Cureus
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Open Access Case Report

Lupus Overlap Syndrome: A Case Report

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Review began 05/06/2023
Review ended 05/23/2023
Published 11/25/2026

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DOI: 10.7759/cureus.120215

Abstract

Lupus overlap syndrome (OS) (also called mixed connective tissue disease (MCTD)) is a condition that shares symptoms with several autoimmune diseases, including systemic lupus erythematosus (SLE), systemic sclerosis (SSc), and polymyositis (PM). Overlap syndrome includes those affected by systemic lupus erythematosus with other features of autoimmune conditions such as rheumatoid arthritis (RA), vasculitis, myositis, and Sjögren's syndrome (SS); it is characterized by the presence of autoantibodies (antibodies produced by the immune system that attack the body's own tissues) that are commonly found in patients with lupus, as well as features of other autoimmune diseases such as Raynaud's phenomenon, arthritis, muscle weakness, and scleroderma-like skin changes. Although MCTD shares some clinical features with other autoimmune diseases, it is considered a distinct condition because it has a unique antibody profile and a more benign clinical course than SLE or other connective tissue diseases (CTDs). Treatment typically involves managing symptoms with medications such as nonsteroidal anti-inflammatory drugs (NSAIDs), corticosteroids, and immunosuppressive drugs. It is important to note that MCTD can be difficult to diagnose and can mimic other conditions of connective tissue disorders, such as progressive systemic sclerosis. A rare case of autoimmune sialadenitis of the parotid gland in a patient with underlying autoimmune disorders such as systemic lupus erythematosus and rheumatoid arthritis is discussed.

Categories: Oral Medicine, Dentistry
Keywords: anti-smith antibody, color doppler ultrasonography, overlap syndrome, rheumatoid arthritis, systemic lupus erythematosus

Introduction

Overlap syndrome (OS) is a medical entity characterized by two or more clinical features of autoimmune disorders such as rheumatoid arthritis, vasculitis, myositis, systemic lupus erythematosus (SLE), and Sjögren's syndrome. Overlap syndromes (OSs) satisfy classification criteria of at least two connective tissue diseases (CTDs) occurring at the same or different times in the same patient. CTDs include systemic lupus erythematosus (SLE), rheumatoid arthritis (RA), systemic sclerosis (SSc), polymyositis (PM), dermatomyositis (PDM), and Sjögren's syndrome (SS) [1]. Mixed connective tissue disease (MCTD) is a rare systemic autoimmune disease with an overlapping feature of at least two connective tissue diseases (CTDs), including systemic lupus erythematosus (SLE), systemic sclerosis (SSc), polymyositis (PM), dermatomyositis (DM), and rheumatoid arthritis (RA) along with the presence of a specific antibody, anti-U1-ribonucleoprotein (RNP), previously known as an antibody to extractable nuclear antigen (ENA) [2]. The anti-U1-RNP antibody is the hallmark of mixed connective tissue disease, and its antigen plays an essential role in the pathogenesis of MCTD [2]. U1-RNP complex is an intranuclear protein that converts pre-mRNA to mature RNA and has three specific proteins, A, C, and 70kDa, the principal target antigen in which anti-RNP antibody binds, resulting in mixed connective tissue disease (MCTD) [2]. The modification of the U1 70kDa antigen by apoptosis is believed to be characteristic of mixed connective tissue disease [2]. Antigens are presented by antigen-presenting cells to T cells that release inflammatory chemical mediators called cytokines, which stimulate B cells to produce antibodies [2]. Anti-U1-RNP antibodies, anti-U1 70kDa antibodies, and anti-U1 70kDa reactive T lymphocytes circulating in peripheral blood are the hallmark of MCTD [2]. A rare overlap syndrome, in which bilateral chronic parotitis occurred with systemic lupus erythematosus, an underlying autoimmune disorder, was discussed here.

