

Inflammatory Bowel Disease and Oral Radiological Manifestions

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Abstract

Original Research Article

Inflammatory bowel diseases (IBD) are known as chronic disorders of the digestive tract with uncertain aetiology. They include Crohn's disease (CD), Gardner's syndrome (GS) and ulcerative colitis (UC). Although IBDs involve primarily the gastrointestinal tract, important extraintestinal manifestations have been reported, notably in the oral cavity. In the last 10 years these diseases have had 20 times more representation among the population, affecting 200.000 people per year in Italy only. Oral manifestations can and must be acknowledged in the dental field using both clinical examination and radiographic techniques. This review's objective is to investigate how the use of radiographic analysis can be a helpful tool in order to highlight the strong correlation between IBD symptoms and oral lesions and, under certain circumstances, enable an early diagnosis.

Keywords: Oral manifestation of IBD, oral lesions of Gardner syndrome, oral lesions of Crohn disease, oral lesions of Ulcerative Colitis.

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INTRODUCTION

Inflammatory bowel diseases (IBD) are defined as chronic inflammatory diseases, represented mainly by Crohn's disease, ulcerative colitis and Gardner's syndrome. The aetiology of IBD is partially unknown but evidence suggests that the underlying cause of this condition is a dysfunction in the immune system of a susceptible individual. The main symptoms of IBD are abdominal pain, diarrhea and fever. Significant extraintestinal manifestations have been found. Their prevalence accounts between 16.7% and 40%. Eyes, skin, joints and oral cavity are majorly involved [1].

The prevalence of oral manifestations varies from 0.7% to 37%. Frequent manifestations are stomatitis, dental caries, mucogingivitis and periodontal tissue involvement. These lesions may precede the development of intestinal symptoms and can therefore be considered as major indicators in early diagnosis and therapy of IBD [2].

Crohn's disease (CD) and ulcerative colitis (UC) affect the digestive tract and are characterized by a persistent inflammatory condition. CD arises in the gastrointestinal tract with a greater involvement of the

terminal ileum while UC originates from the rectum and extends towards the colon.

Crohn's disease oral manifestations occur between 0.5% and 37% of patients [3]. Their classification includes specific and non-specific lesions. Specific lesions include aphthous ulcers and mucogingivitis while non-specific lesions are represented by angular cheilitis, glossitis and gingival hyperplasia [3]. Moreover, individuals affected by Crohn's disease may present orofacial granulomatosis which is typically associated with this disease.

Ulcerative colitis is characterized by many oral manifestations among which pyostomatitis vegetans, gingivitis and periodontitis are the most common. Pyostomatitis vegetans is frequently associated with IBD and more frequently with ulcerative colitis [4]. Some other common lesions are stomatitis and dental caries.

Gardner's syndrome (GS) is a subtype of familial adenomatous polyposis (FAP) caused by mutations in the APC gene. The manifestation of GS consists in multiple intestinal polyps that have a high risk of undergoing malignant transformation. Extraintestinal manifestations include osteomas which

are most frequently found in the mandible and multiple odontomas. Osteomas are reported in 46-93% of individuals affected by FAP and have an incidence four to twenty times greater than the control groups [5]. Odontomas are frequently observed in FAP patients and have a frequency between 9.4% and 83.3% [5]. These oral lesions precede systemic and radiological evidence of Gardner's syndrome and are therefore significant prognostic indicators of the disease [6]. Around 30% of individuals affected by GS develop dental anomalies including non-erupted and supernumerary teeth along with odontomas, dentigerous cysts and hypercementosis [6, 7].

This revision of the literature focuses on highlighting radiological manifestations of IBD in the oral cavity. The aim of the study is to show how the use of diagnostic radiology techniques such as OPT and periapical x-ray are a useful instrument to pursue early diagnosis of these diseases.

MATERIALS AND METHODS

To realize this review literature searches were performed on Pubmed and Scopus. The researched articles focused on oral manifestations of IBD that can be diagnosed with the use of radiography. Inclusion criteria consisted in studies published in the last twenty years, case-control studies, cross-sectional studies, retrospective clinical trials and revisions. Studies carried out on non-human species were excluded. Research terms included "IBD and oral manifestations", "Crohn disease and oral manifestations", "caries and Crohn", "caries and IBD", "caries and colitis", "periodontal and Crohn", "periodontal and IBD", "periodontal and colitis", "Gardner and oral manifestations".

RESULTS

This review has been developed selecting a total of 31 articles. In accordance with the research term "Gardner's Syndrome" 12 articles were utilised of which 6 case reports, 3 case series, 2 reviews and 1 chapter of "Oral And Maxillofacial Pathology" book; for "IBD" 9 articles of which 1 cross-sectional study, 2 case-controls, 1 systematic review, 4 reviews and 1 retrospective clinical study; for "Crohn's disease" 5 articles of which 2 case reports, 1 case series and 2 reviews; for "Ulcerative colitis" 5 articles of which 1 case reports, 2 case-controls, 1 pilot study and 1 review.

