Objective: There is a growing body of evidence to substantiate that cutaneous psoriasis is associated with an increased risk for a multitude of systemic disorders. Although there is an extensive array of medical publications regarding psoriasis, the dental literature has almost exclusively been focused on erythema migrans and occasionally, with oral psoriatic mucositis, chronic periodontitis, and psoriatic arthritis of the temporomandibular joint. This report will review the diversity of systemic comorbidities, namely cardiovascular, neurologic, renal, liver, gastrointestinal, pulmonary, endocrine, ocular, arthritic (including temporomandibular joint), nail, cutaneous, and psychologic (including suicide) disorders; neoplasia; infection; dyslipidemia; vitamin D deficiency; substance abuse; higher mortality; and oral mucosal involvement. A discussion of the oral and maxillofacial relevance of these comorbidities is also provided. Method and Materials: The author conducted a PubMed search from 1975 through August 2017 for articles on comorbidities associated with psoriasis. For select topics, some relevant case reports were examined. Results: A search on PubMed yielded almost 44,000 articles on psoriasis and nearly 1,300 with the keywords psoriasis and comorbidities. Articles selected for discussion consisted mostly of recent systematic reviews and meta-analyses. Case reports were included when there was a restricted number of psoriatic patients with a particular comorbidity. Conclusion: When a patient presents with a history of psoriasis, the dental practitioner should expand the medical history process to ascertain possible correlated diseases. Information gleaned from this interview process may prompt the attending dental clinician to seek consultation with the patient’s physician to gain greater insight to the severity of any prevailing comorbidities and engage in discussions for possible modifications in dental management. Knowledge of psoriatic comorbidities and their possible impact on dental care may improve clinical outcomes. (Quintessence Int 2018;49:209–217; doi: 10.3290/j.qi.a39692)

Key words: comorbidities, dentistry, management, oral, psoriasis

Psoriasis, once considered solely a chronic inflammatory cutaneous disease, is now recognized to be associated with a myriad of organ system burdens and a greater risk of mortality. The presence of one psoriatic comorbidity increases the coexistence of others. Generally, the severity of psoriasis is correlative with the extent of comorbid disease. The etiopathogenesis of psoriasis and comorbidities involves a complex interaction of genetic and environmental factors; immunologic T-lymphocyte dysregulation; chronic inflammatory mediators, such as interleukin 6, 12, 20, and 23; osteopontin; C-reactive protein; homocysteine; microbials; and pharmacologic agents (biologics, tumor-necrosis factors, beta-blockers, lithium, antimalarials).
Demographic studies have demonstrated heterogeneity in various subpopulations, with incidences averaging from 2% to 3% and affecting 125 million individuals worldwide. An assortment of cutaneous presentations has been characterized, with more than 80% of patients affected with plaque (vulgaris) psoriasis, and less frequently with guttate (eruptive), pustular, inverse (flexural), and erythrodermic subtypes. Microscopically, skin lesions exhibit poorly differentiated keratinocytes with hyperproliferation.

Although a vast number of systemic comorbidities has been reported with psoriasis, attention in the dental literature has been dedicated mostly to erythema migrans and occasionally to oral psoriatic mucositis, chronic periodontitis, and psoriatic arthritis (PsA) of the temporomandibular joint. To extend the knowledge of psoriasis for dental professionals, this review will provide a discussion of its multisystem dissemination and possible impact on dental management.

METHOD AND MATERIALS

The author searched PubMed for articles in the English language literature on psoriatic comorbidities from 1975 through August 2017. The search strategy initially employed the key words psoriasis AND comorbidities and psoriasis AND oral. A subsequent search was conducted with each comorbidity AND psoriasis.

RESULTS

A search on PubMed yielded almost 44,000 articles on psoriasis and nearly 1,300 with the key words psoriasis and comorbidities. Articles selected for discussion consisted mostly of recent systematic reviews and meta-analyses. Several case reports were included when there was only a limited number of psoriatic patients with a specific comorbidity. When applicable, the oral and maxillofacial relevance of psoriasis is included in Table 1. Note that references within the table are cited numerically after the discussion of each comorbidity.

DISCUSSION

Cardiovascular disease

Large-based population systematic reviews have found psoriasis associated with an increased prevalence for cardiovascular disease, independent from traditional risk factors (hypertension, diabetes, dyslipidemia). Myocardial infarction has been correlated with a relative risk (RR) of 1.3 with mild psoriasis (95% confidence interval [CI], 1.0 to 1.6) and a RR of 1.7 (95% CI, 1.3 to 2.2) with the severe form; severe psoriasis had a RR of 1.4 (95% CI, 1.1 to 1.7) for cardiovascular mortality. Psoriasis has also been linked to an increased risk for arrhythmia, which has then led to other cardiac sequelae (paroxysmal supraventricular tachycardia, heart block, sick sinus syndrome, cardiac arrest).