Case Presentation

A 30-year-old female reported to our dental outpatient department with a chief complaint of pain and swelling on the right side of her face for the past three days. History reveals that it had been swelling for the past year, subsiding independently with fluid discharge intraorally. Presently, the swelling occurs first and is then gradually accompanied by pain. Swelling occurred smaller in size, and it gradually increased and attained the present size. Pain is sudden in onset, continuous, pricking in character, and mild in intensity. The pain gets aggravated during eating and sleeping and gets relieved by medication. Her past medical history was noncontributory. The patient had no history of diabetes or jaundice. There was no past surgical history under general anesthesia intubation and no other similar swellings on the different parts of her body. There was also no significant history among her family members. On inspection, a diffuse swelling is present on the right side of the face. It measures about 4 × 7 cm approximately, and it extends anteriorly 4

cm in front of the ear lobe, posteriorly 2 cm behind the ear's pinna, and superiorly to the line corresponding to the outer canthus of the eye to the upper helix of the ear, inferiorly to the inferior border of the mandible. The skin over the swelling appears stretched and the same as the adjacent structure; no sinus, bleeding, or pus discharge is present (Figure *1*).



FIGURE 1: Extraoral examination revealed swelling in the right parotid gland region with elevation of the ear lobe (arrow)

On palpation, all the inspection findings are confirmed regarding size, shape extent, firmness in consistency, and tenderness, and the skin over the swelling is pinchable and compressible. There was non-fluctuant evidence of secondary changes. The elevation of the ear lobe was bilaterally present. A diffuse swelling is also seen on the face's left side, which measures approximately 1.5 × 2 cm and extends 1 cm in front of the ear lobe, posteriorly 1 cm away from the ear lobe, superiorly to the line corresponding to the ala tragal plane, and inferiorly to the inferior border of the mandible (Figure *2*).



FIGURE 2: Left lateral profile view revealed an extraoral swelling in the left parotid gland region with elevation of the left ear lobe (arrow)

A single palpable right submandibular lymph node is approximately 1 cm long, firm in consistency, tender, and mobile. Intraoral examination revealed dental caries in 15 and 26, pit and fissure caries in 47 and 48, and discrete greyish pigmentation of buccal mucosa and gingiva (Figure *3A*-*3D*).

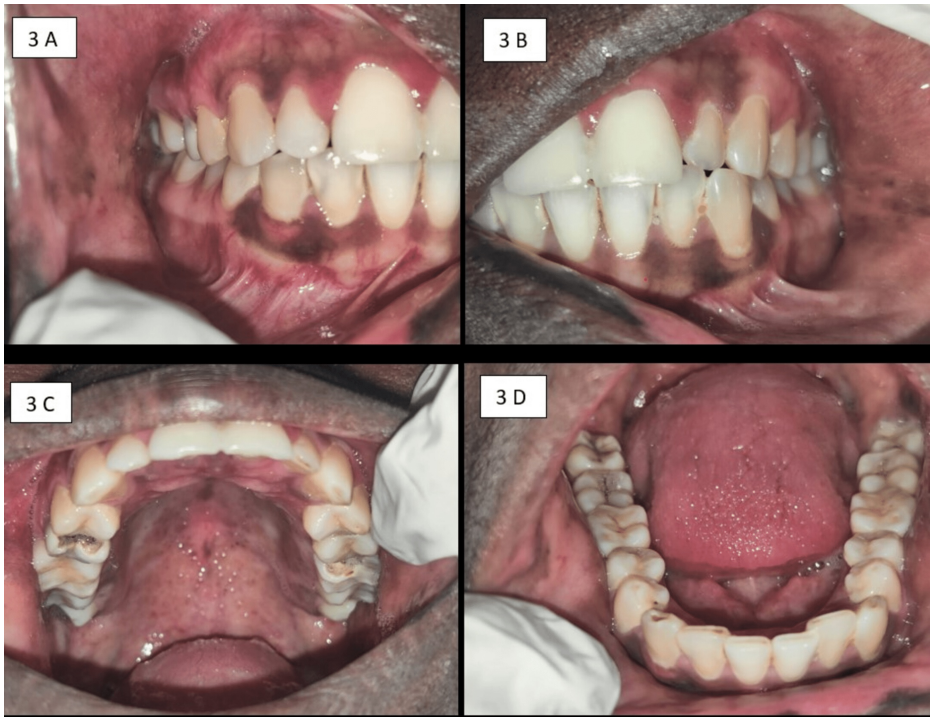


FIGURE 3: Intraoral examination revealed dental caries in 15, 26, 47, and 48 and discrete greyish pigmentation of the buccal mucosa and gingiva

The pulp vitality test was performed using an electric pulp tester, which revealed no response of value 6.1 mA in carious tooth 26. A radiovisiography taken with a Carestream CMOS sensor (Atlanta, GA, USA) in relation to 26 revealed radiolucency in the crown portion of 26 with pulp involvement. However, the lamina dura was intact. No other periradicular changes were evident in the intraoral periapical radiograph (Figure *4*).

