rheumatoid arthritis. Revista Colombiana de Reumatología. 2019;26:105–10, http://dx.doi.org/10.1016/j.rcreue.2019.03.003.
11. Merino-Soto C, Calderón-De la Cruz GA. Validez de estudios peruanos sobre estrés y burnout. Rev Perú Med Exp Salud Publica. 2018;35:353–4, http://dx.doi.org/10.17843/rpmesp.2018.352.3521.
12. Boateng GO, Neilands TB, Frongillo EA, Melgar-Quiñonez HR, Young SL. Best practices for developing and validating scales for health, social, and behavioral research: a primer. Front Public Health. 2018;6:149, http://dx.doi.org/10.3389/fpubh.2018.00149.

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Kabuki syndrome with Sjögren Syndrome: First case reported☆

Síndrome de Kabuki con síndrome de Sjögren: primer caso descrito

Dear Editor,

Kabuki syndrome (KS) is a genetic syndrome characterised by typical facial features (palpebral fissures with inverted lower eyelids, arched eyebrows, depressed nasal tip), musculoskeletal abnormalities (brachydactyly, clinodactyly of the fifth digits and spine abnormalities), abnormal epidermal ridges, short stature, and intellectual deficit[1].

Although the association between KS and autoimmune disease is well documented, probably due to mutations in the dysregulation of lymphocyte differentiation[2,3], this is the first reported case of association with primary juvenile Sjögren's syndrome (jSS).

We present the case of a 9-year-old Caucasian girl diagnosed with KS (15654C>G mutation in exon 48 of gene KMT2B) and father with systemic lupus erythematosus (SLE).

Her symptoms started with xerophthalmia (red eye, stinging sensation and ocular lacrimation) associated with xerostomia (drinking more than 3 l of water per day, including night waking) and occasional mouth ulcers. She reported intermittent polyarthralgia, without oedema or stiffness. No history of parotitis or Raynaud's phenomenon.

On examination, she presented dysmorphic features typical of KS, joint hypermobility without arthritis, cutaneous xerosis, cracked tongue and impalpable salivary glands.

Laboratory tests reported normal haemogram, elevated amylase, ANA 1/1000 with speckled pattern, positive anti-SSa, normal complement and mild hypergammaglobulinaemia. Inflammatory markers, urinary sediment and the remaining immunological study were normal. Salivary gland ultrasound (SGUS) showed normal dimensions, heterogeneous parenchyma, and hypoechoic areas, compatible with jSS. Biopsy of the minor salivary glands was normal.

She was observed by the ophthalmology department who confirmed keratoconjunctivitis sicca, with positive Schirmer test and Ocular Staining Score $\geq$5.

Due to transient liver function elevation, she underwent a liver autoimmunity panel, which was negative. The elevated liver function in this syndrome could be due to autoimmune hepatitis or primary biliary cirrhosis, and was therefore excluded.

She started treatment with general measures for xerostomia and oral hygiene, ocular lubrication, and skin hydration. During follow-up she developed mild photosensitive malar erythema. Due to the risk of overlap with SLE and mild systemic manifestations (arthralgias and hypergammaglobulinaemia), treatment was started with hydroxychloroquine 4 mg/kg/day.

We now know that SS is an autoimmune disease characterised by T-lymphocyte infiltration at the level of the exocrine glands. This infiltration leads to destruction of the exocrine glands and the onset of symptoms related to dryness of the infiltrated mucous membranes. Up to one third of patients may present with more active and severe extraglandular manifestations that affect long-term prognosis[2–4].

In children SS is rarely primary, as in our case, and therefore close monitoring is essential in this type of patient due to the risk of overlap with another connective tissue disease[5].

There are currently no diagnostic criteria for SS in the paediatric age group; adult criteria depend too much on evidence of glandular dysfunction, which takes time to develop and is less evident during childhood. Biopsy at this age has a low sensitivity due to the small size of the glands, diagnostic difficulty and being able to biopsy an area that is normal[5]. Nevertheless, our patient meets the 2016 ACR/EULAR criteria[6].