Other cardiac disorders that are more prevalent with psoriasis include ischemic artery disease, angina, structural heart disease, pulmonary hypertension, coronary artery calcification, arterial stiffness, and increased thickness of the intima media. Moreover, the prevalence for occlusive vascular disease may be even greater among patients who have had psoriasis for > 8 years. An increased incidence with deep vein thrombosis has also been found. Patients with psoriasis may have an increased risk for hypertension and experience greater difficulties to maintain adequate blood pressure control. In comparison to matched controls, psoriatic patients were 5.0-times more liable to take a single antihypertensive agent, 9.5-times more liable to be on two agents, 16.5-times more liable to be on three agents, and 19.0-times more likely to be on four blood pressure medications. The administration of systemic psoriatic agents has reduced the risk for cardiac events.

Neurologic disease

Severe psoriasis has been associated with an increased risk for stroke, with a RR of 1.1 (95% CI, 1.0 to 1.1) for mild psoriasis and a RR of 1.4 (95% CI, 1.1 to 1.9) for severe psoriasis. Other neurologic disorders correlative with psoriasis include dementia and mortality-related death, and Parkinson disease.
Oral diseases

Increased incidence of erythema migrans, psoriatic mucosal lesions, and periodontal disease. Careful periodontal scaling is warranted with the attending physician for severe cardiac disease (unstable angina and congestive heart failure) and whether use of a local anesthetic agent containing a vasoconstrictor or general anesthesia would be contraindicated. Clinicians should be familiar with recognizing signs of cardiac distress and be prepared to institute emergency procedures.

Neurologic disease

To reduce the risk for stroke, patients with BP > 160/100 should be referred to their attending physician for optimization. For patients taking warfarin to prevent cerebral ischemia, see Cardiovascular disease for comments on INR.

Renal disease

Inquire about degree of kidney impairment. For advanced renal disease, request available laboratory studies (glomerular filtration rate, serum creatinine, blood urea nitrogen, proteinuria, serum electrolytes). Exercise caution when prescribing medications metabolized in the kidney (ester-based topical anesthetics, nonsteroidal anti-inflammatory agents, various antibiotics). Dialysis patients should undergo dental procedures on non-dialysis days to allow for heparin manipulation. BP monitoring is advised to reduce the risk for renal damage; patients with readings > 160/100 should be referred to their attending physician for optimization. Obtain preoperative hematocrit before general anesthesia and anticipated extensive bleeding.

Liver disease

As severe liver impairment may reduce the production of coagulation factors, it is advised to perform laboratory studies (liver function tests, CBC, PT, INR) prior to moderate-severe surgical procedures. See Cardiovascular disease for INR commentary. Exercise caution when prescribing medications and using local anesthetics that are metabolized in the liver.

Other gastrointestinal diseases

Immunomodulators and glucocorticoids for inflammatory bowel disease may increase the risk for oral and oropharyngeal opportunistic infections. Chronic steroid intake may lead to adrenal atrophy and enteral steroid augmentation for anticipated stressful procedures. As a consequence of chronic steroid intake, some patients may take anti-resorptive medications (bisphosphonates, denosumab) for osteoporosis, which could predispose to osteonecrosis.

Pulmonary disease

The severity of any pulmonary disorder needs to be determined. For asthmatics, knowledge of triggers and frequency of attacks is warranted and patients should be advised to bring their inhalers. Clinicians should be prepared for a possible respiratory severe episode and take measures to maintain airway competence. If the patient has had tuberculosis, it is important to establish whether the patient has completed their medication regimen, and acetylsalicylic acid should be used with caution with concurrent ioniazid administration. Patients taking warfarin for pulmonary emboli will need a current INR. For patients taking steroids for pulmonary management, see Other gastrointestinal diseases for glucocorticoid relevance.

Diabetes mellitus

The diabetic status and most recent glycated hemoglobin need to be determined before the initiation of oral surgical and periodontal procedures. Immunomodulators and glucocorticoids may increase the risk of oral opportunistic infections. Consideration should be given for postoperative antibiotics in poorly controlled diabetics.

