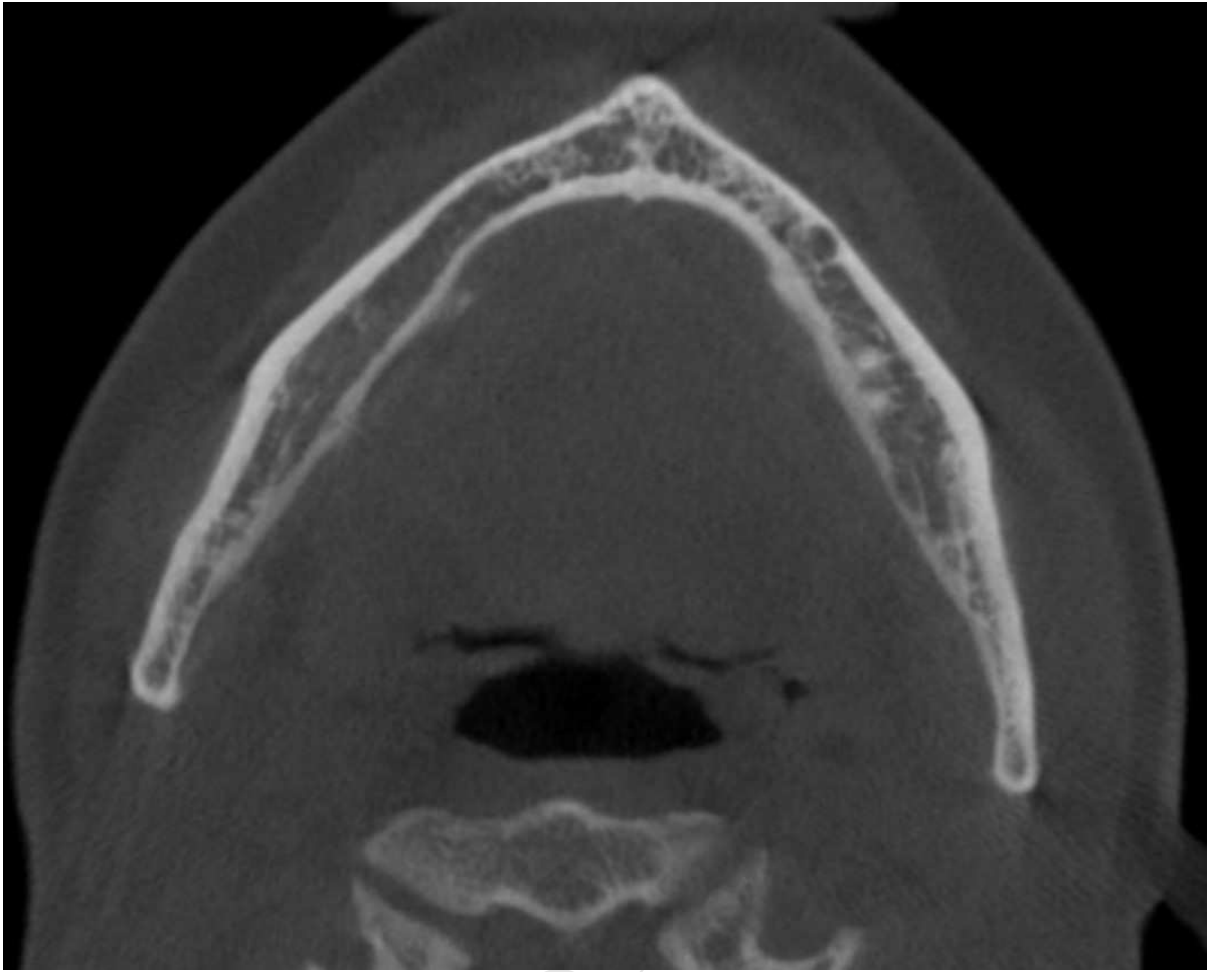
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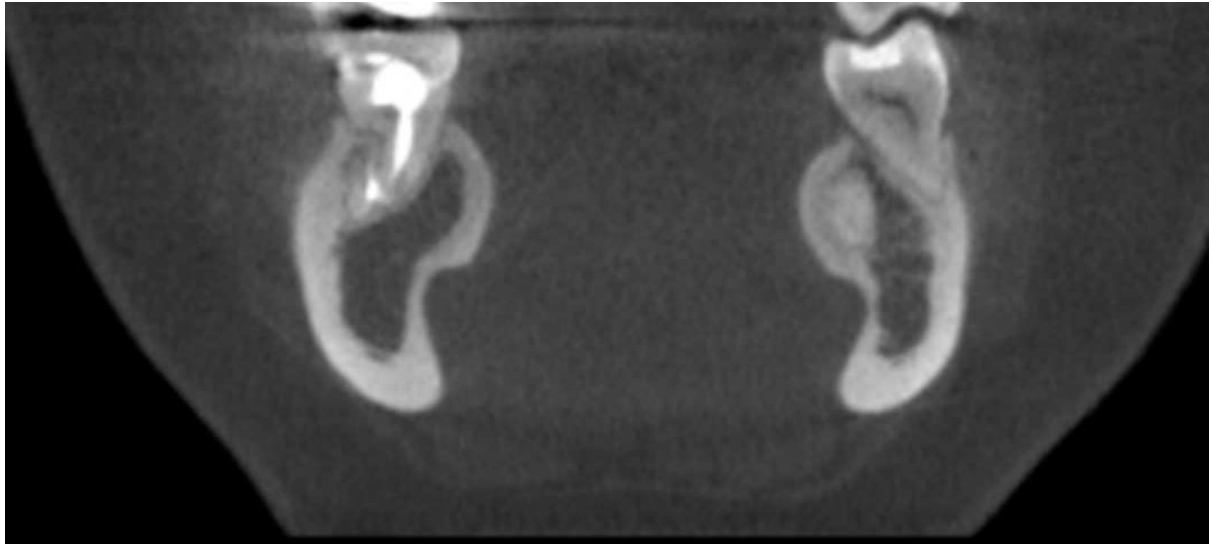
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