There are international groups that are working on diagnostic criteria for SS adapted to the paediatric age group. Since we know that recurrent mumps is the most typical form of presentation in this age group, including this entity in these criteria seems to increase diagnostic sensitivity for jSS. It is possible that the combination of salivary gland inflammation (clinical or subclinical parotitis, SGUS or histopathology changes) and positive autoantibody may be sufficient to diagnose SS in a child.

If there are suggestive symptoms, patients with KS should always be thoroughly assessed for autoimmune disorders. This is the first case described in the literature of both syndromes.

References

1. Niikawa N, Kuroki Y, Kajii T, Matsuura N, Ishikiriyama S, Tonoki H, et al. Kabuki make-up (Niikawa-Kuroki) syndrome: a study of 62 patients. Am J Med Genet. 1988;31:562–9.
2. Stagi S, Gulino AV, Lapi E, Rigante A. Epigenetic control of the immune system: a lesson from Kabuki syndrome. Immunol Res. 2016;64:345–59.
3. Hoffman JD, Ciprero KL, Sullivan KE, Kaplan PB, McDonald-McGinn DM, Zackai EH, et al. Immune abnormalities are a frequent manifestation of Kabuki syndrome. Am J Med Genet A. 2005;135:278–81.
4. Arsov T, Sestan M, Cekada N, Frkovic M, Andrews D, He Y, et al. Systemic lupus erythematosus: a new autoimmune disorder in Kabuki syndrome. Eur J Med Genet. 2019;62:103538.
5. Gómez P, Rojas JP. Síndrome de Sjögren en pediatría: diagnóstico y manejo. Rev Colomb de Reumatol. 2012;19:245–50.
6. Shiboski CH, Shiboski SC, Seror R, Criswell LA, Labetoulle M, Lietman T, et al. 2016 American College of Rheumatology/European League Against Rheumatism Clas-

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sification Criteria for Primary Sjögren's Syndrome: a consensus and data-driven methodology involving three international patient cohorts. Arthritis Rheumatol. 2017;69:35–45.

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Differences and Determinants of Physician's and Patient's Perception in Global Assessment of Rheumatoid Arthritis☆

Diferencias y determinantes de la percepción del médico y el paciente en la evaluación global de la artritis reumatoide

Dear Editor:

Patient's Global Assessment of Disease Activity (PtGA) and Physician's Global Assessment of Disease Activity (PhGA) are assessed as part of disease activity in Rheumatoid Arthritis (RA).[1] Both are important measures in the treat-to-target strategies, but often provide discordant results.[2,3] This can provide an erroneous assessment of the disease activity in patients and mislead treatment decisions.

We aimed to assess the differences and determinants of PtGA and PhGA in RA patients under biologic treatment.

We performed a cross-sectional study, including 46 patients with RA diagnosed according to the ACR/EULAR criteria, under biologic treatment. A written informed consent was obtained. Sociodemographic, clinical data, inflammatory parameters, disease activity (28-joint Disease Activity four variables Score (DAS28 4V) and patient-reported outcomes (PROs) were collected at same medical appointment.

Variables with $p < 0.1$ in the univariate analysis and those with clinical relevance were included in the multivariate analysis.

Clinical and laboratory characteristics of patients are shown in Table 1. PtGA and PhGA were significantly different (36.1 ± 27.6 mm *vs* 8.7 ± 14.2 mm, $p < 0.001$) and a positive discordance (PtGA > PhGA, more than 25 mm in visual analogue scale [VAS]) was found in 54.3% of cases.

PtGA had a strong correlation with PROs. More elevated PtGA was associated with higher pain VAS, Health Assessment Questionnaire [HAQ], and Hospital Anxiety and Depression Scale [HADS]), C reactive protein (CRP), tender and swollen joint counts (TJC and SJC, respectively) and with comorbidities like fibromyalgia or osteoarthritis (OA), and with lower 36-Item Short Form Health Survey [SF-36], Functional Assessment of Chronic Illness Therapy [FACIT], and EuroQol [EQ5D]. No association was found between PtGA and age, sex, education level, profession, employment status, extra-articular manifestations, positivity of rheumatoid factor, erythrocyte sedimentation rate (ESR), years of disease evolution or number of biologic treatments.

