Advances in Clinical Medicine 临床医学进展, 2023, 13(3), 4227-4232
Published Online March 2023 in Hans. https://www.hanspub.org/journal/acm
https://doi.org/10.12677/acm.2023.133606

Hans汉斯

误诊为顽固性低钾血症的干燥综合征一例

曹靖兰[1]，陈　婷[1]，程雪娇[2]，岳红梅[2]

[1]济宁医学院临床医学院，山东 济宁
[2]济宁市第一人民医院神经内科，山东 济宁

收稿日期：2023年2月21日；录用日期：2023年3月16日；发布日期：2023年3月22日

摘　要

目的：探讨以双下肢疼痛伴无力为首发症状的干燥综合征患者的临床表现，诊疗经过及预后情况。方法：回顾性分析就诊于济宁市人民医院的以双下肢疼痛为首发症状的患者的临床资料。结果：干燥综合征发病机制极为复杂，临床表现多样化，极易漏诊、误诊。以双下肢疼痛为首发症状的干燥综合征合并肾损害极其罕见，临床医师应提高警惕。

关键词

双下肢疼痛伴无力，干燥综合征，首发症状

A Case of Sjogren's Syndrome Misdiagnosed as Intractable Hypokalemia

Jinglan Cao[1], Ting Chen[1], Xuejiao Cheng[2], Hongmei Yue[2]

[1]Clinical Medical College of Jining Medical University, Jining Shandong
[2]Department of Neurology, The First People's Hospital of Jining, Jining Shandong

Received: Feb. 21st, 2023; accepted: Mar. 16th, 2023; published: Mar. 22nd, 2023

Abstract

Objective: To explore the clinical manifestations, diagnosis and treatment and prognosis of Sjogren's syndrome with pain and weakness of both lower limbs as the first symptom. Methods: The clinical data of patients with pain of both lower limbs as the first symptom in Jining People's Hospital were retrospectively analyzed. Results: The pathogenesis of Sjogren's syndrome is extremely complex, and its clinical manifestations are diverse, so it is easy to be missed and misdiagnosed. Sjogren's syndrome with renal damage as the first symptom of lower limbs pain is extremely rare, so clinicians should be vigilant.

文章引用: 曹靖兰, 陈婷, 程雪娇, 岳红梅. 误诊为顽固性低钾血症的干燥综合征一例[J]. 临床医学进展, 2023, 13(3): 4227-4232. DOI: 10.12677/acm.2023.133606

Keywords

Pain and Weakness of Both Lower Limbs, Sjogren's Syndrome, First Symptom

Copyright © 2023 by author(s) and Hans Publishers Inc.
This work is licensed under the Creative Commons Attribution International License (CC BY 4.0).
http://creativecommons.org/licenses/by/4.0/

Open Access

1. 引言

干燥综合征是发生在外分泌腺体上皮细胞上的异常免疫炎症反应性疾病，分为诊断明确的结缔组织疾病，如系统性红斑狼疮、类风湿关节炎等结缔组织疾病以及诊断尚不明确的结缔组织疾病[1]。其起病隐匿，病因尚不明确，目前为止，专家学者公认与遗传[2] [3]、EB 病毒[4] [5]、免疫因素[2] [6] [7]有关，此外，生活环境及干燥的气候条件对患者发病有直接影响[8] [9] [10]。本文回顾性分析一例以双下肢疼痛为首发症状的干燥综合征的患者临床资料，并复习相关文献，报告如下。

2. 临床资料

患者女，33 岁，因四肢疼痛 7 天伴无力 5 天，以双下肢疼痛、无力为著，于 2021 年 2 月 17 日收入济宁市第一人民医院。具体疼痛性质不详，无双下肢水肿，无麻木、刺痛等感觉异常，无呕吐、腹泻，无盗汗，无发热，无光过敏、口腔溃疡，无色素沉着，无皮疹，无尿频、尿急、尿痛等症状。既往眩晕症病史，“海鲜”过敏史，患者至患病以来，无呕吐腹泻、大量出汗，大便颜色正常，无尿多、尿少等尿量的变化，无甲亢等病史。饮食睡眠可，体重近期无明显变化。曾就诊于当地医院给予“膏药、口服药丸”(具体不详)。四肢疼痛减轻，无力改善。查血钾是 1.77 mmol/L，常规给予患者静脉补液(0.9%氯化钠 500 ml + 氯化钾 1.5 g + 维生素 C 2.0 g，bid，静滴)和氯化钾缓释片(2.0 g，4 小时 1 次，口服)。第二天上午 10:31 复查血钾 1.51 mmol/L，17:09 血钾 1.80 mmol/L。

