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Melorheostosis and Central Giant Cell Granuloma of the Mandible in a 15-year-old Girl

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Abstract

Melorheostosis is a nonhereditary bone dysplasia primarily affecting the appendicular skeleton. Because clinical and histologic features are often nonspecific, the diagnosis is often based on the radiographic presentation. Involvement of the craniofacial skeleton is rare. We describe a case of a 15-year-old girl with appendicular and craniofacial melorheostosis with adjacent central giant cell granuloma. We discuss the possible significance of this previously unreported finding.

Melorheostosis is a nonhereditary bone dysplasia that primarily affects the appendicular skeleton and may ossify adjacent soft tissues.^{1,2,3} It was initially described in 1922 by Léri and Joanny; the name was derived from the Greek words for limb (*melos*) and flow (*rhein*), because the radiographic appearance resembled melting wax dripping down the side of a candle.⁴ Because the clinical and histologic features are nonspecific, the diagnosis is often based on the radiographic presentation.²

The typical radiographic presentation of melorheostosis includes an irregular hyperostosis affecting the outer cortical bone. Frequently, the hyperostosis extends into the cancellous bone and may be either completely radiopaque or a mixed pattern. Common locations include the diaphysis of long bones, the pelvis, the ribs, and the bones of the hands and feet. Reports of changes in the craniofacial complex are less common.¹ Although 4 distinct types of melorheostosis are described in the literature, the condition is more practically classified as monostotic or polyostotic.⁵ We report a case affecting several areas including the facial bones and jaws of a 15-year-old girl. A detailed description of the radiographic and histologic features is provided, including a possible association of central giant cell granuloma with this condition.

Case Report

Clinical findings

A 15-year-old white girl presented for evaluation of right mandibular swelling of unknown duration and failure of proper eruption of tooth 31. On examination, palpable expansion of the right posterior mandible was noted. Intraorally, the expansion was seen extending from the premolar area to the ramus. The expansion was asymptomatic. No lymphadenopathy was noted, and blood studies were within normal limits. No significant family history of disease was known.

Radiographic findings

A computed tomography (CT) scan of the head and neck was obtained to evaluate the extent of structural changes. Axial and coronal images were acquired using a helical CT with exposure settings of 100 kilovolt peak, 150 mA, slice thickness of 0.8 mm, and resolution of 0.468 mm². Bone changes were noted in the right parietal, temporal, zygomatic, sphenoid, ethmoid, maxillary, and mandibular bone (Figure 1). The lesion presented with mixed density but mostly as ground-glass changes with irregular but well-delimited margins and cortical expansion. In the right parietal and temporal bones, thickening of the cortices with sclerosis was observed. In the sphenoid, the same irregular ground-glass sclerosis was noted, including thickening of the medial and lateral pterygoid plates. The sphenoid sinus was displaced to the left and diminished in size. Constriction of the right superior and inferior orbital fissures was also observed. In the maxilla, 3-dimensional reconstructions clearly exhibited involvement

of only the right side, with expansion of the outer maxillary cortex showing the classic dripping-wax appearance of melorheostosis (Figure 2). In the nasal cavity, the inferior nasal concha was hypoplastic and superiorly displaced. Owing to cortical expansion, the right nasal cavity was partially obliterated. Other radiographic findings in the maxilla included superior displacement of the floor of the right sinus and impaction of the fully developed right second molar tooth and developing third molar. In the mandible, the same ground-glass changes with cortical expansion extended posteriorly from the periapical region of the right mandibular canine to the posterior third of the ramus. Changes extended superiorly from the lower border of the mandible to the sigmoid notch and coronoid process. The right condyle was not involved. The mandibular canal was inferiorly displaced and constricted in some areas. The mandibular right second molar was buccally displaced, and the third molar was lingually displaced. The molar teeth of the right jaws exhibited a somewhat abnormal morphology, with underdeveloped and stunted roots, when compared with the left side. The mandibular right second molar was impacted, with root dilaceration. A multilocular radiolucency with scalloped margins and cortical thinning with expansion was noted in the right posterior mandible. All involved maxillary and mandibular teeth exhibited irregular widening of the periodontal ligament spaces and absence of lamina dura.