SF-36 global score showed a strong correlation ($P > 0.750$, $p < 0.001$) with all of the other PROs and so it was the PRO included in the multivariate analysis.

In the multivariate analysis including SF-36, CRP, TJC and OA (R^2 adjusted = 0.672), the main predictors of PtGA were lower SF36, concomitant OA and higher CRP level.

PhGA had a correlation with pain VAS, CRP, TJC and SJC. Higher PhGA was associated with higher pain VAS, CRP, TJC and SJC. No association was found between PhGA and patient's or physician's age or gender, extra-articular manifestations, positivity of rheumatoid factor, ESR level, years of disease evolution or number of biologic treatments. In the multivariable analysis including ESR,

Table 1
Clinical and laboratory characteristics of patients with rheumatoid arthritis.

Age (years), mean ± SD	58.7 ± 12.3
Gender – female, % (*n*/*N*)	69.6% (32/46)
Years from diagnosis, mean ± SD	14.7 ± 7.39
Biologic DMARD position, % (*n*/*N*)	1st: 58.7% (27/46) 2nd: 28.3% (13/46) Others: 13.0% (6/46)
Patient Global VAS, median (IQR)	40.0 (50.5)
Patient pain VAS, median (IQR)	31.0 (45.0)
Physician Global VAS, median (IQR)	0.0 (*15.0*)
Positive discordance % (*n*/*N*)[a]	54.3% (35/66)
Tender joints (*n*), median (IQR)	0.0 (3.0)
Swollen joints (*n*), median (IQR)	0.0 (2.0)
CRP (mg/dL), median (IQR)	0.3 (0.9)
ESR (mm/hr), median (IQR)	14.0 (24.0)
HAQ, median (IQR)	1.0 (1.6)
DAS28 4V, mean ± SD	2.9 ± 1.9
SDAI, mean ± SD	6.6 ± 6.3
CDAI, mean ± SD	7.5 ± 7.3
Short Form (36) Health Survey (SF36), mean ± SD	Physical functioning: 49.5 ± 32.3 Role limitations due to physical health problems: 58.2 ± 30.3 Pain: 52.8 ± 26.3 General health perceptions: 41.2 ± 23.3 Energy/fatigue: 50.8 ± 23.3 Social role functioning: 66.0 ± 26.0 Role limitations due to emotional problems: 65.7 ± 30.9 Mental health: 62.5 ± 24.8
FACIT, mean ± SD	34.9 ± 10.3
HADS, median (IQR)	Anxiety: 7 (7) Depression: 6 (7.5)
EQ5D, median (IQR)	0.32 (0.44)
Comorbidities, median (IQR)	2 (3)
Mellitus diabetes, % (*n*/*N*)	17.4% (8/46)
Depression/Anxiety, % (*n*/*N*)	8.7% (4/46)
Osteoarthritis, % (*n*/*N*)	28.3% (13/46)
Fibromyalgia, % (*n*/*N*)	4.3% (2/46)
Osteoporosis, % (*n*/*N*)	15.2% (7/46)

VAS: Visual Analogic Scale; CRP: C-reactive protein; ESR: erythrocyte sedimentation rate; HAQ: Health Assessment Questionnaire; DAS 28: Disease Activity Score; SDAI: Simple Disease Activity Index; CDAI: Clinical Disease Activity Index; EQ5D: EuroQol-5 dimension; FACIT: Functional Assessment of Chronic Illness Therapy; HADS: Hospital Anxiety and Depression; SD: Standard Deviation.
[a] Positive discordance: PtGA > PhGA, more than 25 mm in VAS.

☆ Authors declare that the manuscript has not been submitted or published elsewhere with the exception of abstracts published with scientific meetings.