体格检查：T 36.6℃，P 75 次/分，R 18 次/分，BP 114/78 mmHg，疼痛评分 2 分。神志清，精神可。营养中等，肌张力正常，双上肢肌力 4+级，双下肢肌力 3 级，甲状腺未触及肿大，无满月脸，水牛背，乳房无溢液，发毛未见明显稀疏。患者电解质、尿常规、血气分析结果示：血氯 112.3 mmol/L，二氧化碳结合力 16.8 mmol/L，尿 pH 6.5。结果提示肾性低钾，合并肾小管酸中毒，常规给予患者静脉补液和氯化钾缓释片，纠正电解质紊乱，患者仍存在顽固性低钾血症。后追问患者家族史发现患龋齿较多，无口干、眼干不适等不适，患者生长激素、甲状旁腺激素测定、甲功七项、垂体泌乳素、促卵泡生成素、促黄体生成素、雌二醇、孕酮、睾酮、尿常规等检查结果均未见明显异常，抗核抗体：抗 SS-A 阳性(+)、抗 RO-52 阳性(+)、抗 SS-B 弱阳性(+)，类风湿因子 21.70 IU/ml，考虑为：干燥综合征可能，患者低钾，考虑肾小管酸中毒导致低钾血症，给予患者氯化钾缓释片口服纠正电解质紊乱效果补明显。给予患者枸橼酸钾口服适合肾小管酸中毒补钾，并加用泼尼松(15 mg bid)、羟氯喹片(200 mg bid)、维 D 钙咀嚼片(0.1 g bid)、阿发骨化醇片(0.5 μg bid)防止骨质疏松，等治疗后好转出院。

3. 讨论

3.1. 干燥综合征的概述

干燥综合症(Sjögren's Syndrome, SS)是一种以侵犯泪腺、唾腺等外分泌腺体等为特征的一种长期的自

身免疫疾病[11] [12]，多发于 30~50 岁的女性群体[13] [14]。由于外分泌腺体受致病性免疫细胞的攻击[15] [16]，唾液分泌不足，出现口干、眼干的症状[17]，唾液中的杀菌物质不足以满足牙齿的清洁[18]，猖獗性龋齿大量出现[19] [20]；异常免疫细胞可诱导全身多脏器损伤[21]，引起皮肤干燥、慢性咳嗽、阴道干涩、疲倦、肌肉与关节疼痛、甲状腺问题，累及到肾脏可表现为肾小管酸中毒及其并发的低血钾性肌肉麻痹[22] [23]；在神经系统的表现多为认知功能障碍，焦虑、抑郁，疲乏无力[24] [25]。临床诊断以血清标志物检查，泪腺和唾液腺活检为主要参考[26] [27]。

3.2. 干燥综合征性合并肾小管性酸中毒的发病机制

肾小管酸中毒是由于各种原因导致的肾的肾小管功能出现异常。如近端肾小管对碱性物质如碳酸氢盐重吸收和(或)远端肾小管对酸性物质如氢离子分泌障碍，从而引起肾脏酸化功能障碍，不能维持机体正常的酸碱平衡状态，进而引起的一类综合征[28]。肾小管酸中毒分为四类，最常见的是 I 型和 II 型。I 型至远端肾小管分泌氢障碍，是由于远端肾小管分泌的氢离子减少，所以钾离子代替氢离子与钠离子进行交换，导致从肾脏排出钾增多。且酸中毒会直接引起骨质溶解同时以抑制肾小管对钙的重吸收，引起骨质疏松。据统计，5%的原发性干燥综合征(pSS)患者可有肾脏受累，临床症状隐匿[29]。原发性干燥综合征的肾损害多表现为肾间质炎症[30]。肾小管被淋巴细胞浸润或异常免疫复合物沉积于肾脏引起肾小管酸中毒伴低钾血症(发病率为 59.9% [31])、范科尼综合征(发病率为 13.0% [32])、尿崩症(发病率为 8.3% [33])、肾性蛋白尿(发病率为 42.7% [34])及钙性肾结石(发病率为 20.1% [35])等病症。