Neoplastic disease

Clinicians should gain knowledge of any tumor diagnosis, treatment rendered (chemotherapy, radiation), and prognosis. For current disease, a CBC may be indicated preoperatively. There is a risk of 1.5 (95% CI, 1.2 to 1.8) for the development of malignancies of the lips, oral mucosa and pharynx in psoriatic patients, underscoring the need for added vigilance when conducting an oral cancer examination.13 Rarely, benign lesions, such as Warthin tumor have occurred with psoriasis.62

Psoriatic arthritis

Rarely, PsA may affect the temporomandibular joint, often antecedent to other affected joints.14 Several PsA medications increase the risk for osteoporosis, notably glucocorticoids and cyclosporine.14 See section in Other gastrointestinal diseases for glucocorticoid relevance.

Nail psoriasis

Hand discomfort could discourage efforts to engage in regular oral hygiene measures, particularly with using dental floss. Recommend patients wear gloves to reduce dental floss injury and discomfort to the fingertips, which may result in greater oral maintenance. Use of dental flossing aids or oral irrigating devices may be a practical alternative to dental floss.

Psychologic disorders and suicidality

Psychologic illnesses are frequently managed with antidepressants, which often promote xerostomia and consequent dental caries, periodontal disease, and osteonecrosis. Patients with a history of severe alcohol intake may warrant laboratory studies (CBC, PT, INR) prior to oral surgery (see aforementioned section in Liver disease). Alcoholics should be advised to use alcohol-free mouthwashes. More frequent dental recalls and fluoride supplementation may be needed.

Infection

There are no apparent documented cases of serious infections in psoriatic patients subsequent to oral surgical procedures. Nevertheless, immunocompetence should be taken into account when rendering decisions for postoperative antibiotic coverage. Poorly controlled psoriasis may increase susceptibility to oral candidiasis and the need for antifungals.16 The SAPHO syndrome (synovitis, acne, pustulosis, hyperostosis, osteitis), linked with psoriasis vulgaris, may promote erythematous gingival pustules and osteolytic jaw lesions.62

Vitamin D deficiency

As vitamin D deficiency is associated with osteopenia and osteoporosis, patients may be at an increased risk for bone fractures, falling, periodontal disease, and osteonecrosis of the jawbone (consequent to intake of anti-resorptive agents).

Substance abuse

Clinicians should obtain a history of past and present substance abuse and avoid prescribing opioids whenever permissible. Added vigilance for oral and oropharyngeal neoplastic changes and opportunistic infections should be undertaken with histories of alcohol and tobacco abuse. As opioids and alcohol may promote xerostomia, see comments in Psychologic disorders and suicidality, as well as Liver disease for alcohol-related recommendations.

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Table 1: Psoriatic comorbidities and dental concerns

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BP, blood pressure; CBC, complete blood count; CI, confidence interval; INR, international normalized ratio; PT, prothrombin time; RR, relative risk.
Renal disease
Cohorts with psoriasis have a near-doubled risk for chronic kidney disease. Population studies also have found a two-fold increased risk of death from kidney failure with mild psoriasis and a four-fold increased fatality risk with severe psoriasis. Kidney injury has been attributed to coexistent psoriatic cardiovascular disease and potential nephrotoxic consequence of antipsoriatics.

Liver disease
The prevalence of abnormal hepatic laboratory values among patients with psoriasis has ranged from 24% to 36% in various subpopulations and mainly arises secondarily to antipsoriatic agents rather than as an inherent reflection of dermatopathology. These include acitretin, cyclosporine, or methotrexate, often in combination with hepatic comorbidities (alcohol abuse, viral hepatitis, nonalcoholic fatty liver disease). The administration of targeted immunosuppressive medications, often referred to as biologics, has been implicated in viral reactivation in 20.0% (8/40) of chronic hepatitis B carriers and emphasizes the efficacy of antiviral prophylaxis in this cohort. Ninety percent (20/22) of hospitalized patients with generalized pustular psoriasis developed neutrophilic cholangitis. Rarely, psoriatic patients may develop autoimmune hepatitis in the absence of immunosuppressive agents.

Other gastrointestinal diseases
Psoriasis has a bidirectional relationship with inflammatory bowel disease, principally involving Crohn disease and ulcerative colitis; the severity of each disorder also coincides with severity of psoriasis and PsA. Preliminary evidence has suggested an increased prevalence of coeliac disease among psoriatic patients.

Pulmonary disease
Psoriasis has been associated with chronic obstructive pulmonary disease (including asthma), pneumonia, and obstructive sleep apnea. Administration of various tumor necrosis factor antagonists may increase the risk for the reactivation of latent and primary tuberculosis infection due to medication-induced immunosuppression. Another psoriatic association is an increased risk for pulmonary embolism.