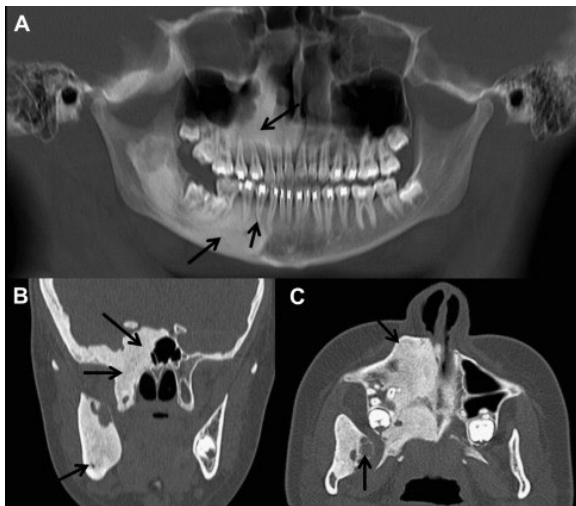


Fig. 1. Computed tomography (CT) examination. **A**, Panoramic reconstruction from CT data. Note ground-glass bone, dental displacement, and widening of periodontal ligament spaces in the right maxilla and mandible. **B**, Coronal CT reconstruction depicts extension of lesion in the sphenoid and mandible. Note lateral displacement of the right sphenoid sinus and thickening of the pterygoid process and mandible, with cortical expansion and inferior displacement of the mandibular canal. **C**, In the axial CT scan, unilateral involvement is noted with typical ground-glass bone and cortical expansion of the anterior maxilla, as well as similar changes of the right mandible. Note multilocular radiolucency in the medial aspect of the right mandible.

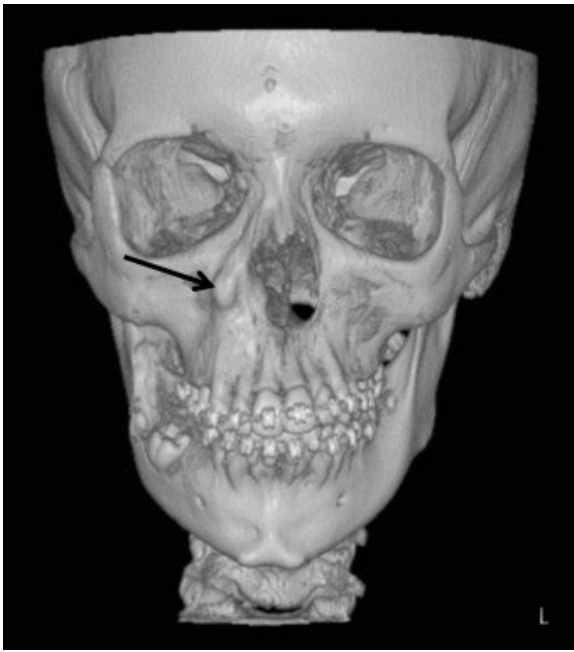


Fig. 2. Three-dimensional model. Note the dripping-wax appearance distinctive of melorheostosis in the anterior aspect of the right maxilla.

In addition to the CT scan, radiographic plain projections of the lower limb were available and demonstrated additional characteristic findings associated with appendicular melorheostosis. In the lateral projection of the left femur (Figure 3, A) and anteroposterior projection of the lower limb (see Figure 3, B), endosteal hyperostosis, linear ground-glass sclerosis, and mild expansion were present in the diaphysis of both the femur and tibia. In the epiphyses of these bones, rounded areas of hyperostosis with irregular contours characteristic of melorheostosis were present. Dorsiplantar and lateral projections of the left foot showed similar irregular endosteal hyperostosis involving the first and second distal, intermediate, and proximal phalanges; metatarsals I and II; the medial and intermediate cuneiforms; and the navicular bones. Lateral deviation of the second toe was also evident (see Figure 3, C).

