Syndromes Affecting Bone

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KEYWORDS

• Dysmorphic facies • Facial bones • Jaw diseases • Genetic bone diseases

KEY POINTS

- Look beyond the primary jaw pathology for clues of syndromic involvement. Observe the skin, and always consider extrafacial skeletal involvement.
- Study Gorlin's *Syndromes of the Head and Neck* and similar references to increase your "rolodex" of known syndromes.
- Review the natural history of the pathology and develop a perspective for whether there is an active process and/or a progressive process.

Introduction

This article is a clinical description of genetic diseases that affect facial bones, giving rise to dysmorphic facies. It is by no means complete, rather it is meant to serve as an outline of skeletal anomalies that can provide structure for oral and maxillofacial surgeons to screen the patients that they encounter. The reader should have access to other sources, such as *Gorlin Syndromes of the Head and Neck*, Sixth Edition; *Smith's Recognizable Patterns of Human Malformation* by Jones; and *The Management of Genetic Syndromes* by Cassidy and Allanson.

When evaluating bone diseases of the jaws and considering a syndromic etiology, the clinician needs to first characterize what is observed. Is the process radiolucent or radiopaque? Does this condition result in skeletal dysplasia, hyperplasia, or hypoplasia? Is this a local, monostotic, regional, or polyostotic phenomena? Finally, what other abnormalities are present in this patient. Is this observed bony pathology a component of a constellation of findings, that is, a syndrome involving multiple pathologic entities? If there are multiple disorders, are they associated with potential for genetic transmission?

Although today there seems to be a limited number of conditions that affect the maxillofacial skeleton that are truly genetic in order, as our ability to understand the human genome and characterize individuals and their genetic sequence increases, undoubtedly many more clusters of genetically coded phenotypic expressions will be identified. In addition, what appears outwardly as an external independent source of disease or deformity may turn out to be genetically predetermined. For example, there is no doubt that medication-related osteonecrosis of the jaw (MRONJ) can be related to the use of bisphosphonates that inhibit osteoclast formation. However, it is becoming apparent that there are clusters of patients with genetic sequences that increase susceptibility to this class of drugs, rendering the patient increasingly susceptible to MRONJ. That being said, there are classic syndromes that affect bone and are associated with other physical abnormalities that are genetically transmitted. These are illustrated in this article.

Osteopetrosis

Genetics

Osteopetrosis is autosomal recessive in its neonatal form and is often called marble bone disease. The autosomal dominant form, often called late onset, is more benign in its clinical nature and is divided into a Type 1 and Type 2 expression. The prevalence is about 1 in 250,000 births. There is a higher incidence of this condition in Costa Rica, Saudi Arabia, and Denmark (1/20,000).

Clinical features

Osteopetrosis is a generalized disease of bone in which there is failure of normal bone remodeling by resorption or an overproduction of bone. Various defects in osteoclast or osteoblast function have been implicated. As a consequence, the bone becomes dense and radiopaque with a radiographic homogeneity between the cortical and medullary bone (Fig. 1). There are various clinical forms of this disease. The worst outcomes are seen with the neonatal form, Albers-Schönberg disease. This entity is generally fatal, although early bone marrow transplantation can slow the progression of the disease process. Most patients do not live beyond adolescence.

The progressive density of affected bones without a resorptive phase promotes early fracture and encroachment on the cranial nerve foramina resulting in diminished vision, hearing, and fifth nerve function. Extramedullary hematopoiesis may result in hepatosplenomegaly and pancytopenia.

