Clinical Pathologic Conference Case 6: Infantile Myofibroma

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Clinical Presentation

A 5-year-old female presented with facial asymmetry, which was first noted by her parents 1 month prior to consultation. The lesion was painful and interfered with speech and swallowing. The girl was otherwise in good health with normal physical and mental development. Her medical history was non-contributory.

Extraoral examination revealed a slight facial asymmetry of the right side covered by normal-colored skin with no signs of paresthesia. Intraoral examination revealed a swelling on the buccal aspect of the right posterior mandible, covered by normal mucosa. Lingual displacement of the first molar was noted. A panoramic radiograph revealed a large well-defined multilocular radiolucent lesion measuring 4 × 3 cm, which involved the ramus and coronoid process of the right mandible, displacing dental follicles and cortical bone, but not affecting the inferior alveolar nerve canal (Fig. 1).

Differential Diagnosis

Considering the clinical history and radiographic features, the differential diagnosis included multilocular radiolucent lesions that might affect pediatric patients. The diagnostic possibilities, therefore, would include lesions such as central giant cell granuloma (CGCG), central hemangioma, infantile myofibroma, aneurysmal bone cyst (ABC), and odontogenic tumors, such as ameloblastic fibroma (AF) and odontogenic myxoma (OM).

CGCG is a benign lesion that occurs in the jaws of young patients, usually before the age of 30 [1, 2]. About 10% of the cases affect patients in the first decade of life, similar to the current case [1]. The anterior region of the maxilla is commonly affected, and mandibular lesions are equally distributed on anterior and posterior regions [1]. The radiographic features of CGCG are variable, including both unilocular and multilocular lesions with scalloped and well-defined borders [2]. As in the present case, CGCG may present with aggressive clinical behavior, exhibiting rapid growth as a large multilocular radiolucent lesion, causing tooth resorption and displacement, and eventually, paresthesia, and pain [1, 2].

Central hemangioma is a benign proliferation of blood vessels that usually affects the vertebrae and skull, and is only uncommonly seen in the jaws [2]. Hemangioma of the jaw commonly affects patients in the first three decades of life, but only ~14% of those are in the first decade [2, 3]. Most central hemangiomas occur in the mandible, with 23% involving the angle and ramus regions [3]. The radiographic appearance is variable, ranging from unilocular cyst-like lesions to multilocular radiolucencies, with variable sized loculations. Occasionally, hemangiomas can present radiographically with spoke-like projections radiating from the center of the lesion [2, 3]. It is not unusual

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Fig. 1 Panoramic radiography of a 5-year-old girl, showing a large well-delimited multilocular radiolucent lesion involving the right angle and ascending ramus of the mandible

for central hemangiomas to measure 2 cm or more [3]. However, other main radiographic features of a hemangioma, such as diffuse borders and enlargement of the inferior alveolar nerve canal, as in neural lesions, were not seen in the present case. Furthermore, only a minority of cases of central hemangiomas exhibit tooth displacement and resorption [3].

Infantile myofibroma typically affects the mandible of pediatric patients, usually boys, in the first decade of life [4]. It is frequently characterized by a painless, slow-growing mandibular swelling with no surface ulceration [4, 5]. Radiographically, myofibromas are unilocular, but ~30% may be multilocular [4, 5]. About 30% of the cases are located in the body and ascending ramus of the mandible, and most cases exhibit displacement of tooth germs and well-defined borders [4]. Moreover, myofibromas can be large, causing cortical expansion and perforation [4, 5].

ABC is a pseudo-cystic bone lesion composed of blood filled spaces and giant cells, mainly found in long bones and vertebral bodies of patients in the first two decades of life [2, 6]. ABC of the head and neck is rare. Those lesions located in the head typically present in the mandible, particularly in the posterior mandible and ascending ramus. Facial swelling is common, with pain being a variable feature [2, 6]. Radiographically, ABC is characterized by unilocular or multilocular lesions with well-defined borders, occasionally causing cortical perforation, tooth displacement and root resorption [2, 6].

AF is a rare odontogenic tumor that mainly affects young patients in the first two decades of life [7]. It presents most often in the posterior region of the mandible as a hard swelling with variable symptoms and size. Radiographically, the AF can present as a well-defined unilocular or multilocular lesion associated with altered tooth eruption [7].

OM is commonly found in the posterior region of the mandible, and presents as a painless swelling. Most OMs

are diagnosed in patients between the second and fourth decades of life with a slight female predominance [8]. It is uncommonly observed in pediatric patients. Very few OM cases were described in children of less than 2 years of age, and all of these cases occurred in the paranasal area of the maxilla [8]. Radiographically, it may have a unilocular or multilocular appearance, containing well-defined and corticated borders, and causing tooth resorption and displacement [8].