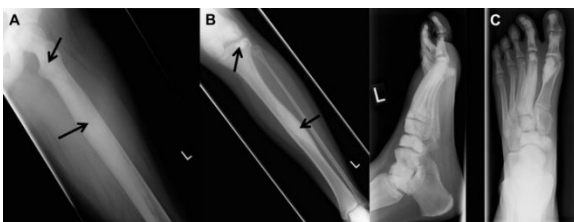


Fig. 3. **A**, Lateral 2-dimensional image of the left femur depicts ground-glass endosteal hyperostosis with cortical expansion in the epiphysis and diaphysis. **B**, Anteroposterior projection of the left tibia and fibula, with involvement of the tibia exhibiting hyperostosis of the epiphysis and diaphysis. **C**, Various 2-dimensional projections depict involvement of the left foot, with hyperostosis and lateral deviation of the second toe.

Histopathologic findings

Microscopic examination of the radiolucent lesion removed from the right posterior mandible showed a benign proliferation of ovoid to spindle-shaped cells within a background of dense fibrous connective

tissue. Scattered throughout the tissue were numerous multinucleated giant cells, with prominent erythrocyte extravasation and hemosiderin deposition (Figure 4). Based on these features, a diagnosis of central giant cell granuloma was made. A subsequent biopsy of the mandibular bony changes was later done, with a diagnosis of dense cortical bone, consistent with melorheostosis.

At the 3-year follow-up in March 2010, no recurrence of the giant cell granuloma was seen clinically or radiographically. However, some clinical deformity was noted involving the right temporal region as the patient's melorheostosis continued to progress. Ocular symptoms, consisting of partial blindness, had also developed, necessitating optic nerve decompression the previous year. Additional sensory disturbances were not reported.

Discussion

Melorheostosis is a rare, benign bone disorder characterized by hyperostosis that, in later stages, radiographically resembles melting candle wax. It is classified among the “sclerosing bone dysplasias,” which also include disorders such as craniometaphyseal and diaphyseal dysplasias, osteopetrosis, pyknodysostosis, osteopoikilosis, and osteopathia striata.⁶ Occasionally, patients exhibit more than one sclerosing disorder; such comorbidity is referred to as mixed sclerosing bone dysplasia or overlap syndrome.⁷

The estimated incidence of melorheostosis is 0.9 per 1 million persons.⁸ There is an equal distribution between males and females.¹ The disease most often manifests in childhood or early adolescence, with most patients showing evidence of the disease by age 20.^{8,9} However, the initial presentation may occur as late as age 61, with a second peak occurring in the fourth and fifth decades.⁸ In rare cases, the deformity or limitation of motion has been noted at birth.¹⁰

Melorheostosis may be monostotic, polyostotic, or monomelic (affecting a single limb).² Although the disease is primarily seen in the long bones, any bone may be affected. The lower extremities are more commonly affected than the upper extremities.¹¹ Uncommon sites of involvement include the skull, spine, and ribs.⁴ Involvement tends to be unilateral, and this case was unusual, owing to its bilateral presentation of lesions in the left appendicular skeleton and right craniofacial bones.

Four distinct types and one combination of types of melorheostosis have been described, based on radiographic presentation.¹¹ Type A is characterized by an osteoma-like appearance. Type B represents the classic “flowing” hyperostosis. Type C shows a myositis ossificans-like pattern, especially around the joints. Type D demonstrates features similar to osteopathia striata. A mixture of patterns is seen in Type E. Although the practical classification of the submitted case would be polyostotic melorheostosis, the involvement of the craniofacial regions and appendicular skeleton with both ground-glass sclerosis and the classic “flowing” hyperostosis would fall under the mixed pattern, or Type E.