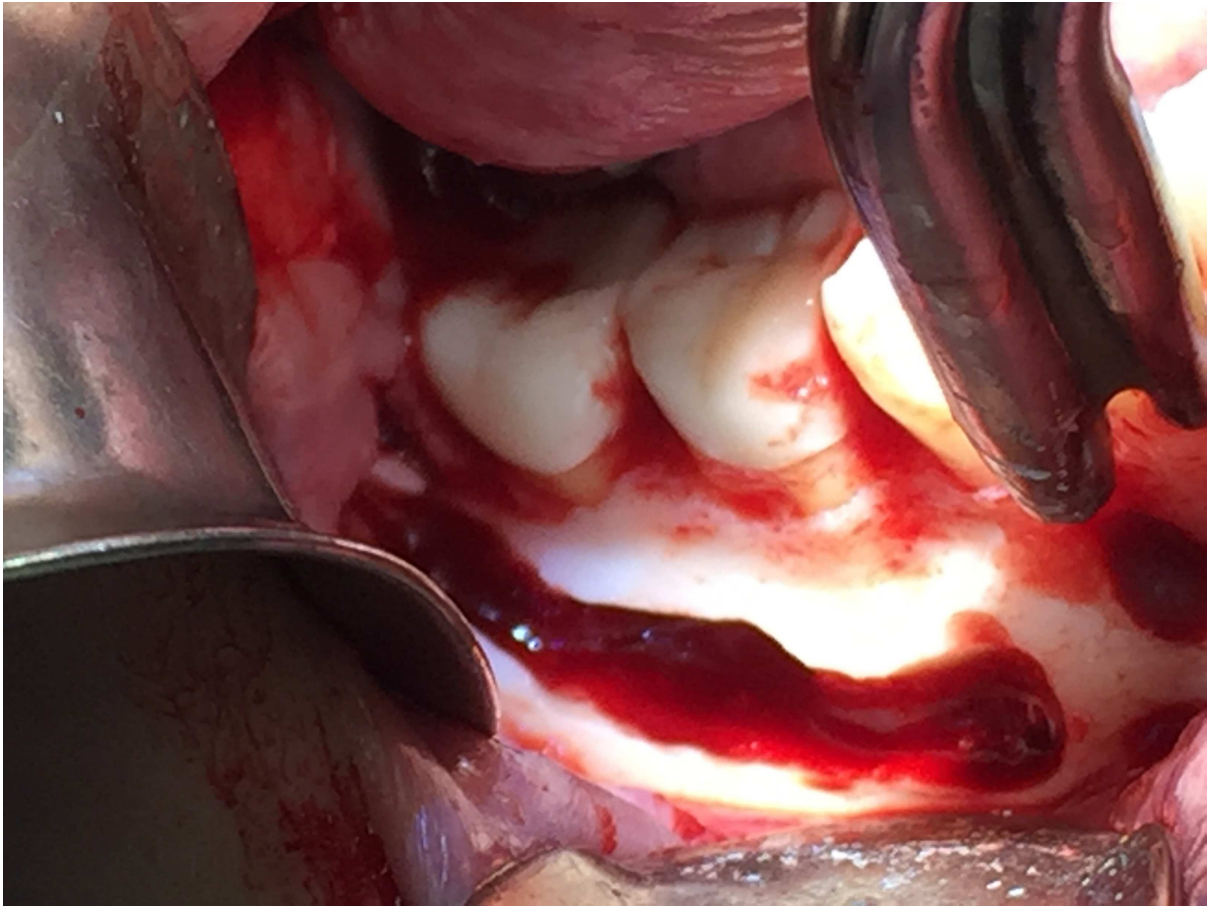
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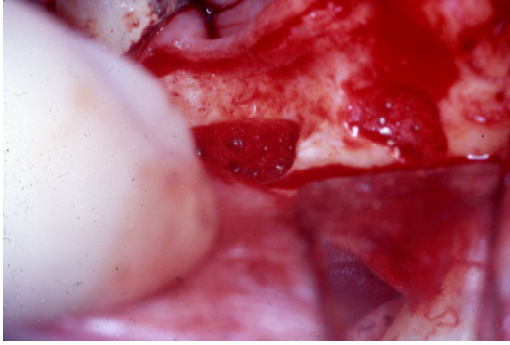
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