Diagnosis and Discussion

Considering the above mentioned differential diagnoses, the patient was referred for an incisional biopsy under general anesthesia. Macroscopically, the specimen consisted of multiple brownish fragments of fibrous consistency (Fig. 2). Microscopic examination of H&E preparations revealed fascicles of spindle cells with tapering ends surrounding small vascular spaces (Figs. 3, 4, 5). The initial diagnosis was of a benign spindle cell lesion. Immunohistochemical evaluation showed tumor cells positive for smooth muscle actin (1A4, 1:400, Dako, Denmark), muscle-specific actin (HHF-35, 1:800, Dako, Denmark), and focal positivity for calponin (CALP, 1:600, Dako, Denmark) (Figs. 6, 7, 8). S-100 protein (Polyclonal, 1:10,000, Dako, Denmark), h-caldesmon (N-CD, 1:400, Dako, Denmark), desmin (D33, 1:1,000, Dako, Denmark), and CD34 (QBEnd-10, 1:50, Dako, Denmark) were negative. The Ki-67 (MIB-1, 1:100, Dako, Denmark) index was less than 1%. The final diagnosis was of infantile myofibroma.

Infantile myofibroma is a benign tumor of fibroblasts and myofibroblasts that represents the solitary form of infantile myofibromatosis [5]. The head and neck region is the most affected site, although other organs can also be involved such as the lungs, kidneys, pancreas, and

Fig. 2 Macroscopic aspects of the biopsy formed of multiple brownish elastic fragments

Fig. 3 General microscopic view at low magnification, showing multiple fragments formed by fibrous tissue with areas of hemorrhage (H&E, 40 $\times$)

Fig. 4 Fascicles of spindle cells, hyperchromatic nuclei, and indistinct cytoplasm, permeated by some hypocellular areas (H&E, 100 $\times$)

gastrointestinal tract [4]. It may affect the bones of the craniofacial region, including the orbit, and a small number of cases of solitary myofibromas have been reported within the mandible [4, 5].

Myofibroma of the mandible is typically diagnosed in children, usually in the first decade of life, and has a male predominance [4]. Clinically, it is characterized by a painless, slow-growing swelling of the jaw covered by normal-appearing mucosa. Bone expansion and cortical perforation have also been reported [4, 5].

Radiographically, the mandibular myofibroma is a radiolucent lesion, commonly unilocular (70%), with well-defined borders (67%), and occasional cortical expansion and/or perforation [4, 5]. Approximately one-third of the

Fig. 5 Higher magnification of variable densities of spindle cells in longitudinal and transversal sections, exhibiting myofibroblastic morphology and eosinophilic background (H&E, 200 $\times$)

Fig. 6 Tumor cells were strongly positive for smooth muscle actin (IHC, 200 $\times$)

Fig. 7 Most of the tumor cells were positive for muscle-specific actin (HHF-35; IHC, 200 $\times$)

Fig. 8 Many tumor cells were also strongly positive for calponin (IHC, 400×)

central myofibromas present as aggressive lesions, appearing as an ill-defined radiolucency. In young patients, these should be differentiated from desmoplastic fibroma, Langerhans cell histiocytosis, or malignancies, such as fibrosarcoma, rhabdomyosarcoma, Ewing's sarcoma, and more rarely, metastatic neuroblastoma [4]. The present case showed a multilocular appearance with well-defined margins, thus favoring a benign biologic process and long-term behavior, as mentioned above.

Microscopic features of myofibromas include a biphasic pattern of light- and dark-staining areas [4, 5]. Tumor cells are round to spindle, with slightly hyperchromatic nuclei arranged in short fascicles or whorls around hemangiopericytoma-like vessels, and presenting occasional areas of hyalinization [5]. Immunohistochemistry findings are important for the determination of the myofibroblastic nature of the cells. Specifically, evidence of smooth muscle actin positivity, and variable staining for other muscle markers, as well as demonstrating negativity for h-caldesmon, are all important for differentiating myofibroblasts

from smooth muscle cells. Myofibromas are also negative for neural and epithelial markers [4].

The treatment of choice for the central myofibroma is conservative surgery. Historically, relatively few cases have been treated by aggressive surgical jaw resection. The current patient was treated conservatively and shows no signs of recurrence after 6 months of follow-up [4, 5].

Although rare and usually unilocular, myofibroma of the mandible should also be considered in the differential diagnosis of aggressive multilocular radiolucent lesions in pediatric patients.

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