Radiographic changes of melorheostosis typically show endosteal sclerosis of the long axis of the bone, primarily limited to one limb.⁸ The hyperostosis is usually confined to one lateral side of the bone, but small bones of the hand may be completely involved.¹² There is usually a distinct demarcation between lesional and normal bone, a feature readily seen on CT scans.⁶ Extrasosseous bone deposition may also occur.¹² In infancy and childhood, the hyperostosis may not be a prominent feature. However, with the

natural progression of the disease, radiographic changes become more apparent. Early lesions show a streaky or patchy endosteal distribution, with the more distinct “flowing” periosteal distribution seen later and primarily in adults.^{3,4} The linear hyperostosis often extends along a limb, from one bone to the next, continuing into the carpus or the tarsus, and potentially as far as the phalanges.⁴ Typically, the diagnosis of melorheostosis is based on the radiologic signs and bone histology showing sclerosis without cellular abnormalities.⁸ Although CT or magnetic resonance imaging is not needed in most cases, scintigraphy reveals abnormal tracer uptake in melorheostosis and can be helpful in the diagnosis of equivocal cases.⁶

Numerous clinical features have been described in patients with melorheostosis, and signs and symptoms may appear before any radiographic changes.⁴ Typically, more severe symptoms are associated with extensive hyperostosis, as well as a greater number of affected bones.¹¹ Chronic pain, which ranges in severity, is a relatively consistent finding. However, it is often less prominent in children than in adults.¹¹ When present, the pain is usually felt when the patient is at rest and during the night.

In younger patients, the initial presentation may involve limb length discrepancy or joint contractures, sometimes several years before the onset of pain.^{2,3} Premature closure of the epiphyseal plate results in shortening of the limbs or angulation.¹² Reported soft tissue findings include joint stiffness, limitation of motion, muscle atrophy, subcutaneous fibrosis, circumscribed scleroderma, skin hyperpigmentation, paresthesia, palpable soft tissue masses, and vascular malformations.^{4,8,11,12} Blood test results are within normal limits.¹ Involvement of the craniofacial skeleton by melorheostosis is exceedingly rare, and most of these patients will also have involvement of the appendicular skeleton.¹ Currently, 8 cases of craniofacial melorheostosis have been reported in the English-language literature and are summarized in Table I, along with the current case. Most cases have been seen in girls and women and initially present as swelling of the maxilla or mandible. Pain is not a consistent finding. Displacement of teeth is not seen. Although symptoms may also include paresthesia or sensory disturbances, no loss or impairment of sensory or motor function has been reported in cases of the craniofacial region.⁷

Table I. Published reports of craniofacial melorheostosis

Reference	Person affected (age, gender)	Year published	Craniofacial involvement
Franklin and Matheson ¹³	41-year-old woman	1942	Enlargement of the right skull and mandible
Williams et al. ²	Elderly woman	1990	None*
Tueche et al. ¹⁴	21-year-old man	1999	None*
Mariaud-Schmidt et al. ⁹	11-year-old girl	2002	Facial asymmetry and contractural deformities
Ethunandan et al. ¹	66-year-old woman	2004	Left facial swelling
Kuttenberger et al. ⁸	18-year-old (gender not given)	2006	Left mandibular pain
Parashar et al. ⁷	11-year-old girl	2007	Right maxillary swelling
Parashar et al. ⁷	27-year-old man	2007	Left mandibular swelling

Anderson et al. (current case)	15-year-old girl	2013	Right mandibular swelling
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*Craniofacial involvement was subclinical and was discovered after discovery at other skeletal sites.

The radiographic features of craniofacial melorheostosis can be quite different from those of appendicular melorheostosis. In contrast to the classic melted-wax appearance seen in the long bones, melorheostosis of the craniofacial skeleton shows either homogeneous sclerosis, with an increase in volume, or focal irregular sclerosis, without changes in volume.⁸ Melorheostosis of the jaws can mimic other bone tumors such as osteoma and osteosarcoma. As observed in this case, a ground-glass radiographic appearance similar to fibrous dysplasia may also be seen.