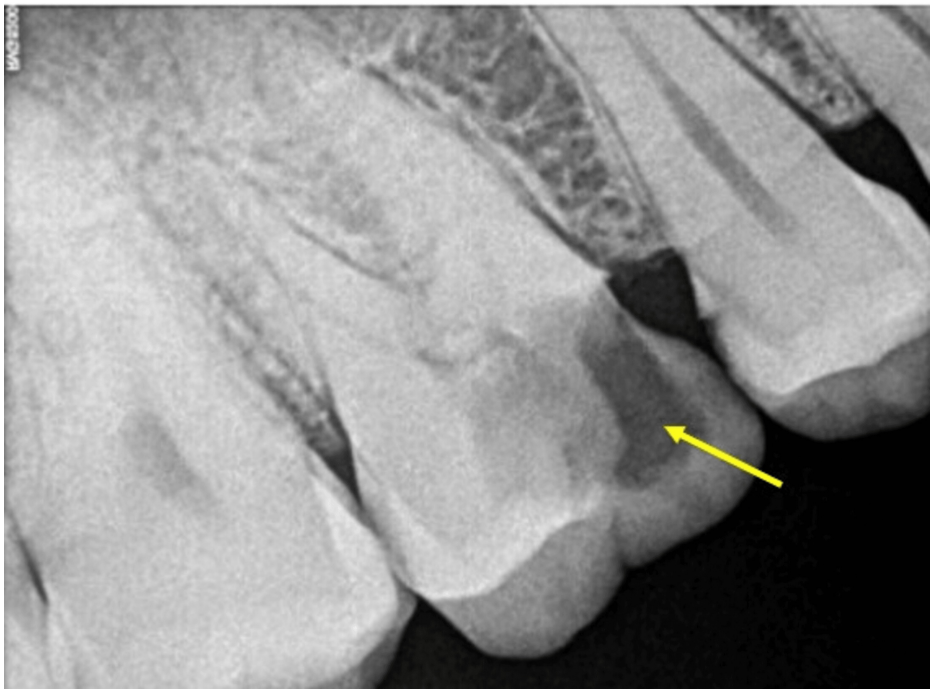


FIGURE 4: RVG in relation to 26 with CMOS sensor revealed dental caries with pulp involvement in 26, intact lamina dura, and no other periradicular changes (arrow)

RVG: radiovisiography

Based on the clinical findings, a provisional diagnosis of bilateral chronic parotitis was made. Color Doppler ultrasound revealed increased signal flow due to increased vascularity and multiple tiny hypoechoic nodules within the salivary gland parenchyma (Figure *5A*, *5B*).

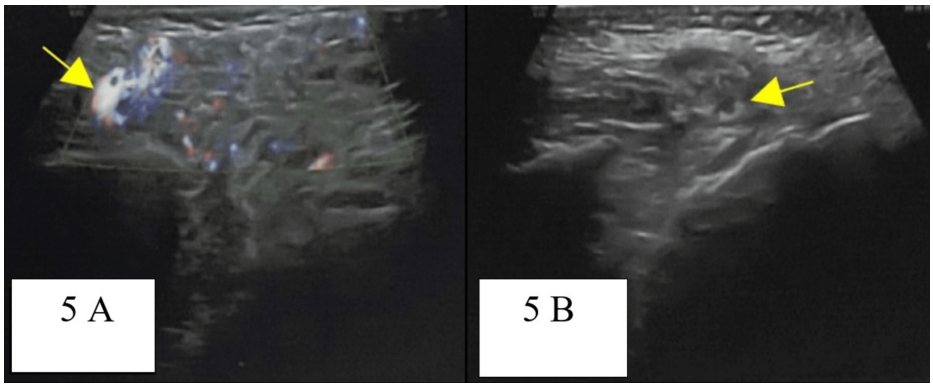


FIGURE 5: Color Doppler ultrasound revealed increased signal flow due to increased vascularity (A) and multiple tiny hypoechoic nodules within the salivary gland parenchyma (B) (arrows)

Conventional extraoral radiograph anteroposterior skull view revealed multiple specks of calcification distributed uniformly within the right and left parotid glands (Figure *6*).