Diabetes mellitus
Pooled studies have found an odds ratio (OR) of 1.6 (95% CI, 1.4 to 1.8) for diabetes mellitus among psoriatic cohorts and a subset has been associated with metabolic syndrome (central obesity, hypertension, insulin resistance, dyslipidemia). Diabetic patients with severe psoriasis also may have poorer glycemic control and an increased reliance on oral hypoglycemics and insulin. There is tentative evidence that use of these agents or weight loss may ameliorate the severity of psoriasis.

Other endocrine diseases
There have been conflicting studies defining the relationship of psoriasis and autoimmune thyroiditis. Kiguradze et al determined an OR of 2.5 (95% CI, 1.8 to 3.5) for developing Hashimoto thyroiditis with psoriasis, whereas Vassilatou et al had not established any association. Antonelli et al demonstrated increased anti-thyroid peroxidase antibodies and ultrasonographic evidence of autoimmune hypothyroidism in cohorts with PsA. Mild serum parathyroid hormone levels, without clinical manifestations or hypercalcaemia, occasionally have been seen with psoriasis and commensurate with disease severity. There is also a higher incidence of polycystic ovary syndrome in cohorts of psoriatic patients (47% versus 11% controls) concordant with insulin resistance, hyperinsulinemia, dyslipidemia, and possibly increased complications for pregnancy.

Ocular disease
In a cohort of psoriatic patients, 58% (58/100) developed ophthalmologic complications (blepharitis, conjunctivitis, corneal disease, cataract) versus 25% (25/100) of controls, most of whom had PsA. Severe psoriasis with PsA has been associated with an increased risk for uveitis.
Neoplastic disease
The attenuated immunosurveillance, implicated with psoriasis, is also believed to be protumorigenic.54 Psoriatic patients have demonstrated increased risks for various solid and hematologic malignancies, including cancers of the respiratory tract, upper aerodigestive tract, urinary tract, liver, pancreas, Hodkgin lymphoma and non-Hodgkin lymphoma, and leukemia.54-56 Alcohol intake and cigarette smoking may act as permissive factors to increase the risk for some solid cancers among psoriatic patients.54
Psoriasis is associated with a greater risk for cutaneous squamous cell and basal cell carcinoma, particularly with psoralen ultraviolet A (PUVA) treatments, cyclosporine, or methotrexate.54,57 The risk for melanoma with PUVA therapy and psoriasis has been contradictory, with increased58 or decreased54,59 frequencies ascertained. Administration of biologics for management of psoriasis has been implicated in the promotion of melanoma, seen with a RR of 1.8 (95% CI, 1.2 to 3.0) with adalimumab and a RR of 2.4 (95% CI, 1.5 to 3.8) with etanercept.60

Psoriatic arthritis
PsA occurs in 30% of cohorts with psoriasis and is manifested by inflammation, deformation, and possibly bone resorption in the peripheral and axial joints; enthesitis (inflammation of tendons, ligaments); and dactylitis (“sausage” digits).63 The preponderance of cases begins 10 years after the onset of psoriasis.63 Preliminary evidence has determined an increased association of PsA and renal impairment, as demonstrated by reductions in glomerular filtration rate and elevations of creatinine, urea, and proteinuria.64

Nail psoriasis
The prevalence of nail disease with psoriasis has ranged from 10% to 78%, with greater affinity for fingernails.66 Psoriatic nail malformation includes pitting, onycholysis, discoloration, subungual hyperkeratosis, and splinter hemorrhage.67 Nail psoriasis tends to occur with PsA or scalp psoriasis.68 More than half of affected patients complain of reduced qualities of life due to the nail appearance or nail pain, which often restricts daily activities (housekeeping, occupational).66 Non-dermatophytic fungal nail infection has been reported in 48% of individuals with psoriatic nails.69

Other cutaneous diseases
Isolated case reports have documented the concurrence of psoriasis with systemic lupus erythematosus,70 pemphigus vulgaris,71 lichen planus,72 and primary cutaneous amyloidosis.73

Psychologic disorders and suicidality
The magnitude of the physical (pain, pruritus, fatigue) and emotional (stigmatization, social isolation) parameters of chronic psoriasis may have a significant negative impact on qualities of life and result in clinical depression, anxiety, and psychosis.74 Psoriatic patients have increased rates of suicidal ideation and attempts, and fatal outcomes, occurring more frequently in younger individuals.75 Alcohol may further worsen psoriatic-based depression.76 Use of various biologics for cutaneous disease has mitigated depressive rating scores.77