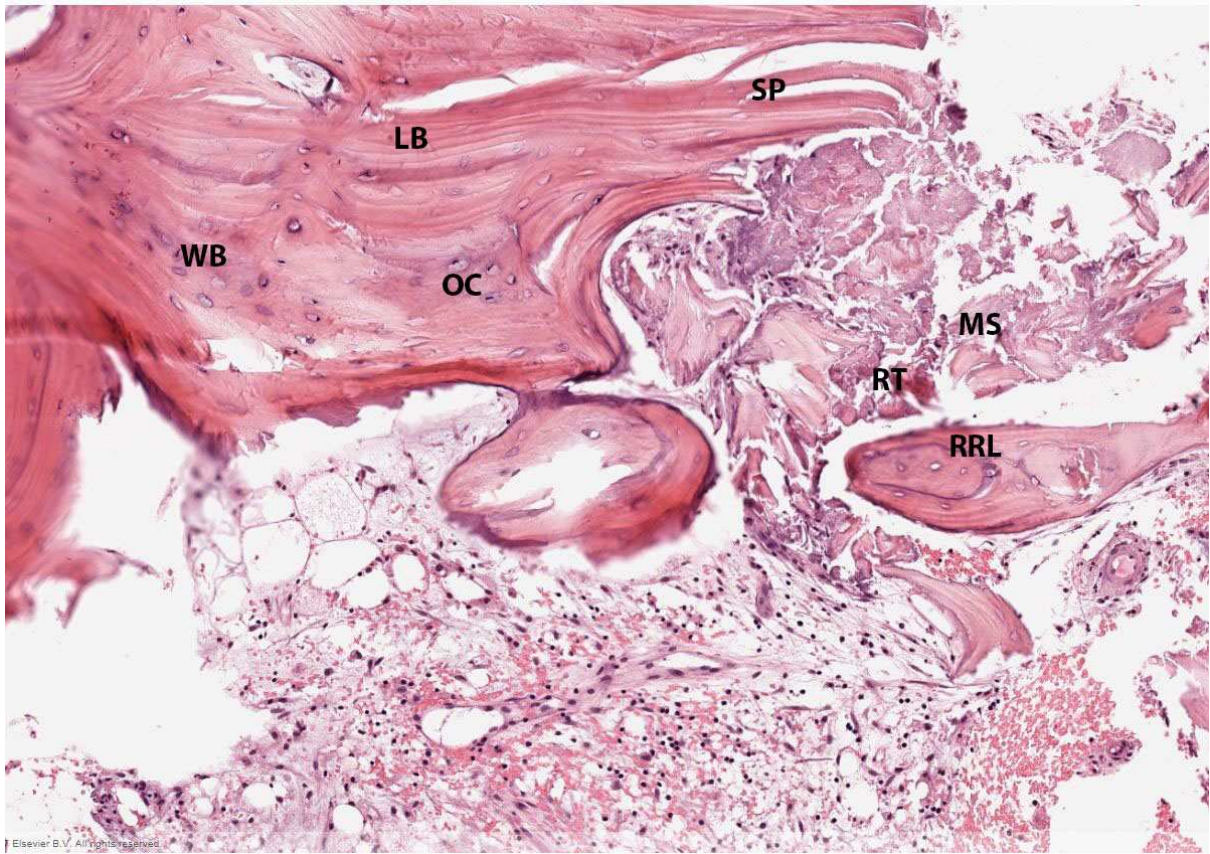
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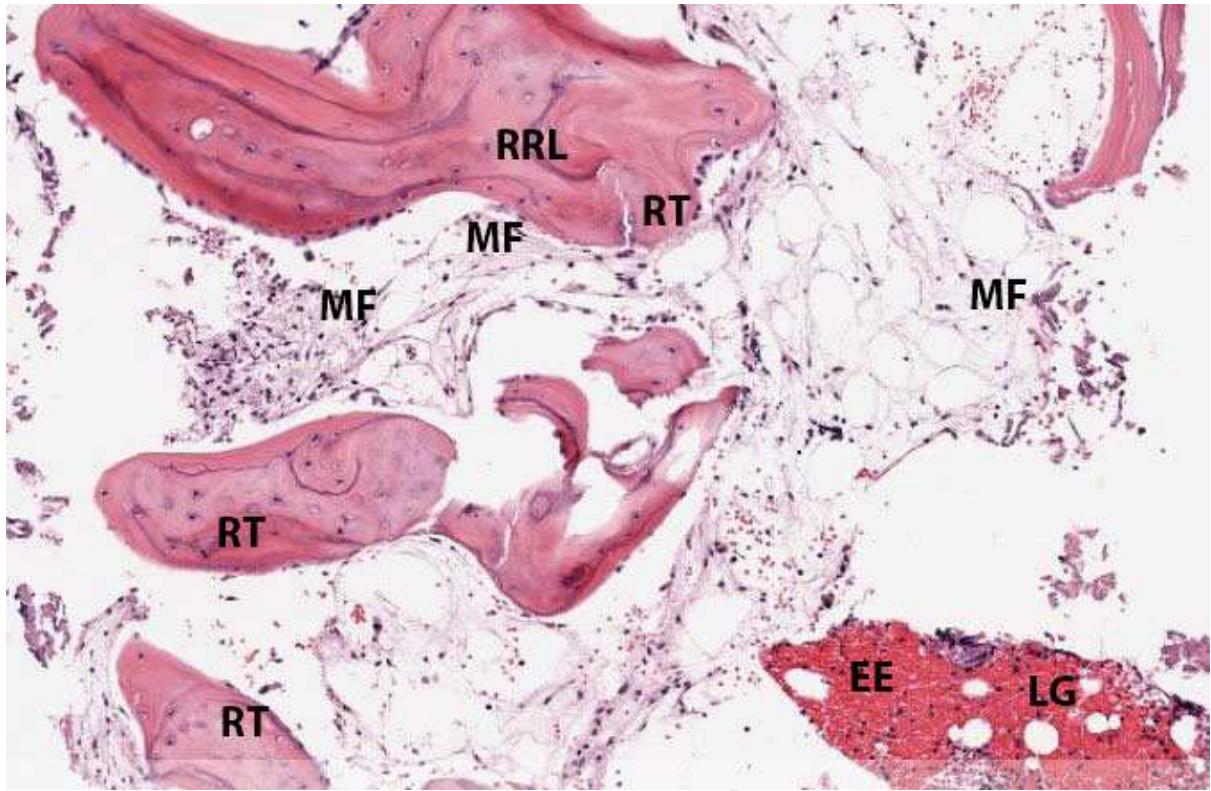
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