DISCUSSION

Gardner's Syndrome

Gardner's syndrome (GS) is a type of intestinal polyposis characterized by extraintestinal manifestations. Familial Adenomatous Polyposis (FAP) is a medical condition in which more than a hundred polyps are found in the colon and rectum.

In the diagnosis of Gardner's syndrome dentist's role is essential, particularly in pediatric age since maxillo-facial osteomas, sebaceous cysts and

dental abnormalities are suggestive of the disease. These signs anticipate the appearance of intestinal polyps that have a high risk of subsequently becoming malignant around the fourth decade of life. This causes a rise in the mortality rate of subjects affected by the disease.

Distinctive elements of GS are polyps in the stomach and small intestine, dental and skeletal anomalies, pigmentations of the retina, skin tumors as desmoid tumors, sebaceous cysts, dermoid and epidermoid cysts.

The disease is caused by germline mutations in the APC gene (Adenomatous Polyposis Coli gene), located in the long arm of chromosome 5. The family anamnesis may be positive or negative to GS. The syndrome has an incidence ranging between 1:8300 to 1:16000 live births and the mean age at the time of diagnosis of the polyposis is approximately 25 years. GS manifestations in the gastrointestinal tract include adenomatous polyps of the colon and rectum that can develop into adenocarcinomas before the 30th year of age in 50% of individuals. The rate narrows to 100% with the increase of age [7]. To prevent the fast growth of malignant tumors in the colon and rectum a resection of the low intestine is performed. The alternative to surgery is the pharmacological therapy with Sulindac [8].

Patients affected by undiagnosed GS often require a dental consult due to swellings of the mandible.

90% of patients present skeletal abnormalities including osteomas that grow during puberty and precede the development of polyps [7]. The growth of osteomas is slow and stabilizes with the increase of their dimensions [9]. Osteomas are slightly thick or big masses more frequently located in the mandible (angle and right margin) and the maxillary sinus. Osteomas can also be located in the cranium, paranasal sinuses and in the long bones. The presence of three or more osteomas in the mandible provides a diagnosis of GS.

Gardner's Syndrome is frequently associated with dental abnormalities as odontomas, odontogenic cysts, supernumerary teeth and impacted teeth [7].

The oral examination shows bone swellings or palpable exostosis on the mandibular angles that may limit the opening of the mouth. Sometimes the lesions can lead to facial asymmetry [10, 11].

Orthopantomography (OPG) shows well defined radiopacities around the margin of the mandible and multiple radiopacities in the mandible and maxilla which suggest the presence of enostosis. The enostoses are usually found in the molar or premolar region of the mandibles. Their number and dimensions increase

slowly with age. In some cases, enlarged enostoses may cause the absorption of adjacent dental roots [11]. Computerized tomography is also useful as it can show the involvement of bone and cement proliferations and measure their width. In many cases skeletal abnormalities lead to unerupted permanent teeth [12].

Osteomas are benign osteogenic lesions that slowly evolve from spongy or compact bone. They can be central, peripheral or extraosseous with a corresponding development in the endosteum, periosteum and soft tissue. Peripheral osteomas may be present in the paranasal sinuses, mostly in the frontal and ethmoidal. Histology shows trabecular bone and fibroadipose tissue. OPG can often be sufficient to identify osteomas but computerized tomography is usually a better diagnostic instrument. The detection of osteomas is necessary to diagnose GS since they precede the clinical and radiological evidence of FAP.

In Gardner's Syndrome sebaceous, epidermoid or dermoid cysts are observed. These are more frequently found on the face, scalp, arms and legs and are also very relevant for the diagnosis of GS.

Epidermoid cysts are the most common cutaneous manifestation of Gardner's syndrome and are detectable in 50-60% of patients.

Other manifestations of GS are fibromas, soft tissue fibromatosis also known as desmoid abdominal or extra abdominal tumors.

It is rare but possible to detect odontogenic myxoma in GS patients. This lesion is benign and locally invasive of the mandible.

Current literature shows the correlation between age and development of specific pathological signs as polyps of the colon, desmoid tumors, mandibular exostosis or enostosis, supernumerary teeth, odontomas and unerupted permanent teeth. Most frequently unerupted teeth, mandibular enostosis and exostosis are associated with GS therefore they must be detected for an early diagnosis of the disease.

In order to diagnose Gardner's syndrome a detailed medical examination is needed. Clinicians must verify the presence of sebaceous cysts and should perform an OPG along with craniofacial radiographies. A biopsy is suggested in case osteomas or bone radiopaque lesions are identified.

It is therefore necessary to visit the dentist regularly since childhood. During the dental examination, basic radiological exams as OPG must also be performed periodically. In case of suspicious lesions, TC or magnetic resonance (MR) are carried out.

