Vascular Floor of Mouth Mass with Unanticipated Intracranial, Orbital, and Vertebral Associated Involvements

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Abstract

We report on a case in which a blanching, unobtrusive oral growth proved to be a systemic threat. A blind, epileptic child presented with a bleeding oral floor mass of 4 weeks. Biopsy showed small, dilated vascular spaces with reactive fibroblasts. MRI indicated distribution of expansile lesions in the mandible, cranial base, and right orbit that had possibly contributed to the patient's years-long neurologic deficits. A subsequent bone scan indicated lesions in multiple axial bones. Histologic markers confirmed the presentation of a rare cystic vascular pathology. Cystic Angiomatosis is a disease of intraosseous vascular malformations with occasional visceral involvements. Oral and craniomaxillofacial cases are especially rare and presentations can involve neuropsychiatric deficits, sensory issues, and mucosal bleeding. While clinicians are often dismissive of intraoral bleeding because of the prevalence of periodontal disease, careful evaluation is nonetheless critical to rule out underlying diseases with a possibly significant systemic involvement.

Keywords Vascular neoplasm · Epilepsy · Blindness · Cystic angiomatosis

History

Vascular entities of the mouth pose clinical challenges because of the prevalence of mucosal vessels. Diagnosis may be complicated not only by the bleeding risk of the lesion but its nonspecific nature and their proximity to central neurovascular structures. Even relatively common pathoses—such as hemangioma—have earned the nickname “the great imitator” to highlight their nondescript phenotypes. Differential diagnoses range from conditions like periodontal abscesses to malignancies like lymphoma with equally profound variations in treatment. To simplify diagnosis, considerations for malignant entities could be deprioritized if mitotic figures

and atypia are not present, though the benign nature of a lesion does not always guarantee a nonaggressive course [1].

Here we demonstrate a unique case of a seemingly solitary entity of the oral mucosa with significant systemic repercussions. The report demonstrates that unassuming oral masses may (1) present as nondescript entities with nonetheless distinct molecular phenotypes, (2) produce a far-reaching cohort of neurovisceral symptoms, and that (3) appropriate management could be devised for significant improvements in quality of life even in such diseases.

Radiologic and Clinical Findings

A 13 year-old male presented for intermittent intraoral bleeding of 4 weeks. His medical history at presentation was significant for seizures, blindness, and cerebral palsy with quadriplegia as well as intellectual delay limiting direct communication. The bleeding was attributed to the floor of the mouth (FOM) without consistent triggers. The patient's family denied a recent history of nausea, vomiting, fevers, chills, or infections.

Examination revealed a nonambulatory, normocephalic, and aphasic teenager. Maximal interincisal opening was within normal limits, but further examination was

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compromised by the patient's inability to verbalize or follow commands. No port-wine stains or varicosities were noted. A 3 cm×2.5 cm firm, smooth, immobile, pink mass was noted on the right FOM without overt surface changes. (Fig. 1) Compression of the lesion elicited slight blanching without pain or discomfort. The mandibular region did not exhibit motor deficits or structural anomalies save for a slight right-sided bucco-lingual expansion. Pathoses, including the mass itself, were not noted during a dentist visit 2 months prior. Manipulation of the right FOM led to bleeding that was controlled via gauze pressure. Per family, the lesion would often bleed during brushing and mastication, leading to visible distress.

A magnetic resonance imaging (MRI) was taken, which indicated a multicystic, gadolinium contrast-enhancing lesion occupying the right mandibular intracortical space (Fig. 2). Lingual cortex perforation was noted near teeth #28–29 and into the right FOM. Masses of similar intensities were also found in the right maxillary alveolus and sinus, superior–posterior–inferior surfaces of the right orbit, as well as the frontal, biparietal, and occipital cranium with displacement of corticocerebellar structures. (Fig. 3) A follow-up bone scan suggested abnormal cyst-like entities in nearly all cervicothoracic spine and proximal humeri with loss of vertebral body height.

