Differential Diagnosis: Gingival Hyperplasia

Calcium Channel Blockers (e.g., Amlodipine, Nifedipine)
- *Associations*: History of hypertension +/- presence of firm nodular enlargement of the interdental papillae
- *Pathophysiology*: Nifedipine appears to be more commonly associated with this condition. Thought to occur from their ability to inhibit the influx of calcium leading to reduced uptake of folic acid that limits active collagenase production and accumulation of collagen.

Cyclosporine
- *Associations*: Past medical history of an autoimmune disorder, psoriasis, organ transplantation, bone marrow transplant, ulcerative colitis (severe)
- *Pathophysiology*: Increases the levels of signaling messengers IL-6 and TGF-beta1, which regulate the influence of MAPKs and PI3K which are known to be involved in cell proliferation of gingival tissue.

Familial Gingival Fibromatosis
- *Associations*: Family history demonstrating an autosomal dominant pattern of transmission +/- gingival growth over the teeth +/- problems with mastication or speech
- *Pathophysiology*: It is an inherited autosomal dominant trait that is low in incidence resulting in gingival overgrowth due to excessive collagen production in the gingival corium.

Gingivitis
- *Associations*: Bleeding gums especially with eating, flossing or brushing teeth
- *Pathophysiology*: Inflammation involving the mucosal epithelial tissue around the cervical portion of the teeth and alveolar process. Most commonly this induced by plaque

Leukemia
- *Associations*: Gingiva with erythematous or cyanotic hyperplasia +/- necrosis, bleeding or petechiae + elevated leukocyte count along with low hemoglobin, hematocrit and platelets.
- *Pathophysiology*: A hematological disorder that results in excessive and disordered proliferation of neoplastic hematopoietic stem cells that infiltrate tissues and organs, one of which is the gingiva.

Phenytoin (Dilantin)
- *Associations*: History of seizures
- *Pathophysiology*: Unknown, but may be due to an accumulation of extracellular matrix (ECM), such as collagen from an imbalance between the synthesis and breakdown of the ECM.

Scurvy from Vitamin C Deficiency
- *Associations*: Poor nutritional intake of vitamin C containing foods such as fruits + bleeding gums + red painful gums +/- generalized weakness, +/- petechiae of the skin
- *Pathophysiology*: Defective collagen synthesis that leads to impaired wound healing and ruptured capillaries that support the connective tissues.

Trench Mouth (Ulcerative Gingivitis)
- *Associations*: Acute onset of pain + bloody gums +/- foul smelling breath + grayish exudate covering the interdental papillae
- *Pathophysiology*: It is caused by infection from fusospirochetes, *Prevotella intermedia*, *Actinomyces* species

Valproic Acid

- *Associations*: Past medical history of either seizures, bipolar disorder, migraine headaches where valproic acid might be used for management +/- presence of hyperammonemia
- *Pathophysiology*: Associated with congenital gingival enlargement (known as fetal valproate syndrome)

References:

1. Livada R et al. Calcium channel blocker-induced gingival enlargement. J Hum Hypertension 2014;28:10-14.
2. Rodriguez-Vazquez M, et al. Congenital gingival hyperplasia in a neonate with foetal valproate syndrome. Neuropediatrics 2007;38(5):251-2.
3. Thomason JD, et al. Gingival hyperplasia associated with the administration of amlodipine to dogs with degenerative valvular disease (2004-2008). J Vet Intern Med 2009;23(1):39-42.
4. Thomason JM et al. The prevalence and severity of cyclosporin and nifedipine-induced gingival overgrowth. J Clin Periodontol 1993;20(1):37-40.
5. Hyland PL, et al. The effects of cyclosporin on the collagenolytic activity of gingival fibroblasts. J Periodontol 2003;74(4):437-45.
6. Chae HJ et al. Mechanism of cyclosporine-induced overgrowth in gingiva. J Dent Res 2006;85:515-9.
7. Dhadse PV et al. Hereditary gingival fibromatosis. J Indian Soc Peridontol 2012;16(4):606-609.
8. Menezes L et al. Acute myelomonocytic leukemia presenting with gingival enlargement as the only clinical manifestation. J Indian Soc Peridontol 2012:19:597-601.
9. Correa JD et al. Phenytoin-induced gingival overgrowth: a review of the molecular, immune, and inflammatory features. ISRN Dent 2011:497850.
10. Modeer T, et al. Enhanced prostaglandin biosynthesis in human gingival fibroblasts isolated from patients treated with phenytoin. J Oral Pathol Med 1992;21(6):251-5.
11. Schincaglia GP, et al. Cyclosporin-A increases type I procollagen production and mRNA level in human gingival fibroblasts in vitro. J Oral Pathol Med 1992;21(4):181-5.
12. Fu E, et al. Dose-dependent gingival overgrowth induced by cyclosporin in rats. J Periodontol 1995;66(7):594-8.