OPG enables the detection of dental or bone lesions that have not fully developed. Periapical x-ray are moreover used to identify non clinically detectable caries that are important for GS diagnosis. The early evidence of the disease improves patients' quality of life. From the moment diagnosis the individual will undergo frequent gastrointestinal examinations and possibly colectomy.

This revision of the literature analyzed a group of articles in order to underline the relevance of performing radiologic examinations as an instrument of early diagnosis of Gardner's Syndrome.

Panjwani S *et al.*, reported the case of a 25-year-old female patient with Gardner's syndrome [6]. The clinical examination revealed multiple supernumerary teeth, odontomas, sebaceous cysts on the scalp and osteomas. The patient also presented a history of multiple swellings of the mandible. A significant facial asymmetry was noticeable due to a diffused swelling on the left side of the mandible that measured 3 cm x 4 cm and had a wide extension going from the parasymphysis to the posterior border of the mandible [6]. There were clinically missing teeth, 21 and 23 (no history of extraction revealed) and an over-retained tooth, 63. The following examinations were carried out to investigate the patient's condition: OPG (Fig-1), posteroanterior radiograph (Fig-2) and maxillary and mandibular occlusal radiograph (Fig-3) [6].



Fig-1: OPG demonstrates impacted teeth 21 and 23, homogenous radiopaque masses over the right and left inferior aspect of the mandible suggestive of osteomas (large arrows). Also multiple small, homogenous radiopaque masses surrounded by a radiolucent halo could be seen throughout the maxilla and mandible suggestive of complex odontomes (small arrows). Diffuse sclerotic masses are present throughout the body of mandible giving it a mottled appearance – Courtesy of Dr. Sapna Panjwani



Fig-2: Posteroanterior radiograph shows extra-oral osteomas along the mandible (white arrows). – Courtesy of Dr. Sapna Panjwani

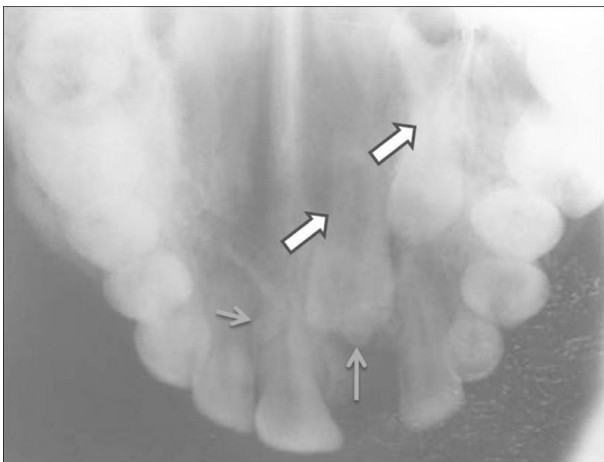


Fig-3: Maxillary occlusal radiograph shows impacted teeth 21, 23 (large arrows) and odontomes (small arrows) in the near vicinity. – Courtesy of Dr. Sapna Panjwani

OPG demonstrates impacted teeth 21 and 23, homogenous radiopaque masses over the right and left inferior aspect of the mandible suggestive of osteomas. The patient did not exert any symptoms of rectal bleeding, cramping abdominal pain, weight loss, diarrhea or small bowel or colonic obstruction. A colonoscopy was not performed to rule out the presence of polyps in the intestine, colon and rectum. In the next year the patient

has remained asymptomatic, with no relapse of the lesions [6].

Chimenos-Küstner *et al.*, [13] reported the case of a female patient, 42 years of age, claiming nonspecific pain present for several days, in the lower right hemiarcuate particularly on the first molar 46. The patient reported numerous painful episodes over approximately one year, which had a spontaneous resolution. Palpation of the soft and hard structures of the maxillofacial area showed the presence of protuberances of a bony consistency, compatible with exostosis, of some 5 mm in diameter, in the second and third quadrant, near the mandibular angle. A periapical x-ray of the affected zone (molar 46) showed radio-opaque cotton wool like images. The orthopantomograph of the patient revealed well defined radio-opaque images with similar characteristics to those described in the intra-oral periapical projection, regarding the whole mandibular area. During the anamnesis the patient declared familial adenomatous polyposis diagnosis in puberty. A total colectomy with ileorectal anastomosis was performed when she was 21 years old. She also presented with epidermoid cysts on the back and gastric polyps. The patient's children were carriers of the same genetic mutation. A radiographic study was carried out on the mother and her two children. In an orthopantomograph of the daughter, the presence of multiple radio-dense mandibular lesions was confirmed whereas in the orthopantomograph of the son inclusion of tooth 23 was observed [13].

Salti *et al.*, reported a rare case of a 14-year-old male patient with Gardner's syndrome and odontogenic myxoma [14]. The patient was referred by his dentist twice in the span of a year. The clinical examination showed a slight painless swelling of the left mandible (Fig-4).