Genetic testing showed 7.1% of chromosomes with homozygosity greater than 3 Mb in length, though no signs of aneuploidy or overt genetic diseases were found. Urine organic acid, oligosaccharide, and mucopolysaccharide study results were unremarkable.

Fig. 1 Smooth, soft, immobile, and pink mass of the right floor of the mouth without overt surface changes

Fig. 2 Multicystic, gadolinium contrast-enhancing lesion occupying almost the entirety of the intracortical space in the right mandible

Diagnosis

FOM and mandible biopsies were taken under general anesthesia, whose recovery was lengthened to observe for post-operative bleeding. The entire intraoral exophytic mass was removed for patient comfort. Intermittent bleeding was controlled via pressure hemostasis. Microscopy revealed dilated, endothelium-lined small vessels with intervascular

Fig. 3 Various sized cystic masses in the right maxillary alveolus and sinus, orbital bones, and the cranial chamber with displacement of neuronal tissue

fibroses and limited atypia. Immunostains were positive for the GLUT-1 and CD31 proteins in the vascular walls. Histologic and radiologic findings together were consistent with a diagnosis of cystic angiomatosis (CA).

Discussion

CA is a rare, idiopathic proliferation of vascular tissue typically in the medullary spaces of long bones and axial skeleton [2, 3]. Its oft-lytic lesions are multilocular, well-defined, cystic entities with visceral spread commonly noted in the spleen, liver, kidney, pleura, and peritoneal membrane [1–4]. Polyostotic presentations may mimic metastatic disease [1, 5]. The distended, thin-walled vessels on histology likely represent lymphangiomatous proliferations marked by vascular endothelial growth factor (VEGF) and podoplanin [1, 2]. CD31 (or PECAM-1) and factor VIII antigen are other notable markers of CA, indicating a hematopoietic lineage [3, 6].

Literature on CA is sparse, with several studies suggesting a young male predominance [1, 4–6] while others purport a preference for middle-aged females [2, 3]. A survey of the MEDLINE database showed approximately 50 known cases in the English literature [1]. Though calvarial presentations are documented, maxillary and mandibular variants have each been reported in fewer than 5 cases as of 2016 [3, 5]. The mean age of presentation within the documented cases was 22.8 with a slight male predominance [1]. Three patients demonstrated mandibular lesions and another a maxillary lesion upon radiography. One individual complained of rhinorrhea also indicating naso-maxillary involvement [3]. The first known case of posterior fossa and cerebellar compression was also published in 2015, but this presentation did not involve the facial bones [1, 3, 5]. Extraosseous involvements could prove fatal via lesional displacement of irreplaceable tissue, especially when present in the liver [1, 4]. Approximately 35% of CA cases were shown to involve the viscera, especially the spleen [1]. Differential diagnoses for polyostotic, slow-growing, multilocular diseases include Langerhans cell histiocytosis, chordoma, and Ollier-Maffucci disease.

Langerhans cell histiocytosis (LCH) is a rare, likely a neoplastic entity of the dendritic myeloid progenitors especially in children under 15 years of age [7]. Approximately 60% of patients experience lytic intraosseous disease most commonly in the skull and the femur [8]. These masses are characterized by pain and multilocular radiographic appearance but unlike CA, demonstrate increased metabolic activity as well as eosinophilia [7, 8]. Intraoral lesions are also rare but share similar histopathology indicative of inflammation rather than lymphangiomatous proliferation. Interestingly, many LCH cases co-present with another neoplasm of the cranium, somewhat mimicking the current case [8].

Chordoma may originate from notochord remnants to present most commonly in males between the ages of 50 and 70, and is accompanied by pain and neurologic disturbance, presumably from nerve compression [9]. Soft tissue presentations are uncommon but possible via metastases to the lungs and the brain. More than 90% of the cases occur in the axial skeleton with a predilection for the skull and the sacrum [9, 10]. Intracranial manifestations may result in seizures or ocular deficits [9]. Preferred treatment is surgical resection (often followed by chemotherapy), but the complex anatomy of the skull and sacrum lead to a high rate of complication [9, 10]. Chordoma typically demonstrates positive immunohistochemistry for oncogenic markers such as the fibroblastic growth factor receptor (FGFR) and B-catenin with likely associations to both embryonic and carcinogenic processes [10]. Aneuploidy appears to be a common finding as well, with approximately 50% of all cases demonstrating chromosomal aberrations [10].