FIGURE 6: Extraoral radiograph anteroposterior skull view revealed multiple tiny specks of calcification uniformly distributed within the right and left parotid gland (arrows)

Computed tomography revealed discrete specks of calcification in both right and left parotid glands (Figure *7A*, *7B*).

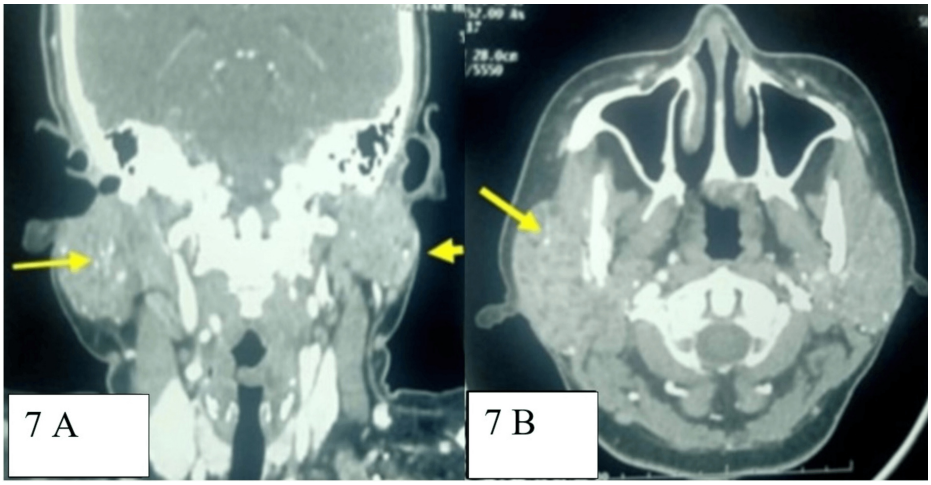


FIGURE 7: CT coronal section revealed discrete specks of calcification within the right and left parotid glands (A), and CT axial section revealed multiple flecks of calcifications within the right and left parotid glands (B) (arrows)

CT: computed tomography

Indirect immunofluorescence of the patient's serum revealed a coarse speckled nuclear pattern of immunofluorescence with 3+ (+++) intensity using 1:80 dilution of Hep2 cells and antigenic positivity for U1 RNP and anti-Smith antigens (Sm antigens). The differential diagnosis for bilateral parotid gland swelling includes parotid sialadenosis due to diabetes mellitus or chronic consumption of alcohol, viral parotitis caused by mumps, and pneumoparotid. The differential diagnosis of bilateral parotid gland swelling and clinical similarities and differences are described in Table *1*.

Differential diagnosis for bilateral parotid gland swelling	Clinical similarities	Clinical differences
Bilateral painless parotid gland enlargement		
Bilateral parotid sialadenosis (chronic alcoholism)	Bilateral parotid gland enlargement resulting in facial asymmetry	Absence of consumption of any forms of alcohol in our case
Bilateral parotid sialadenosis (diabetes mellitus)	Bilateral parotid gland enlargement resulting in facial asymmetry; the patient may have episodes of pain when infection of the parotid gland occurs in uncontrolled diabetes	No medical history of diabetes mellitus in our case
Pneumoparotid	Bilateral parotid gland swelling resulting in facial asymmetry	No history of using percussion instruments such as trumpet and flute in our case
Autoimmune parotitis	Bilateral parotid gland enlargement resulting in facial asymmetry; no odontogenic origin, such as spread of infection from a carious tooth; positive for immunofluorescence from the patient's serum revealed coarse speckled nuclear pattern (+++)	Our case matched with the clinical features of underlying lupus erythematosus, confirmed by positive Smith (Sm) antigens; autoimmune parotitis usually painless; painful parotid gland swelling seen in our case due to underlying infection of the parotid glands
Anesthesia mumps	Bilateral parotid gland swelling resulting in facial asymmetry	No surgical history under general anesthesia such as general anesthesia intubation
Bilateral painful parotid gland enlargement		
Acute bilateral parotitis	Viral infection from mumps resulting in painful bilateral enlargement of the parotid gland	No history of fever in our case; absence of Koplik spots on the buccal mucosa