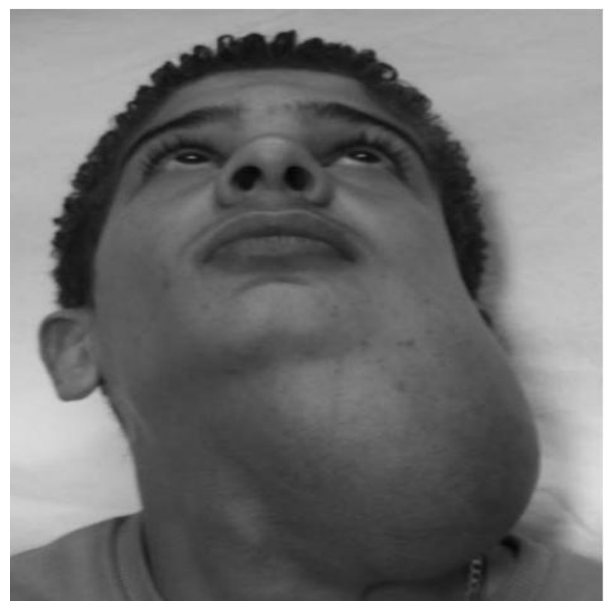


Fig-4: Photo of the patient – Courtesy of Dr. Louffi Salti

OPG (Fig-5) shows multiple impacted teeth, unerupted and retained deciduous teeth [14]. Additionally, non-corticated, conglomerates of indistinct radiopacities structures were noted apical to the roots of first mandibular molars and maxillary premolars and molars and in the ascending ramus. Two non-corticated, distinct, radiopacities were located between the right maxillary first premolar and canine and in the left zygomatic-maxillary process. Moreover, a multilocular radiolucent area, with “soap bubble” pattern, was noted at the left angle of the mandible [14].



Fig-5: Panoramic radiograph shows unerupted teeth, osteoma at the left ascending ramus and in the left zygomatic-maxillary process. Multilocular lesion is at the left mandible angle – Courtesy of Dr. Loufi Salti

CT demonstrated unerupted teeth and several hyperdense areas in the mandible and left maxilla apical to the roots and in the left ascending ramus. The left maxillary sinus along with the left zygomatic bone, ethmoidal cells and right ascending ramus presented

multiple osteomas. Moreover, the coronal CT revealed partial destruction of the facial bone.

Eleven months later the patient presented himself with gross facial asymmetry and considerable painless swelling of the left side of the mandible measuring 10 cm × 7 cm, extending from the parasymphysis to the angle of the mandible. The OPG (Fig-6) showed multilocular radiolucency in the body of the left mandible with a smooth, scalloped, well-defined margin, and of variable cortication [14].



Fig-6: Panoramic radiograph demonstrates multilocular radiolucency in the body of the left mandible extending from the mesial root of the left first molar to the unerupted third molar – Courtesy of Dr. Loufi Salti

The axial CBCT (Fig-7) showed loculated irregularly shaped radiolucency with well-defined corticated margin in the body of the left mandible. The coronal and sagittal images revealed extensive bone destruction at the left body of the mandible and the ascending ramus.

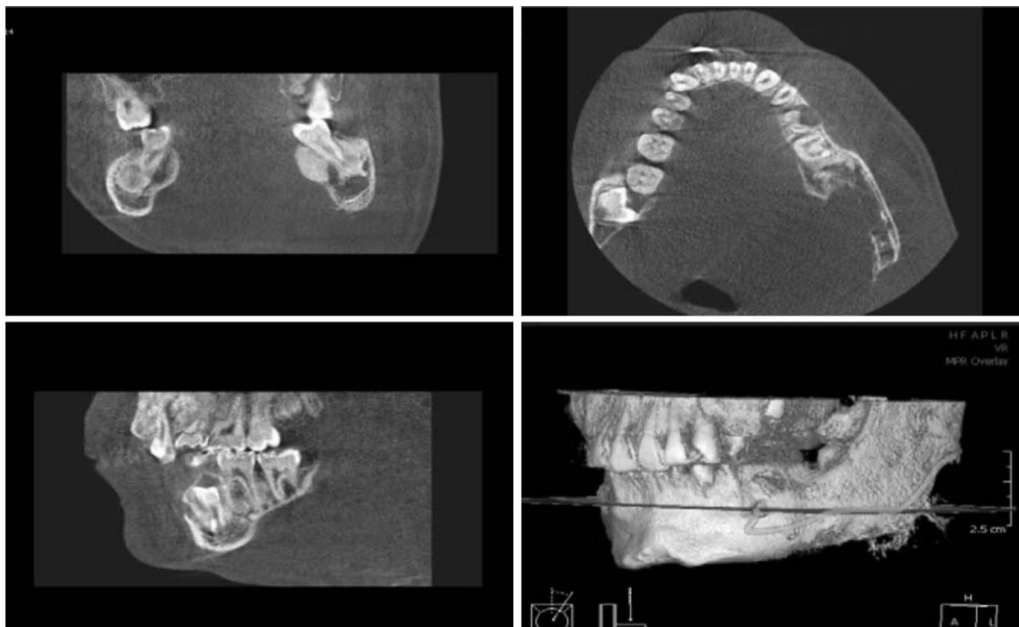


Fig-7: CBCT of the mandible shows loculated irregular radiolucency and well-defined corticated margin in the body of the left mandible (axial). The coronal and sagittal views reveal bone destruction at the left body of the mandible and the ascending ramus. – Courtesy of Dr. Loufi Salti

The patient was referred to the hospital to surgically remove the tumor on the left angle of the

mandible and excise the left hyperplastic coronoid process (Fig-8).