低钾血症通常指静脉血中测定血清钾浓度低于 3.5 mmol/L [36] [37]。低钾血症是人体的电解质紊乱，电解质紊乱可以导致人体出现全身系统的损害。在出现低钾血症时，对骨骼和神经系统会造成一定的影响，通常以反复发作的骨骼肌迟缓性瘫痪为特征为首发症状，例如我们所熟知的疾病：低钾性周期性麻痹[38]。低钾血症还会导致心脏出现异常，心电图通常表现为：胸导联 U 波增高，U 波与 T 波融合成驼峰样，或 U 波重叠与 T 波上，导致 QT 间期延长。导致人体出现心律失常，特别是出现快速性的心律失常，甚至诱发患者出现猝死的可能。所以针对低钾血症时需要及时积极的对症处理。低钾血症患者在检查体内电解质含量的同时，血气指标也应作为检查项。低钾血症的原因可分为肾内失钾和肾外失钾两种类别，应仔细询问患者近期有无肾病史以及服用肾毒性药物后做甄别。根据患者病史，可以确定患者为肾性失钾。根据有无酸碱失衡可分为带酸性低钾血症和代碱性低钾血症及酸碱正常的低钾血症。该患者从目前的诊断来看是代酸性低钾血症，且患者所以可能的原因最常见的是干燥综合征引起的肾小管酸中毒。干燥综合征合并肾损害治疗旨在抑制局部和全身的自身免疫反应。肾小管性酸中毒可以通过症状体征及相关辅助检查进行确诊[39]。纠酸是治疗肾小管酸中毒的关键，用于其治疗时补碱剂量应偏小，以免引起低钾性抽搐[40]。针对补钾，可以选择口服补钾。患者通过服用枸橼酸钾颗粒等药物，能够有效缓解肾小管酸中毒的情况，能够增加丢失的碳酸氢根，从而促进钾离子的摄入。在没有枸橼酸钾的情况下，口服氯化钾可作为备选方案，但是口服氯化钾生理反应性较大，患者会产生恶心、呕吐腹部不适等不良反应，建议饭后服用；如果口服氯化钾的方式没有得到明显效果，也可以选择静脉补钾，特别是低钾血症比较严重的程度，静脉滴注氯化钾见效快，但不良反应大，应少量多次，不宜快速补钾，时刻注意血钾浓度和尿量[41]。

3.3. 干燥综合征性肾损害的康复预后及注意事项

Jessica 等人使用生存分析策略评估了来自纽卡斯特尔的干燥综合征患者生活质量，结果显示在 377 名原发性干燥综合征参与者中，16%经历了健康相关生活质量下降到与更糟糕的健康状态甚至死亡，症状负担的改善有对原发性干燥综合征患者的远期生存率产生显著影响[42]。早发性 pSS 患者与晚发性 pSS

患者相比，外周淋巴结病和血细胞减少的发生率更高[43] [44]。无论患者年龄大小，累及肺组织和关节以及干燥症状在 pSS 中是常见的。RF 在 pSS 发展的病理机制中起作用[45]。一项调查性研究显示，吸烟、肥胖、极端环境条件对于干燥综合征的预后有不利影响[9] [46]。干燥综合征是一种罕见的疾病，没有治疗方法能够改变其自然病程，近些年来皮质类固醇和免疫抑制剂以及新的生物制剂的出现为 pSS 患者的治疗开辟了一个新的时代，长期遵医嘱规律服药可明显改善减慢疾病进展[47]。原发性干燥综合征和 TIN 或肾小球疾病患者的肾脏预后通常良好，但对一些患者而言，慢性肾脏疾病的风险仍然很大，因此定期复查可减慢肾功能的进行性恶化，提高患者生存质量[48]。