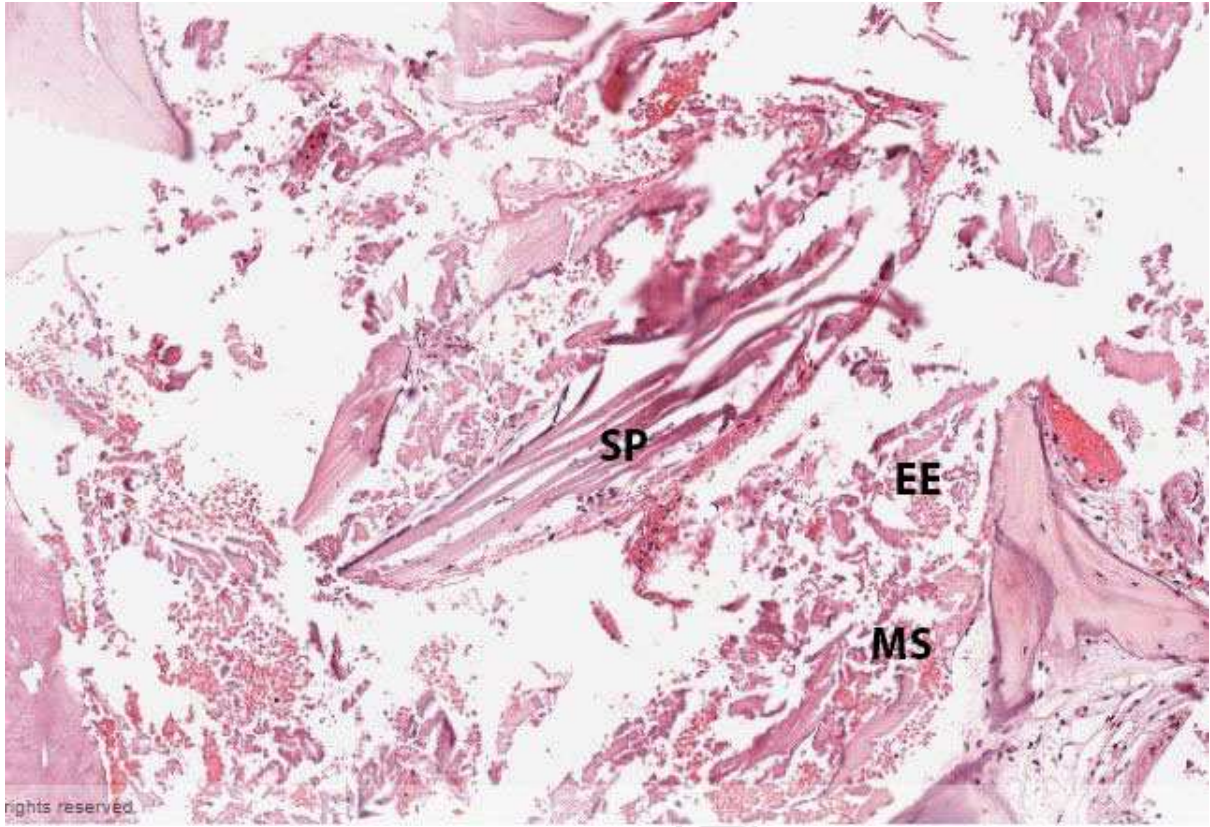
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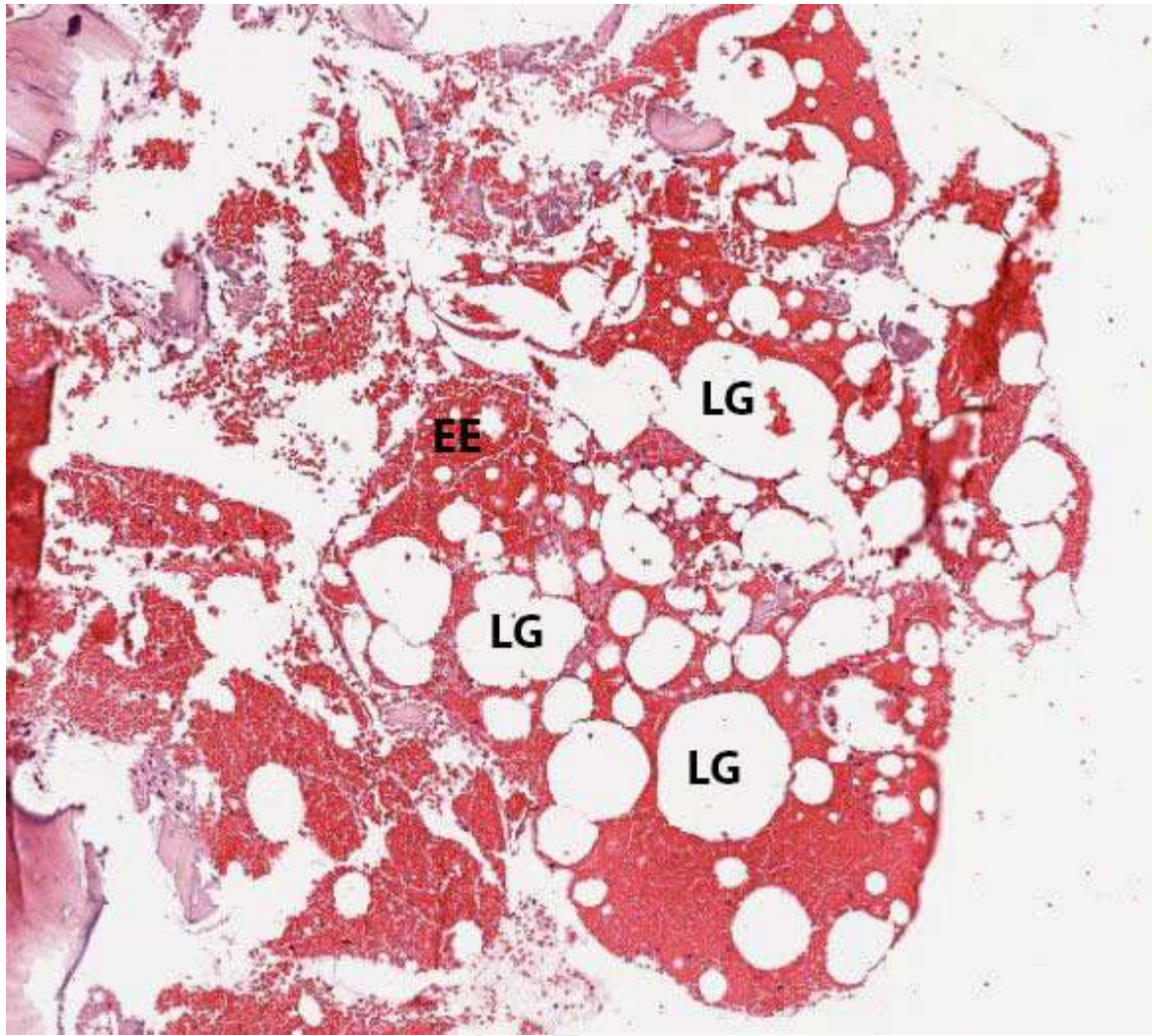