TABLE 1: Differential diagnosis for bilateral parotid gland swelling

Our patient showed glycated hemoglobin (HbA1C) of 5.4, suggesting non-diabetes. Our patient also did not have a habit of alcohol consumption. Episodes of fever usually accompany bilateral parotitis caused by mumps. No outbreaks of fever were present in our patient. Bilateral parotid gland swellings in chronic percussion instrument players such as the trumpet characterize pneumoparotid. Our patient does not use any percussion instruments. The incisional biopsy was performed on the mandibular labial mucosa. The soft tissue specimen sent for histopathological examination revealed numerous mucous acini and salivary ducts infiltrated by inflammatory cells, chiefly lymphocytes not more than five cells per 4 mm^2 of salivary gland tissue, suggestive of the absence of focus score (dense foci of inflammatory cells (lymphocytes) more than 50 cells per 4 mm^2 of salivary gland tissue), characteristic in Sjögren's syndrome. Hence, Sjögren's syndrome was ruled out. A final diagnosis of lupus overlap syndrome was made. The patient was prescribed the following medications: tablet Augmentin (amoxicillin 500 mg + potassium clavulanate 125 mg) and tablet Flagyl (metronidazole 400 mg) twice daily for five days and tablet ketorolac tromethamine 10 mg twice daily for three days for pain relief. The patient was followed up after five days, which revealed complete resolution of her swelling on the right and left side of her face and ease from pain (Figure *8A*-*8C*).



FIGURE 8: Follow-up extraoral clinical photographs after one week

Discussion

"Overlap syndrome" refers to a diverse group of conditions with clinical features of, and meets the classification criteria for, more than one well-characterized autoimmune disorder [3]. It usually presents subacutely with clinical manifestations, including different organ systems [3]. Overlap syndrome is a medical condition characterized by clinical signs and symptoms that overlap with each other in various autoimmune disorders, such as systemic lupus erythematosus, progressive systemic sclerosis, vasculitis, myositis, and Sjögren's syndrome [4]. The anti-Sm and anti-RNP bind on the surface of human monocytes and synergistically enhance the production and expression of interleukin-6 (IL-6) [4]. Ramya et al. (2022) [5] reported a case of chronic parotid sialadenitis in a 69-year-old female with complaints on the left side of the face for the past month. The patient was diagnosed with systemic lupus erythematosus [5]. Patients with overlap syndrome present to the outpatient department with acute clinical manifestations, which can affect different organ systems [5]. Autoimmune sialadenitis usually occurs as painless bilateral swellings but becomes painful when infected [6]. Autoimmune sialadenitis can also occur secondary to an autoimmune disorder such as systemic lupus erythematosus, Sjögren's syndrome, or progressive systemic sclerosis [5]. Inflammatory sialadenitis occurs as a result of salivary stasis due to obstruction by salivary calculi and alteration of the electrolyte composition of saliva [5]. The pathogenesis of sialadenitis is controversial, although the interplay of other factors, such as reduced salivary flow in acinar tissue, favors retrograde ascending infection [5]. The two theories favoring retrograde infection as a chief cause of sialadenitis include opportunistic oral pathogens that can cause retrograde infection, a more likely reason for chronic recurrent sialadenitis [5].

Episodes of repeated infection can lead to metaplasia of ductal epithelium resulting in increased mucus and salivary stasis due to the sticky mucinous nature of mixed saliva [5]. Recently, biologically targeted drug therapies, which include anti-CD20 monoclonal antibodies or antitumor necrosis factor, are indicated as interventions for refractory cases of overlap syndrome. Still, they have more adverse effects of exacerbating the disease [5]. Activated phosphoinositide 3-kinase-δ syndrome 1 is characterized by chronic herpes viremia (herpes virus and Epstein-Barr virus), recurrent sinopulmonary infections mimicking systemic lupus erythematosus, and Sjögren's syndrome [6]. Acute bilateral parotid swelling occurs in anesthesia mumps as a consequence of postsurgical treatment procedures and resolves spontaneously by itself within a few days or hours [7]. Pneumoparotid is a sporadic condition of the parotid gland that occurs due to no physiological stagnation of air in the parotid parenchyma and is associated with a retrograde insufflation of air and saliva via Stensen's duct into the secondary ducts and glandular acini [8]. Table *2* presents a summary of literature reviews on other overlap syndromes.