Fig-8: Postoperative panoramic radiograph after one month – Courtesy of Dr. Loufti Salti

Pereira *et al.*, published a case series of GS [15]. The first patient examined was an 18-year-old girl with abnormal mouth opening lasting 8 months. Additionally, she complained of abdominal pain and frequent diarrhoea for the past 18 months. The extraoral examination showed a fixed nodular swelling in right side of the mandible (angle region) without any significant alterations at the intraoral examination. Panoramic radiograph and computed tomography (CT) were performed. They both revealed two well-defined radiopaque/radiodense lesions arising on the ramus (27 mm × 19 mm) and the mandible angle (23 mm × 15 mm). These lesions suggested the diagnosis of osteomas and GS was hypothesised in accordance with the anamnesis and mandible lesions. A colonoscopy of the patient showed colonic and rectal polyposis and a germline mutation in APC gene was confirmed.

The second patient was a 49-year-old woman who reported the occurrence of jaw abnormalities. Her medical history showed FAP diagnosis at 30 years old and the dental history revealed the excision of the left superior incisor impacted in an odontoma. At the intraoral examination 4 supernumerary teeth were observed, 3 in the mandible and one in the maxilla. The panoramic radiography revealed an osteoma in the left condylar region and multiple diffused radiopaque lesions on the lower teeth periapices, which led to the diagnosis of osseous dysplasia [15].

The case report from Cankaya *et al.*, [16] analyses a 21-year-old patient who was referred to the dentist for the management of craniofacial manifestations of GS [16]. An initial clinical examination showed a nodular formation that was palpable along the mesial portion of the right mandibular angle. A panoramic radiograph and an anteroposterior radiograph showed the presence of multiple round radiopaque lesions in both the maxilla and mandible, multiple impacted teeth and multiple odontomas, each measuring approximately 0.5 to 2 cm in diameter. On palpation, these lesions were hard, well confined, and non-adherent to the skin. Dental volumetric tomography (DVT) images showed multiple osteomas of the buccal cortex of the right mandibular angle and left mandibular angle. Coronal and sagittal section view of the right condyle showed a large

osteoma that limited mouth opening. The dental anomalies, mandibular osteomas and the family history of the patient, led to the diagnosis of Gardner's syndrome [16].

Cahuana *et al.*, published a case series on three patients [8]. Patient one was a 10-year-old boy who complained of a hard bilateral swelling on the angle of the mandible. There was no family history of GS. Bilateral palpable bony irregularities on both mandibular angles were present, although the one on the right side was significantly larger. Moreover, the patient presented exostoses on the right maxilla, the parietal and occipital regions, and a soft tumour at the level of the L5, present since birth. The dental OPG showed multiple mandibular exostoses and enostoses and dental anomalies: mandibular right first premolar was unerupted due to persistence of the first primary molar. The CT scan showed many mature osteomas on the right and left angles, pterygoid plates and zygomatic arches. The patient underwent a fibrocolonoscopy and no malignant transformations were revealed. One year later the growth of the right-side tumour required the resection of the osteomas. Histologic examination identified sclerotic bone tissue. During the following three years, since the osteomas on the left side grew considerably, the tumors were therefore resected [8].

The second patient was a 9-year-old girl. She had previously been diagnosed with GS and her family history revealed that her maternal grandfather had presented multiple desmoid cysts and had died of colon cancer. Her mother had several sebaceous cysts and mandibular exostoses, but no history of digestive pathology. At only six months old, the patient had presented a desmoid tumour on her back and small bony tumors on her skull, for which she underwent a resection at the age of two. However, the tumours of the skull recurred at the age of four when she also developed multiple exostoses on her frontal and parietal bones. At age 9 the absence of the maxillary right permanent central incisor (11) was detected. The dental OPG showed a supernumerary tooth, later extracted, impeding the eruption of the maxillary right central incisor. Furthermore, the fibrocolonoscopy revealed the presence of four colonic polyps at the age of 10 [8].