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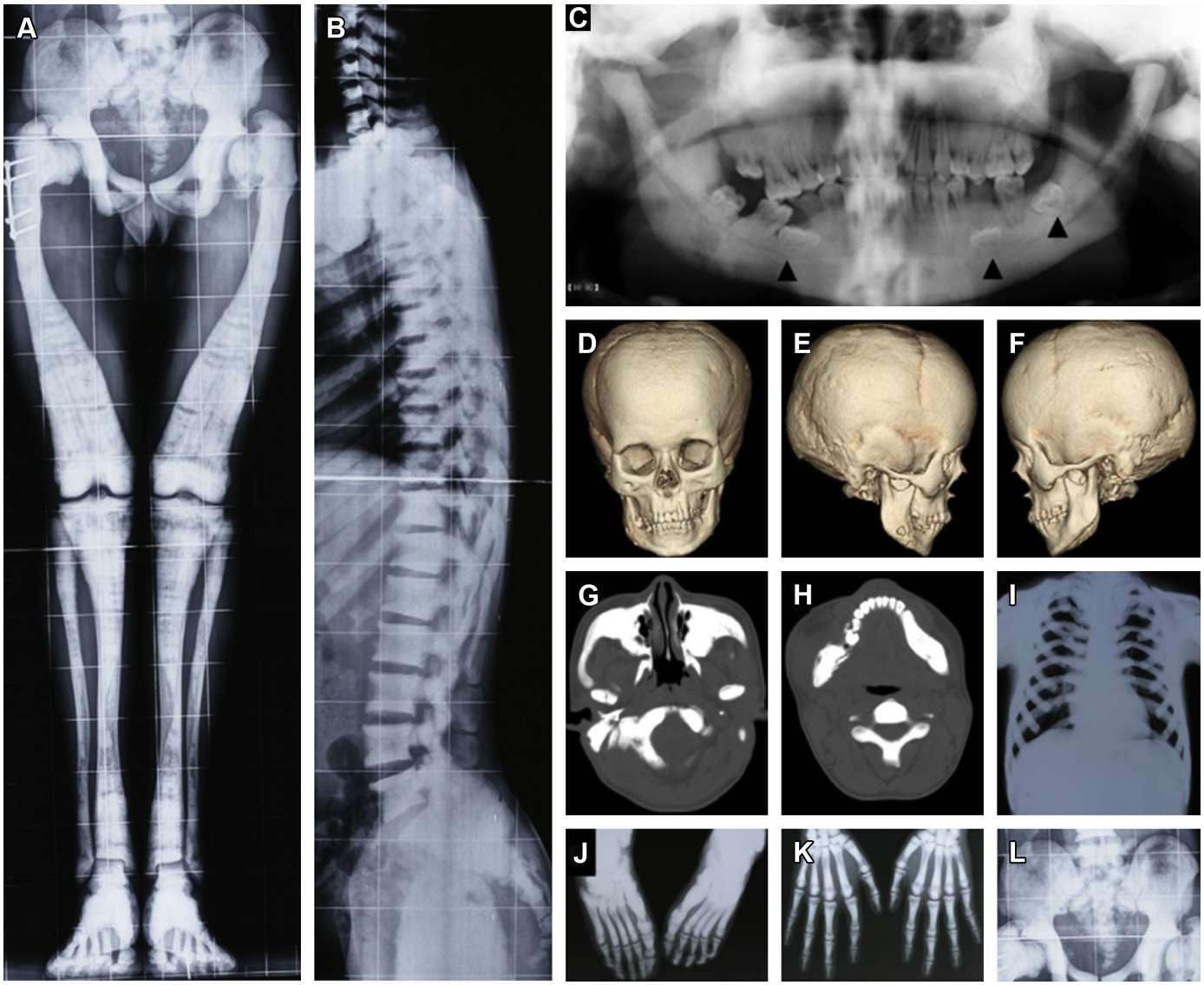

Fig. 1 Montage of patient with sclerotic bones associated with osteopetrosis. (*A*) Bowed femur. (*B*) Dense vertebra with lack of normal spine. (*C*) Sclerotic mandible with multiple unerupted molars. (*D—F*) Enlarged calvarium. (*G, H*) Sclerotic and thickened zygoma and mandible. (*I*) Diffuse ostesclerosis noted on chest x ray. (*J—L*) Radiodense feet, hands, and pelvis. (*From* Xue Y, Wang W, Mao T, et al. Report of two Chinese patients suffering from CLCN7-related osteopetrosis and root dysplasia. J Craniomaxillofac Surg 2012;40:416—20; with permission.)

Facial deformities, including frontal bossing and broad face, occur along with delayed dental eruption.

Differential diagnosis

Although the infantile neonatal form presents with a unique clinical presentation, the benign form of the disease, which can affect the mandible, cranium, and cervical spines with a sclerotic process, needs to be differentiated from other forms of osteosclerosis, such as Van Buchens disease, osteopathia straita, and sclerosteosis.

Treatment considerations for the oral and maxillofacial surgeon

Many unerupted teeth may occur. More than 30% of cases develop osteomyelitis de novo after dental extractions (Fig. 2).

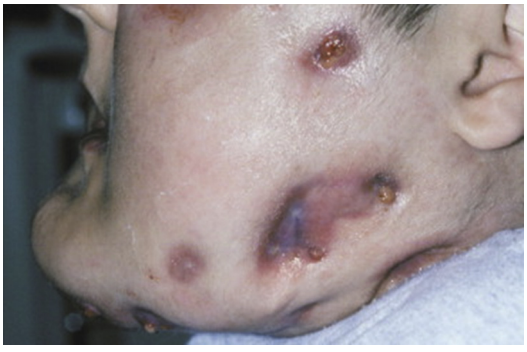

Fig. 2 Draining cutaneous fistulae secondary to chronic osteomyelitis, a common finding when the osteopetrotic jaws are subject to trauma, including dental extractions. (*Courtesy of* D. Sarasin, DDS, Cedar Rapids, IA.)