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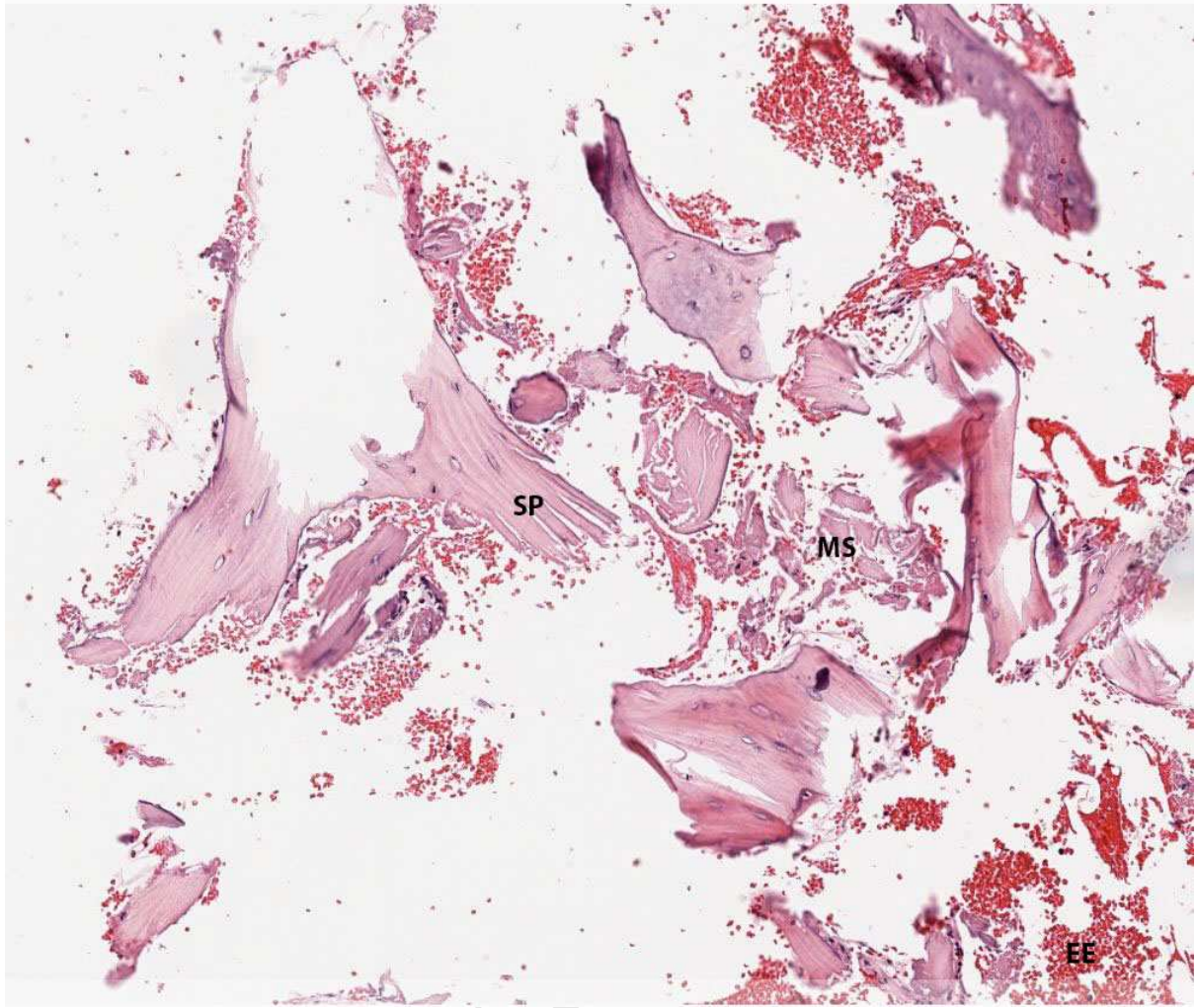
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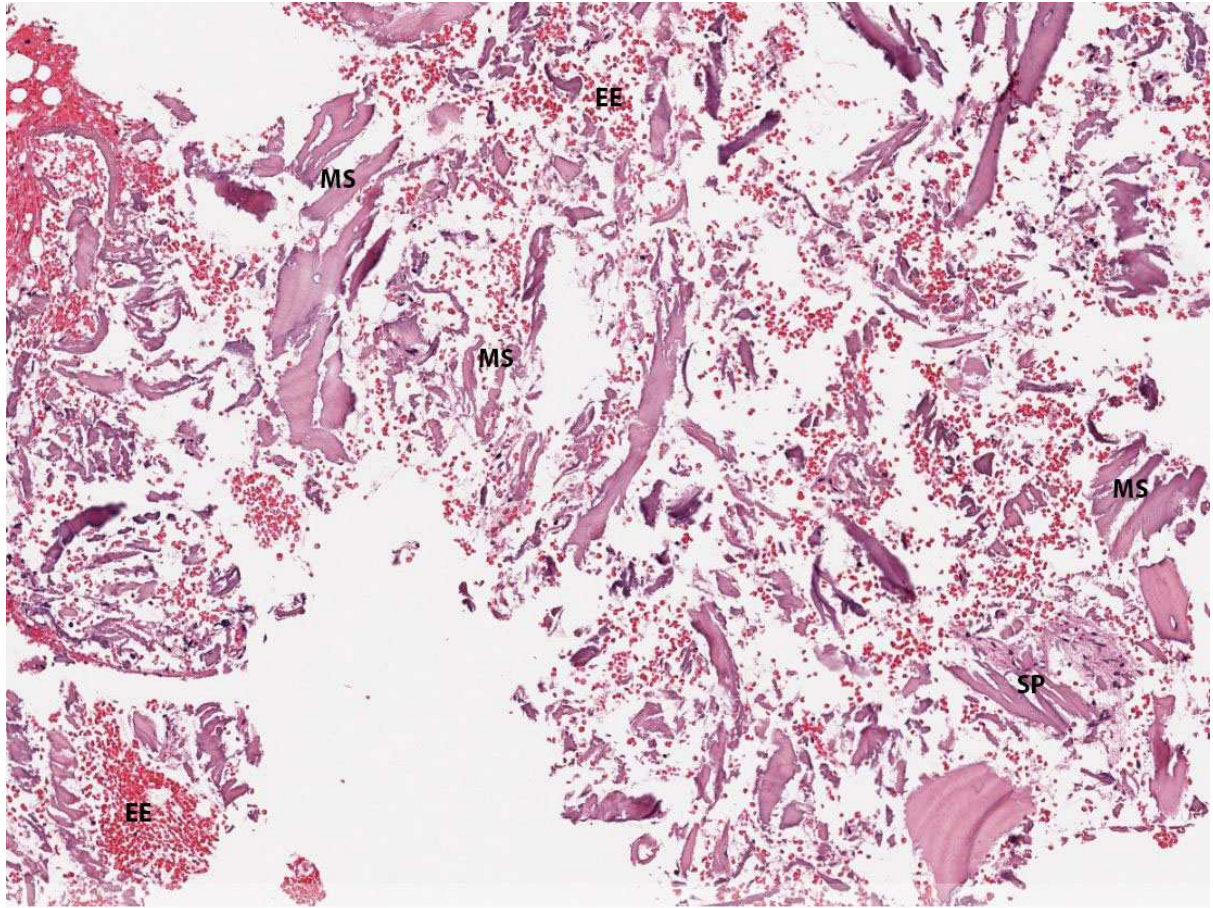