Patient three was a 17-year-old girl referred to the dentist with multiple dental anomalies. Her medical history reported two tumours in her abdominal wall resected at age 2 and 6, diagnosed as non-specific myofibromatosis. Moreover, at the age of 15 a desmoid cyst in her back was observed and resected. Extensive caries in eight permanent molars and several premolars were discovered during the dental examination. The presence of primary teeth (5.2 and 6.3) was noted, with the respective absence of the maxillary right permanent lateral incisor (1.2) and left canine (2.3). The OPG confirmed the inclusion of 1.2 and 2.3, as well as the presence of two odontomas, one impeding the eruption

of 12, and the other between incisors 21 and 22. A supernumerary tooth between the apical regions of 22 and 63 was also observed. The osseous mandibular base showed a marked antegonial notch on the right side. The differences in bone density, especially in the mandible, and the enostoses between the roots of 35 and 36 were significant findings. Since these results were indicative of GS, a colonoscopy was recommended [8].

IBD

Inflammatory bowel diseases (IBD) mainly include two inflammatory conditions: Crohn's disease (CD) and ulcerative colitis (UC). The aetiology of these diseases remains partially unknown, but current scientific evidence recognizes a combination of risk factors such as genetic, environmental and immune factors as possible causes.

A statistically significant association was found in literature between IBD and dental lesions, such as dental caries, infections and periodontitis [17].

The pathogenesis of IBD and periodontal disease implies a complex interaction between bacteria and the host's immune response, which is strongly influenced by genetic and environmental factors [18].

Apical periodontitis (AP) is a chronic inflammatory disease of periapical tissues caused by an infection of endodontic origin. AP is the consequence of a dynamic interaction between the root canal microbes and the host's defence system. It is characterized by local inflammation, reabsorption of hard tissues and destruction of surrounding periapical tissues guided by complex interactions between inflammatory cells and soluble mediators [19]. In the radiographic image, chronic periapical inflammations are evident as radiolucent areas around the apex of the affected tooth. The therapeutic gold standard for AP-affected teeth is root canal treatment (RCT) [18].

A 2017 study published by Piras *et al.*, assessed the presence of periapical periodontitis (AP) and oral health status in 110 IBD patients (49 men and 61 women) treated with corticosteroids or biological drugs (BMs). The oral health of the patients was evaluated using the DMFT index, the initial screening OPGs and the periapical radiographs for further elaboration. The periapical X-rays were assessed via the periapical index score (PAI). The results revealed a higher prevalence of AP in female subjects with IBD than in healthy subjects, especially if treated with BMs, and that subjects with IBD had larger periapical lesions than healthy subjects [19]. However, the scientific evidence available in this regard differed.

In 2020 Poyato-Borrego *et al.*, published a case-control study [18] with the aim to verify the frequency of apical periodontitis, evaluated as a periapical radiolucent lesion, and root canal treatment (RCT) in patients with IBD and healthy patients. The

radiographic examination regarding the state of periapical tissues was conducted through digital orthopantomographies and the periapical index (PAI). In the case of multiradicated teeth, the highest score obtained from the analysis of the individual roots was taken as the tooth PAI score. A PAI value greater than 2 (PAI 3) corresponded to the diagnosis of periapical disease.

The classification of previously endodontically treated teeth (RCT) was done through the identification of radiopaque material inside the root canal [18].

This study revealed a significant association between patients with IBD and the presence of radiolucent periapical lesions (RFL). More precisely, patients with IBD had a frequency of periapical periodontitis 5.7 times greater than those in the control group ($P = 0.005$). In contrast, the frequency of RFT was similar in patients with IBD and patients in the control group ($P > 0.05$). The results suggest that both types of IBD, ulcerative colitis and Crohn's disease, are associated with a higher prevalence of apical periodontitis.

This study highlights how radiographic examinations performed in the oral cavity can contribute to an early diagnosis of IBD [18].

Crohn's Disease

Crohn's disease (CD) is a chronic inflammatory bowel disease, characterized by "skipping" lesions at the intestinal wall level. These lesions can affect any portion of the gastrointestinal tract, from the oral cavity to the anus, but mainly affect the terminal ileum and colon.

In central Europe the disease appears to occur in both sexes with the same frequency. In more than 50% of cases, Crohn's disease manifests itself before the age of 30 and often develops in childhood [20]. Clinical symptoms of Crohn's disease include abdominal pain, diarrhea, loss of blood from the rectum, decreased appetite, weight loss, fever and a decrease in child growth. The disease usually shows exacerbations altered with asymptomatic periods or remissions.

Crohn's disease has several oral manifestations, with a higher prevalence in children than in adults and in patients with proximal and/or perianal gastrointestinal tract involvement. Often lesions in the oral cavity may precede intestinal involvement [3], for this reason they must be investigated through diagnostic procedures that can be executed by dentists.

At oral inspection, diffused labial and buccal swelling is one of the most frequently associated manifestations of CD. The swelling is generally persistent, fixed on palpation and painless; involvement of the lip can lead to vertical fissures. The patient with

CD can present an oral granulomatous swelling, with a "cobblestone" appearance, similar to that found in the intestinal mucosa with endoscopy. Other specific lesions associated with Crohn are deep linear ulcerations, mucogingivitis, granulomatous cheilitis. In addition, non-specific lesions such as aphthous ulcerations may occur, present in about 20% of the general population and in about 20-30% of CD patients. Dental caries, gingivitis and periodontitis occur in about 20% of CD patients. Other non-specific manifestations include angular cheilitis, glossitis, gingival hyperplasia, lichen planus, halitosis, dysphagia, impaired taste perception, reduced salivation, lymphadenopathy, secondary fibrosis and candidiasis.