Infection
The intrinsic diminution in the immune system of psoriatic patients may potentiate various opportunistic infections, chiefly with methicillin-resistant Staphylococcus aureus, and to a lesser extent with cellulitis, herpes simplex virus infection, fungal infection, infectious arthritis, osteomyelitis, meningitis, encephalitis, human immunodeficiency virus, and mycobacteria.78,79 Use of targeted biologic therapy for psoriasis may further increase the risk for both serious infections (pulmonary, abdomen, skin) and the number of days of hospital admission.78,80 In addition, use of these systemic agents has been associated with increasing the risk of cutaneous and genitourinary candidiasis.81

Dyslipidemia
Reviews of psoriasis and dyslipidemia noted 80% (20/25) of investigations established a positive correlation.82 Affected patients may present with greater
atherogenic occlusive risks (elevated total cholesterol and low density lipoproteins, reduced high density lipoproteins). Vitamin D deficiency
A study of 145 patients with chronic plaque psoriasis established statistically lower normal vitamin D levels (20.7 ng/mL versus 37.1 ng/mL in healthy controls, normal > 20 ng/mL), yet actual deficiencies tended to occur in spring (19.1 ng/mL) and winter (16 ng/mL). Oral and topical vitamin D have been efficacious for psoriasis and PsA.

Substance abuse
Various subpopulations have established a reciprocal relationship of alcohol consumption and psoriasis, increasing rates of depression, anxiety, psychosis, and mortality. Psoriasis is also associated with an increased prevalence of current and previous smoking.

Mortality rate
Although the overall consequence of having mild psoriasis does not seem to alter one’s lifespan, cohorts with severe psoriasis may be faced with a 1.5-fold increased mortality risk from all age brackets, with more than a two-fold increased risk between the ages of 35 and 45 years. The most frequent cause of death from severe psoriasis is attributed to cardiovascular disease. With the exclusion of major comorbidities (tobacco; elevated body mass index; cardiovascular, respiratory, liver, renal disease; dementia; malignancies; diabetes; paraplegia and hemiplegia), males with severe psoriasis may die 3.5 years younger, whereas similarly affected females may die 4.4 years younger than unaffected individuals.

Oral diseases
Oral psoriatic involvement, occasionally referred to as psoriasiform mucositis, may be a reflection of the underlying inflammatory cutaneous disease. The most common psoriatic lesion, erythema migrans, principally occurs on the tongue dorsum and less often on the labial and buccal mucosa, ventral tongue, floor of mouth, soft palate, lip, and uvula. These lesions appear as multiple, circular red macules with slightly raised yellowish-white borders; most are incidental findings and pain is infrequent. When non-glossal lesions are found, almost all coexist with tongue lesions. The incidence of erythema migrans is 1.0% to 3.0% in the general population; however, in cohorts with cutaneous psoriasis, the incidence has ranged from 3.8% to 9.1%. Psoriatic patients also maintain a greater risk for periodontal disease. Nakib et al found a RR of 1.4 (95% CI, 1.0 to 1.8) for mild periodontitis and

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a RR of 1.5 (95% CI, 1.1 to 2.1) for severe alveolar bone loss. Antal et al found an OR of 4.4 (95% CI) for severe periodontitis with psoriasis; more importantly, psoriatic patients who smoked had a dramatic OR of 24.3 (95% CI) for bone loss.

A rare manifestation of oral psoriasis is the presence of moderately red macules of the gingiva (Fig 1a), hard palate (Fig 1b), and buccal mucosa, some of which are painful; the gingival erythema may appear disproportionate to the extent of inflammation induced by bacterial-based periodontal disease. Affected gingiva may be friable and display white scaly streaks. The index for suspicion is raised when oral lesions are accompanied with cutaneous psoriasis. Recently, it has been shown that management of cutaneous psoriasis with adalimumab simultaneously resolved oral psoriatic lesions.

CONCLUSION

The effects of psoriasis often extend into a vast array of organ systems, potentially resulting in comorbidities that promote pathophysiologic liabilities. The medical history process of psoriatic patients should include ascertainment of systemic involvement for establishing any potential impact on dental management. Conduction of the patient interview is an evolving skill honed with inquisitive measures to solicit relevant medical information, such as the open-ended question format, allowing the patient to offer specifics about which the clinician had not inquired. Consultation with the patient’s attending physician may clarify salient features of medical burdens that might prompt modifications in dental management. Knowledge of the constellation of psoriatic comorbidities coupled with early recognition of their signs and symptoms may improve clinical outcomes.

REFERENCES


SUPPLEMENTAL READING