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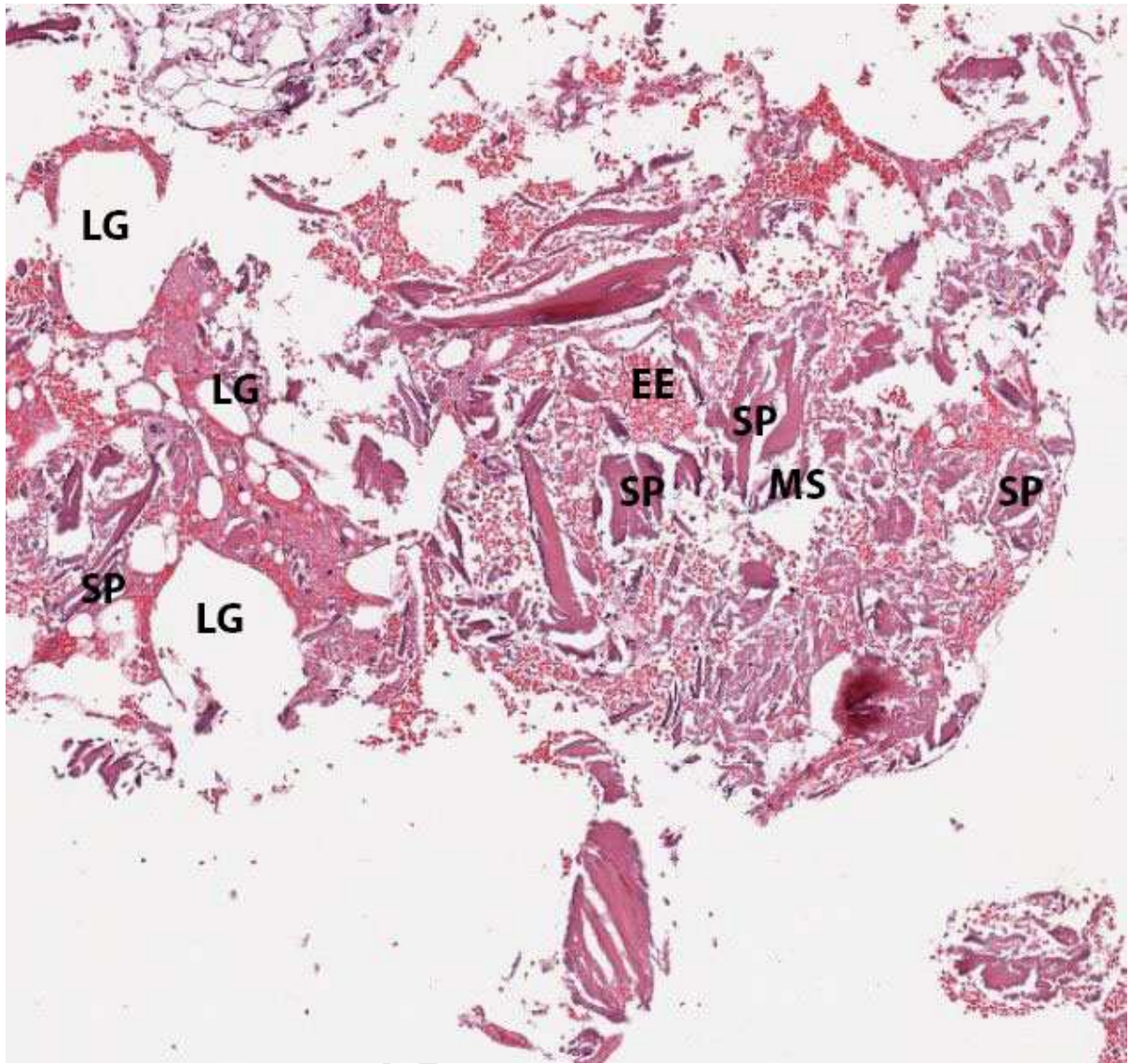
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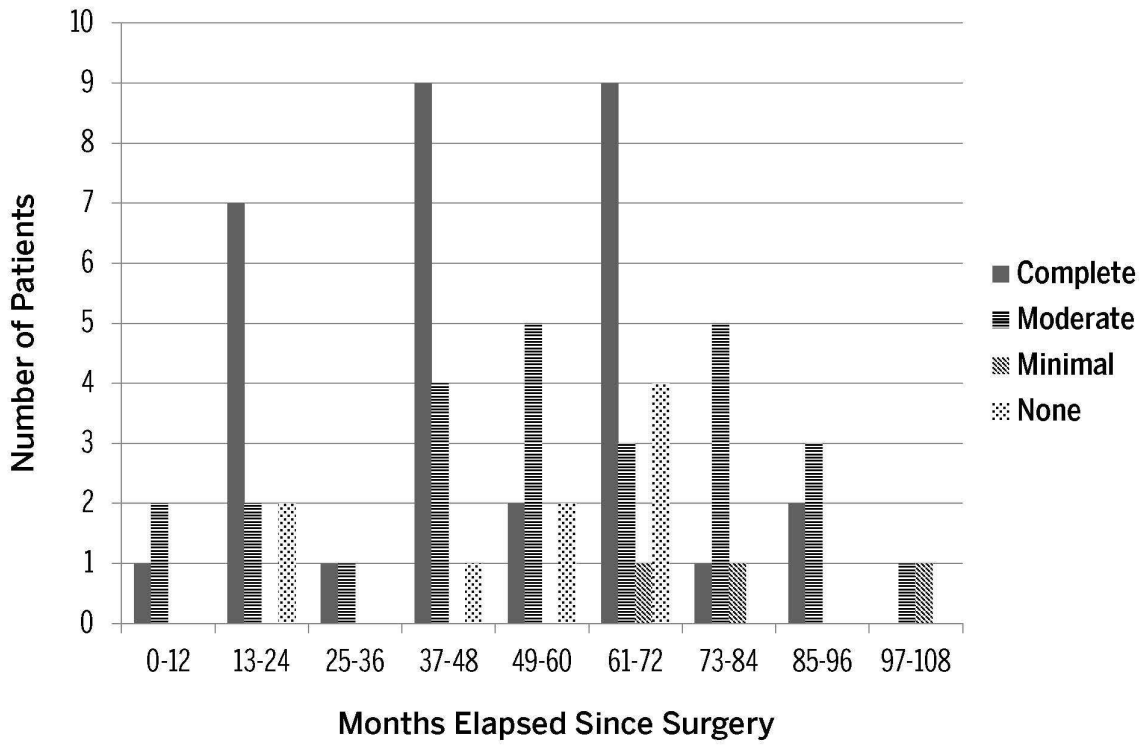