Crohn's disease affects an increasing number of children around the world, with an almost equal incidence in industrialized and developing countries. In children under the age of 15 the male: female ratio is 1.5: 1.0 [21]. The cause of this increase remains unknown to this day.

Children and adolescents with CD can often present a more critical disease course than adult patients and it is therefore extremely important to obtain an early diagnosis, which can be determined on the basis of the presence of oral lesions. Furthermore, the potential impact of Crohn's disease on pubertal growth, emotional development and the quality of life of patients, underlines the need to have a close interaction between all the figures involved in the observation of intestinal and extra-intestinal manifestations (pediatricians, dentists, dermatologists, general surgeons, immunologists).

The study of Favia *et al.*, conducted on 8 patients, aged between 9 and 13 years, reported salient oral manifestations as early signs of CD, later confirmed by biopsies of the gastrointestinal tract [22]. In 4 patients, typical signs of orofacial granulomatosis were detected, such as swelling with a "cobblestone" appearance, "mucosal tags", cheilitis, labial and lingual fissures and gingivitis. In 3 out of 8 patients aphthae or aphthous stomatitis were detected, while glossitis and ulceration of the palate were found in 1 and 2 patients respectively. Biopsies of uncertain lesions were performed confirming the presence of non-caseous granulomas [22].

The study by Eckel *et al.*, described the presence of oral manifestations in a 15-year-old Caucasian boy [23]. On the first visit, the boy presented areas of retromolar swelling, gingival bleeding and swelling of the cheeks, associated with superficial ulcers at the level of the soft palate and vestibules. The patient was referred to a gastroenterologist for further examination. The medical history reported significant weight loss in the previous year, abdominal pain on the

right side and the presence of blood on defecation. Family history was positive for IBD [23].

It is important to carry out the objective clinical examination in conjunction with the radiographic examinations to investigate oral lesions, such as periodontitis, peri-apical periodontitis and caries that need further investigation. Several studies have shown that patients with Crohn's disease are most affected by these oral diseases.

In the prospective study of Vavricka *et al.*, which lasted 8 months, systematic oral tests of 113 patients with IBD (69 patients with CD and 44 patients with ulcerative colitis) were compared with those of a group of healthy patients [24]. The clinical examination was based on established oral health markers for periodontitis (bleeding on probing, loss of attachment and periodontal pocket depth) and gingivitis (papilla bleeding index). In addition, visible oral lesions were also documented. Both markers of gingivitis and those of periodontitis resulted higher in patients with IBD compared to the control group. From this study, IBD, and in particular perianal disease in CD, was found to be associated with periodontitis. Optimal therapeutic strategies should focus on treating oral and systemic inflammation [24].

The cross-sectional study by Limin *et al.*, compared the prevalence, severity and extent of dental caries and periodontal disease in Crohn's disease patients and healthy patients [25]. This study revealed that the indexes of carious, missing and clogged dental elements were significantly higher in patients with CD and UC compared to the control group ($P < 0.001$). Patients with CD [OR = 4.27, 95% CI: 2.63-6.95, $P < 0.001$] and UC [OR = 2.21, 95% CI: 1.24-3.94, $P = 0.007$] had a greater risk of dental caries than controls. Significantly higher percentages were observed in patients with CD and UC compared to pocket depth controls on probing ≥ 5 mm and clinical attachment loss ≥ 4 mm ($P < 0.001$). The results obtained confirmed that CD and UC were risk indicators for periodontitis (respectively OR = 4.46, 95% CI: 2.50-7.95, $P < 0.001$; OR = 4.66, 95% CI: 2.49-8.71, $P < 0.001$) [25].

CD and UC patients showed no significant difference between the risk of dental caries and periodontal disease. In conclusion, IBD patients have a higher degree of prevalence, severity and extent of dental caries and/or periodontal disease than controls and require oral health education and multidisciplinary treatment.

Ulcerative Colitis

Ulcerative colitis (UC) is a chronic intestinal disease characterized by diffused inflammation of the colon mucosa. The disease always affects the rectum but can also extend to the entire colon

(pancolitis). Ulcerative colitis alternates periods of remission with periods of exacerbation.

Oral manifestations of UC can be defined as extraintestinal manifestations or systemic complications. Oral lesions may precede the disease, exacerbate or regress following changes in UC severity. The most characteristic oral manifestation is pyostomatitis vegetans (PV), considered as a specific oral indicator of UC. Other non-specific oral lesions such as aphthous ulcers, lichenoid lesions, halitosis, dysgeusia, dry mouth, coated tongue, gingivitis, oral ulcerations, caries and periodontitis are frequently observed in patients with UC [26].