The histopathology of melorheostosis is typically nonspecific and rarely provides a definitive diagnosis. Rather, its utility lies in the exclusion of other conditions, and biopsy is therefore recommended to rule out osteosarcoma, which is also painful.⁷ Microscopic specimens show a mixture of immature woven bone and somewhat disorganized lamellar bone. The haversian patterns are often irregular and may be obliterated by thickened trabeculae. Vessels are frequently surrounded by woven bone or osteoid rather than lamellar bone. Within the marrow spaces, osteoid and fibrous tissue may be seen surrounding areas of new bone formation. Osteoblastic or osteoclastic activity is not prominent, and cellular atypia or anaplasia is absent.^{1, 8, 11, 15}

Lesions resembling giant cell granuloma have not been previously reported in the setting of melorheostosis. Central giant cell granuloma of the jaws typically presents as a unilocular to multilocular radiolucency. The differential diagnosis of these lesions includes odontogenic keratocyst, ameloblastoma, intraosseous vascular malformation, and odontogenic myxoma. Our patient was diagnosed with a giant cell granuloma of the mandible associated with an unerupted tooth and within an area of increased bone density. It is unclear whether this lesion is related to the patient's melorheostosis or is a concurrent but separate process. Giant cell granulomas have been reported in association with fibro-osseous processes, such as ossifying fibroma or Paget disease of bone. In these conditions, it is thought that the giant cell granuloma may be a reaction to changes in stroma within the original lesion. These changes could involve osteoblasts, which in turn have the capacity to activate osteoclasts. It is possible that a similar mechanism may be in effect in the present case and may be a previously unreported feature in the evolution of this condition.^{16, 17}

The differential diagnosis of melorheostosis is extensive and includes sclerosing osteomyelitis, osteosarcoma, fibrous dysplasia, and the sclerosing bone dysplasias.^{6, 8} Differentiating melorheostosis from these other conditions requires careful assessment of the clinical, radiographic, histopathologic, and laboratory findings in combination. Osteopetrosis is typically a bilateral condition and can often be excluded clinically. Fibrous dysplasia and osteosarcoma can be differentiated from melorheostosis microscopically. Bone scintigraphy also can be a useful diagnostic tool. Increased uptake of technetium 99 m pyrophosphate is seen in melorheostosis, but not in osteopoikilosis or osteopathia striata.⁵ Melorheostosis may be differentiated from sclerosing osteomyelitis by a normal blood cell count and C-reactive protein level.

The etiology of melorheostosis is unclear. Proposed theories include vascular disturbances, inflammatory and degenerative processes, defects in embryogenesis, and abnormalities in

innervation.¹ The segmental bony and soft tissue pattern lends support to the theory of an embryonic insult to the sensory nerves.^{6,11} The distribution of lesions in melorheostosis corresponds to distinct sclerotomes, or areas of bone innervated by individual spinal sensory nerves.⁵ Although germ line mutations have been identified in some cases, a consistent genetic defect remains unidentified.¹⁸

Treatment primarily consists of symptomatic care, surgical correction of deformity, and physical therapy.¹² Nonsteroidal anti-inflammatory medications are effective in the relief of pain, and some benefit has been seen with vasodilators or diphosphonates.⁸ Because the contractures are difficult to manage and recurrence is not uncommon, surgical intervention should ideally be postponed until skeletal maturity is achieved.³ Beyond the associated deformity and variable disability, the overall prognosis is good. The condition is typically benign; however, osteosarcoma arising in melorheostosis has been reported.⁷ Although progression is rapid during active growth, the disease tends to slow during adulthood, with periods of recurrence.⁹ Spontaneous cessation is occasionally seen, and surgery is not always necessary.^{6,8}

In conclusion, we report a case of craniofacial melorheostosis with concomitant central giant cell granuloma. Although previously unreported, the relationship between these 2 processes is considered. Further reports of craniofacial melorheostosis may clarify this relationship.

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