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Degree of Pain Relief



STATEMENT OF CLINICAL RELEVANCE

This large clinicopathologic and followup study strongly supports chronic fibrosing osteomyelitis **of the jaws** as a distinct entity with recognizable clinical, radiographic and histopathologic features, allowing it to be differentiated from other types of facial pain and successfully treated in most cases.

Survey for Chronic Fibrosing Osteomyelitis of the Jaws: A Clinicopathologic, Treatment and FollowUp Study of **Multiple** Cases

Subject Number: _____

The following questions relate to your experiences before your jaw surgery at one of the Indianapolis Endodontic offices. Please circle the answer that best describes your experience and/or clearly print your answer, where indicated.

- 1) How many dentists, physicians, or other health care providers did you seek consultation or treatment from before your surgery at the Indianapolis Endodontics office?
 - a) I did not seek consultation or treatment from anyone other than the Indianapolis Endodontics office.
 - b) I consulted or sought treatment from one or more of the following professionals before my surgery at the Indianapolis Endodontics offices. Please write the number of professionals you saw next to each group that applies:
 1. _____ General Dentist
 2. _____ Endodontist (root canal dentist) other than Indianapolis Endodontics Office
 3. _____ Oral Surgeon (dentist who specializes in pulling teeth)
 4. _____ Physician (like a family doctor or specialist)
 5. _____ Other, Please identify: _____

- 2) Who referred you to the Indianapolis Endodontics office?
 - a) I was not referred by anyone.
 - b) I do not remember who referred me.
 - c) I was referred by my:
 1. General Dentist
 2. Endodontist (root canal dentist) other than Indianapolis Endodontics Office
 3. Oral Surgeon (dentist who specializes in pulling teeth)
 4. Physician (like a family doctor or specialist)
 5. Other, Please identify: _____

- 3) By indicating how many months or years, please give a number for approximately how long you had pain in the jaw (either off and on or constant) before you had surgery at the Indianapolis Endodontics office?
 - a) I had pain in my jaw for _____ months before I had surgery at the Indianapolis Endodontics office.
OR
 - b) I had pain in my jaw for _____ years before I had surgery at the Indianapolis Endodontics office.