Author	Year	Other overlap syndromes
Uddin et al. [9]	2023	Polymyositis and systemic sclerosis overlap syndrome
Yacoub et al. [10]	2023	Overlap syndrome of primary biliary cholangitis and primary sclerosing cholangitis
Lin et al. [11]	2022	Overlap syndrome: systemic lupus erythematosus and anti-OJ antibody-positive polymyositis
Muralidharan et al. [12]	2022	Hutchinson-Gilford syndrome (progeria) with mandibuloacral dysplasia and acrogeroid features: overlap of premature aging syndromes
Zhao et al. [13]	2022	MELAS and PEO
Zeeck et al. [14]	2022	VEXAS syndrome caused by a mutation in the UBA1 gene, which encodes for the E-1 enzyme, which in turn is responsible for the ubiquitination of inflammatory proteins; clinical symptoms often overlap of hematologic, dermatologic, and rheumatologic syndromes
Patnaik et al. [15]	2020	Myelodysplastic syndrome/myeloproliferative neoplasm overlap syndromes
Slade et al. [16]	2020	Overlap of five chronic pain conditions: headache, back pain, irritable bowel syndrome, TMD, and fibromyalgia
Ali et al. [17]	2019	A dermatomyositis/lichen planus overlap syndrome presenting with erythroderma
Budsamongkol et al. [18]	2019	Osteogenesis imperfecta/Ehlers-Danlos overlap syndrome with brachydactyly
Morgan et al. [19]	2019	OFCD syndrome with infantile hemangiomas: phenotypic overlap with PHACE syndrome
Schmitz et al. [20]	2018	Lichen planus with lupus erythematosus overlap syndrome

TABLE 2: Literature reviews on other overlap syndromes

MELAS: mitochondrial encephalopathy, lactic acidosis, and stroke-like episodes, PEO: progressive external ophthalmoplegia, VEXAS: vacuoles, E1 enzyme, X-linked, autoinflammatory, somatic, TMD: temporomandibular disorder, OFCD: oculofaciocardiodental, PHACE: posterior fossa anomalies, hemangioma, arterial anomalies, cardiac defects, eye anomalies

Conclusions

Patients clinically presenting with parotid swelling must not be superficially overlooked by the clinician. Patients with parotid swelling must be evaluated for other autoimmune conditions such as systemic lupus erythematosus, Sjögren's syndrome, progressive systemic sclerosis, vasculitis, myositis, or other connective tissue disorders. A thorough history and clinical examination are essential to prevent complications later. A multidisciplinary approach between dentists, ear-nose-throat physicians, and physiotherapists is vital to overcome such lupus overlap syndrome, with mixed clinical signs and systems with multi-organ involvement. Overlap syndrome is challenging to diagnose, and early diagnosis and treatment help prevent morbidity and improve one's quality of life.

Additional Information

Disclosures

Human subjects: Informed consent for treatment and open access publication was obtained or waived by all participants in this study. **Conflicts of interest:** In compliance with the ICMJE uniform disclosure form, all authors declare the following: **Payment/services info:** All authors have declared that no financial support was received from any organization for the submitted work. **Financial relationships:** All authors have declared that they have no financial relationships at present or within the previous three years with any organizations that might have an interest in the submitted work. **Other relationships:** All authors have declared that there are no other relationships or activities that could appear to have influenced the submitted work.

Acknowledgements

The authors would like to thank Deepaa Micro Lab, Salem, Tamil Nadu, Vinayaka Mission's Kirupananda

Variyar Medical College and Hospitals, and Faculties from the Department of Oral Surgery, Vinayaka Mission's Sankarachariyar Dental College, Vinayaka Mission's Research Foundation (Deemed to be University), Salem, Tamil Nadu, India.