Less than 10% of UC patients have extraintestinal manifestations (EIM) at the time of diagnosis, but around 25% of patients will develop EIM over their lifetime. Oral manifestations appear to be related to the severity of UC; a severe form of ulcerative colitis is associated with a higher prevalence of oral ulcerations, tongue coating and halitosis [4].

In the study of Kumar *et al.*, [26] 15 patients (8 men and 7 women) with UC diagnosis were subjected to an intraoral examination to assess the possible presence of oral manifestations. The results revealed specific and non-specific oral manifestations. PV, minor aphthous ulcers and lichen planus (LP) showed recurrence and remission concomitant with UC severity. Oral manifestations can be used as indicators of UC. This study aimed to evaluate whether EIMs could predict UC's remission and relapse [26].

PV is a characteristic but rare inflammatory stomatitis that can lead to complications in IBD, particularly in ulcerative colitis [27]. The Pyostomatitis Vegetans is more prevalent in males, with a ratio of male: female of almost 3:1. The lesions can occur at any age, with greater frequency between 20 and 59 years (average age is 34 years). PV can involve the entire oral cavity but affects the labial and vestibular portions of the gingivae, the soft and hard palate and the buccal mucosa more frequently. Intestinal symptoms usually precede the oral manifestations of PV by several months or years [4].

Ulceration is the most common oral sign of UC. Ulcers can occur simultaneously with the exacerbation of the disease or independently of UC activity [4].

Some oral manifestations of UC can be defined as side effects from malabsorption or drug therapy. Aphthous ulcer in UC is due to the malabsorption of micronutrients and the simultaneous presence of oral lichen planus [26]. A drug used to treat aphthous ulcers can reduce salivation; reduced salivary flow may be associated with an increased risk of dental erosion, caries, discomfort associated with the use of

dental prostheses, soft tissue abrasions and infections [28]. The use of intraoral x-rays and OPG is a useful tool for detecting carious lesions.

IBD patients have a significantly higher prevalence of caries and plaque due to poor eating habits. The study by Tan *et al.*, performed on 80 patients with UC encountered significantly more cases of periodontitis, greater pocket depth and fewer dental elements in patients with UC compared to controls. UC patients also had greater clinical attachment loss (≥ 3 mm) than CD patients [4].

In the study carried out by Elahi *et al.*, [28] out of 50 UC patients, 20% reported a change in taste, which became more acidic. There was also a significantly higher prevalence of regurgitation in patients with UC compared to controls [28].

Treatment of intestinal manifestations of IBD has a favourable effect on lesions of the oral mucosa. Furthermore, remission has been shown to reflect treatment control and response to therapy [29].

The specialist article of 2017 written by Takeshi *et al.*, [27] reported the clinical case of a 69-year-old Japanese man who had a chronic oral ulcer in the gingiva, with initial diagnostic suspicion of gingival carcinoma. For the past 5 years, the patient had been taking mesalamine and corticosteroids for the treatment of ulcerative colitis. Computed tomography revealed a high uptake in the right maxillary gingiva. On the basis of the clinical results, the patient was diagnosed with PV, which was the reason for exclusion of gingival carcinoma [27].

The study by Sondergaard *et al.*, has shown that the prevalence of osteomas in 50 patients with ulcerative colitis is 4%, while it is 2% in the control group [30]. Osteomas can be detected through routine clinical and radiographic examinations. Panoramic radiography and computed tomography (CT) are therefore essential for the diagnosis [30].

Colectomy is considered as a last treatment option for patients with UC and with untreatable or highly resistant oral lesions that significantly affect the quality of life. Colectomy has also been reported to result in a regression of the UC-associated pyostomatitis vegetans [31].

Oral manifestations in pediatric UC patients may be present in one third of subjects and are usually non-specific [31]. A complete assessment of children with potential UC is essential for early disease identification in order to optimize short and long-term outcomes. The most important step in the treatment of oral signs and symptoms is the control of the intestinal disease [4].

CONCLUSION

Oral manifestations of IBD may contribute to the deterioration of the patient's health and could also precede the development of typical intestinal manifestations of the disease. The role of the dentist in promptly identifying oral signs of the disease is crucial. The identification can be performed by using clinical examination and radiographic analyses. It is also important to pursue a personalized therapy focused primarily on prevention. For preventive purposes oral practitioners must address the patients with diagnostic suspect of IBD to the gastroenterologist.

Evidence collected in this study underlines the relevance of performing an OPG on every patient during his first visit to highlight oral signs of IBD that are not evident during oral examination.

In case of suspect lesions as osteomas, odontomas and periapical lesions further investigations are required (CT, intraoral x-rays). The dentist is responsible for treating identified oral lesions and addressing the patient to a specialist in order to anticipate the malignant development of intestinal manifestations and to improve the patient's overall quality of life.

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