- 4) On a scale of 1 to 10, with 10 being unbearably severe, what was your pain level before your jaw bone surgery at the Indianapolis Endodontics office?

1 2 3 4 5 6 7 8 9 10

Survey for Chronic Fibrosing Osteomyelitis of the Jaws: A Clinicopathologic, Treatment and FollowUp Study of **Multiple** Cases

Subject Number: _____

- 5) On a scale of 0-10, with 0 meaning your jaw pain did not cause any problems with your daily life and 10 meaning your jaw pain completely upset your daily life, how did your jawbone disease before surgery interfere with your usual activities and attitudes (social, concentration, sleep, mood, stress level, etc.)?

0 1 2 3 4 5 6 7 8 9 10

- 6) Before your surgery, what medications were you taking for pain (you may circle more than one)?
- I took over the counter medication to relieve pain, please identify: _____
 - I took prescription medication to relieve pain; please identify: _____
 - I took antibiotics (to kill infection, like penicillin) to relieve pain, please identify: _____

 - I am not sure what medication I was taking for pain or infection before my surgery.
 - I did not take medication for pain or infection before my surgery.
- 7) Did your jaw pain start after you had an accident or a dental procedure?
- Yes, please describe the incident: _____

 - No
- 8) Before your surgery were there any activities or situations that increased your jaw pain?
- Yes, please list: _____

 - No

The following questions relate to your experiences after your jaw surgery at one of the Indianapolis Endodontic offices. Please circle the answer that best describes your experience and/or clearly print your answer, where indicated:

- 9) According to our records you had jaw surgery for pain in one of the Indianapolis Endodontic offices. Did you have jaw surgery for pain at any other office either before or after you had surgery at the Indianapolis Endodontic office?
- No, I only had surgery at the Indianapolis Endodontic office.
 - Yes, I had jaw surgery for pain before the surgery at the Indianapolis Endodontic office.
Please identify where: _____
 - Yes, I had jaw surgery for pain after the surgery at the Indianapolis Endodontic office. Please identify where: _____

Survey for Chronic Fibrosing Osteomyelitis of the Jaws: A Clinicopathologic, Treatment and FollowUp Study of **Multiple** Cases

Subject Number: _____

- 10) In dentistry, we divide the mouth into four sections or quadrants to help identify a certain location (upper right, upper left, lower right, lower left). Considering the surgery you had at the Indianapolis Endodontics office AND any other jaw bone surgery you may have had at another office, did you have jaw pain in more than one quadrant of your mouth?
- a) Yes, I had jaw pain in more than one quadrant. Please circle how many quadrants: 2 3 4
- b) No, I only had jaw pain in one quadrant.
- 11) Considering the surgery you had at the Indianapolis Endodontics office AND any other jaw bone surgery you may have had at another office, did you have more than one surgery in the same quadrant of your mouth?
- a) No, I did not have surgery more than once in the same quadrant of my mouth
- b) Yes, I did have surgery more than once in the same quadrant of my mouth. Please circle how many surgeries you had in the same quadrant of your mouth: 2 3 4 more than 4
- 12) On a scale of 1 to 10, with 10 being unbearably severe, what was your pain level after you recovered from your jaw bone surgery at the Indianapolis Endodontics office?
- 1 2 3 4 5 6 7 8 9 10
- 13) On a scale of 0-10, with 0 meaning your surgery site does not cause any problems with your daily life and 10 meaning what you feel in your surgery site completely upsets your daily life, how does what you feel at your surgery site interfere with your usual activities and attitudes (social, concentration, sleep, mood, stress level, etc.)?
- 0 1 2 3 4 5 6 7 8 9 10
- 14) Since your surgery, what pain medication, if any, have you taken for jaw pain (you may circle more than one answer?)
- a) I have taken over the counter medication to relieve jaw pain. Please identify: _____
- b) I have taken prescription medication to relieve jaw pain; please identify: _____
- c) I am not sure what medication I have taken for jaw pain since my surgery.
- d) I have not taken medication for jaw pain since my surgery.
- 15) Since your surgery are there any activities or situations that increase your jaw pain?
- a) Yes, please list. _____
- b) No
- c) Since recovering from my surgery, I have not had jaw pain.

Survey for Chronic Fibrosing Osteomyelitis of the Jaws: A Clinicopathologic, Treatment and FollowUp Study of **Multiple** Cases

Subject Number: _____

16) How would you evaluate the result of your surgery or surgeries?

- a. complete pain relief
- b. moderate relief
- c. minimal relief
- d. no relief at all

17) Do you feel going through the jaw surgery and its recovery was worth it in relationship to how your jaw feels now after surgery?

- a) Yes
- b) No

For either answer, in a few sentences, please explain your answer _____

These questions can be related to both before and after your surgery. Please circle the answer that best applies and/or provide an answer, where indicated, to each of the following medical questions.

18) Have you ever had blood tests which show that you have a bleeding or clotting problem?

- a) Yes
- b) No

19) What is the name of your bleeding or clotting problem?

- a) I do not have a bleeding or clotting problem.
- b) I do not know the name of my bleeding or clotting problem.
- c) The name of my bleeding or clotting problem is _____

20) Did you experience any other disease conditions which you feel might have been related in some way to your jaw bone disease?

- a) Yes, please list and explain why you believe they were related: _____

- b) No

Thank you for completing this survey. Please place the completed questionnaire in the postage paid envelope we provided with this mailing and return it to us at your earliest convenience.