References

1. BMJ Best Practices: Overlap syndromes . (2023). Accessed: May 5, 2023: https://bestpractice.bmj.com/topics/en-gb/1018.
2. Sapkota B, Al Khalili Y: Mixed connective tissue disease . StatPearls Publishing, Treasure Island, FL; 2022.
3. ScienceDirect: Overlap syndrome . (2023). Accessed: May 5, 2023: https://www.sciencedirect.com/topics/immunology-and-microbiology/overlap-syndrome.
4. Paradowska-Gorycka A: U1-RNP and TLR receptors in the pathogenesis of mixed connective tissue diseasePart I. The U1-RNP complex and its biological significance in the pathogenesis of mixed connective tissue disease. Reumatologia. 2015, 53:94-100. 10.5114/reum.2015.51509
5. Ramya R, Swarnalakshmi R, Preethi A, Pradeep R: A case of progressive systemic sclerosis/lupus overlap syndrome: presenting with parotid swelling. J Oral Maxillofac Pathol. 2021, 25:372. 10.4103/0973-029X.325259
6. Yin J, Ma J, Xia J, Cao Y, Li C: Activated PI3Kδ syndrome 1 mimicking systemic lupus erythematosus and secondary Sjögren's syndrome-like phenotype without recurrent infections: a case report. Front Pediatr. 2022, 10:1077324. 10.3389/fped.2022.1077324
7. Chidipothu K Jr, Verma NC, Madavi S, Jadhav JA: Acute bilateral swelling of the parotid gland after general anesthesia in lateral decubitus position. Cureus. 2022, 14:e29154. 10.7759/cureus.29154
8. Gazia F, Freni F, Galletti C, et al.: Pneumoparotid and pneumoparotitis: a literary review . Int J Environ Res Public Health. 2020, 17:10.3390/ijerph17113936
9. Uddin MK, Vempati R, Bhavanam S, et al.: A rare case of polymyositis and systemic sclerosis overlap syndrome: diagnosis and treatment. Cureus. 2023, 15:e36434. 10.7759/cureus.36434
10. Yacoub H, Ben Azouz S, Hassine H, et al.: Overlap syndrome of primary biliary cholangitis and primary sclerosing cholangitis: two case reports. J Med Case Rep. 2023, 17:169. 10.1186/s13256-023-03908-y
11. Lin KH, Kao JK: Overlap syndrome in a 12-year-old girl with systemic lupus erythematosus and anti-oj antibody-positive polymyositis: a case report. Pediatr Rheumatol Online J. 2022, 20:92. 10.1186/s12969-022-00753-z
12. Muralidharan S, Nair SP, Hariharan SV: Hutchinson-Gilford syndrome (progeria) with heterozygous mutation in the LMNA Gene-ENST00000368300.9 presenting with mandibuloacral dysplasia and acrogeroid features-overlap of premature aging syndromes. Indian Dermatol Online J. 2022, 13:640-2. 10.4103/idoj.idoj_635_21
13. Zhao QY, Zhang WZ, Zhu XL, et al.: Case report: a double pathogenic mutation in a patient with late-onset MELAS/PEO overlap syndrome. Front Neurol. 2022, 13:927823. 10.3389/fneur.2022.927823
14. Zeeck M, Kötter I, Krusche M: [VEXAS syndrome]. Z Rheumatol. 2022, 81:782-6. 10.1007/s00393-022-01169-6
15. Patnaik MM, Lasho T: Myelodysplastic syndrome/myeloproliferative neoplasm overlap syndromes: a focused review. Hematology Am Soc Hematol Educ Program. 2020, 2020:460-4. 10.1182/hematology.2020000163
16. Slade GD, Greenspan JD, Fillingim RB, Maixner W, Sharma S, Ohrbach R: Overlap of five chronic pain conditions: temporomandibular disorders, headache, back pain, irritable bowel syndrome, and fibromyalgia. J Oral Facial Pain Headache. 2020, 34:s15-28. 10.11607/ofph.2581
17. Ali AA, Basharat P, Lovegrove F: A dermatomyositis/lichen planus overlap syndrome presenting with erythroderma: a case report. SAGE Open Med Case Rep. 2019, 7:2050313X19845174. 10.1177/2050313X19845174
18. Budsamongkol T, Intarak N, Theerapanon T, Yodsanga S, Porntaveetus T, Shotelersuk V: A novel mutation in COL1A2 leads to osteogenesis imperfecta/Ehlers-Danlos overlap syndrome with brachydactyly. Genes Dis. 2019, 6:138-46. 10.1016/j.gendis.2019.03.001
19. Morgan TM, Colazo JM, Duncan L, Hamid R, Joos KM: Two cases of oculofaciocardiodental (OFCD) syndrome due to X-linked BCOR mutations presenting with infantile hemangiomas: phenotypic overlap with PHACE syndrome. Case Rep Genet. 2019, 2019:9382640. 10.1155/2019/9382640
20. Schmitz S, Vatanchi M, Alapati U: Seven-year itch: a perplexing case of lichen planus-lupus erythematosus overlap syndrome. Dermatol Online J. 2018, 24:13030/qt40g268t4.