Unlike LCH and chordoma, Ollier-Maffucci disease (OMD) is a rare disorder of endochondromatous proliferation most commonly affecting both males and females equally during or close to their first decade of life [11, 12]. It may arise from nasosphenoid cartilage to develop multilocular, sclerotic radiolucencies of the face, and the Maffucci variant is known to develop soft tissue hemangiomas similar in appearance to the intraoral lesion noted in our patient [12]. Unlike our case, however, OMD is more commonly associated with cartilaginous tissues of the long bones and its microscopy is unmistakable for ovoid cartilagenous nodules [11]. The genetic changes in OMD appear to predispose patients to malignancies including glioma, resulting in polyostotic intra- or paraosseous lesions with intracranial masses [12].

CA exhibits unique traits that aid in diagnosis. For one, it typically demonstrates enhancement on T1-weighted MRI images with gadolinium, indicating a cystic or fluid-filled pathology [1, 5]. Immunohistochemistry is also often positive for the CD31 and GLUT-1 molecules indicative of lymphatic or angiomatous proliferations [1, 3]. Correlation of clinical and molecular characteristics allow management of mass effects via radiotherapy, delay of bony spread with bisphosphonates, and prevention of pathologic fractures using prophylactic fixation [3, 6, 13]. Radiotherapy is a known treatment for lesional expansion in below-neck CA. Bisphosphonates are osteoclast inhibitors with efficacy in delaying osteolysis from neoplasms, osteoporosis, and vascular malformations. Prophylactic fixation utilizes implants to fasten segments of bone against stress. These treatment modalities may help manage craniomaxillofacial CA, though the degree of improvements to prognosis is not yet clear [4, 13].

Craniomaxillofacial CA poses risks akin to and perhaps greater than those posed by disease elsewhere in the body. Intracranial spread produces neuropsychiatric risks unique

to this region of human anatomy [5]. Measures like surgical fixation are not always plausible inside the skull, while radiotherapy near facial glands and follicles could induce alopecia, xerostomia, keratoconjunctivitis sicca, and osteoradionecrosis [14, 15]. Proliferative tissues producing hair and secretions are particularly sensitive to radiation and are easily injured upon exposure. Bisphosphonates are associated with a similar gnathic necrosis now termed medication-related osteonecrosis of the jaw (MRONJ) [16].

In cases of aggressive intracranial, orofacial vascular masses such as these, selective debulking and seizure prophylaxis (often with levetiracetam) could significantly improve psychologic and functional well-being. Post-operatively, our patient is able to better tolerate daily hygiene and activities without notable difficulty. He may also undergo bisphosphonate therapy with concurrent radiotherapy to address possible mass effects. Studies show that utilizing oral (versus intravenous) bisphosphonates and limiting dental trauma minimize the risk of MRONJ. Compromised dentition may be removed prophylactically prior to bisphosphonate administration to minimize the need for future dental work. Focused radiotherapy may be conducted to limit exposure of the jaws and secretory glands [16]. Prophylactic fixations of the orbit, maxilla, and mandible may be considered upon risks of pathologic fracture. As new aspects of CA are discovered, treatment remains ongoing with further genetic and sensitivity assays.

Compliance with Ethical Standards

Conflict of interest The authors declare that they have no conflict of interest.

Ethical Approval The study is a retrospective study of the clinical course of a patient seen at our institution. However, all procedures performed in studies involving human participants were nonetheless in accordance with the ethical standards of the institutional and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards.

Informed Consent Informed consent was obtained from all individual participants included in the study.

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