4. 总结

本例患者以双下肢疼痛无力为首发的主要症状，伴随低钾指标，易误诊为低钾性周期性麻痹，并错误地给予患者补充氯化钾。代谢性酸中毒是由于体内缺乏碳酸氢盐，如果补充氯化钾，会引起氯离子增加，导致体内碳酸氢根进一步下降，进而加重酸中毒。后果是细胞内的钾离子会转运到细胞外，经肾脏排泄后加剧钾的丢失。患者应该补充枸橼酸钾而不是氯化钾，是因为枸橼酸钾在补钾的同时，还会提供碳酸氢盐，提高体内碳酸氢根含量。最后完善血自身抗体等相关辅助检查后，确诊为干燥综合征。然而，干燥综合征病并不都是以口干、眼干症状为首发，同一患者的临床表现及症状体征也各有不同。这要求临床医生在加强理论知识学习的同时，做到对干燥综合征临床表现的症状的熟练掌握和全面分析，避免漏诊、误诊。

参考文献

[1] Sanchez-Zuno, G.A., Oregon-Romero, E., Hernandez-Bello, J., *et al*. (2021) Rheumatic Diseases and Allergies, the Duality of the Immune System. *Revista Alergia México*, **68**, 264-275. https://doi.org/10.29262/ram.v68i4.984

[2] Jonsson, R., Nakken, B., Halse, A.K., *et al*. (2000) Heredity and Immunology in Sjogren's Syndrome. *Tidsskrift for Den Norske Legeforening*, **120**, 811-814.

[3] Yoshio, S. (1997) Association of Sjögren's Syndrome with Hereditary Angioneurotic Edema: Report of a Case. *Clinical Immunology and Immunopathology*, **84**, 95-97. https://doi.org/10.1006/clin.1997.4347

[4] Maria, M. (2019) The Role of Epstein-Barr Virus Infection in Primary Sjögren's Syndrome. *Current Opinion in Rheumatology*, **31**, 475-483. https://doi.org/10.1097/BOR.0000000000000622

[5] Nakamura, H., Shimizu, T. and Kawakami, A. (2020) Role of Viral Infections in the Pathogenesis of Sjögren's Syndrome: Different Characteristics of Epstein-Barr Virus and HTLV-1. *Journal of Clinical Medicine*, **9**, 1459. https://doi.org/10.3390/jcm9051459

[6] Huang, Y.F., *et al*. (2013) The Immune Factors Involved in the Pathogenesis, Diagnosis, and Treatment of Sjogren's Syndrome. *Clinical and Developmental Immunology*, **2013**, Article ID: 160491. https://doi.org/10.1155/2013/160491

[7] Roberta, P., Guido, V., *et al*. (2015) Sex Differences in Sjögren's Syndrome: A Comprehensive Review of Immune Mechanisms. *Biology of Sex Differences*, **6**, 1-13. https://doi.org/10.1186/s13293-015-0037-7

[8] Alani, H., Henty, J.R., Thompson, N.L., *et al*. (2018) Systematic Review and Meta-Analysis of the Epidemiology of Polyautoimmunity in Sjogren's Syndrome (Secondary Sjogren's Syndrome) Focusing on Autoimmune Rheumatic Diseases. *Scandinavian Journal of Rheumatology*, **47**, 141-154. https://doi.org/10.1080/03009742.2017.1324909

[9] Xin, L., *et al*. (2021) Exposure-Lag-Response Associations between Extreme Environmental Conditions and Primary Sjögren's Syndrome. *Clinical Rheumatology*, **41**, 523-532. https://doi.org/10.1007/s10067-021-05910-5

[10] Mavragani, C.P. and Moutsopoulos, H.M. (2009) The Geoepidemiology of Sjögren's Syndrome. *Autoimmunity Reviews*, **9**, A305-A310. https://doi.org/10.1016/j.autrev.2009.11.004

[11] Trevisani, V., Pinheiro, A.C., de Magalhaes, S.F.S., *et al*. (2022) Recommendations for Evaluation and Diagnosis of Extra-Glandular Manifestations of Primary Sjogren Syndrome: Results of an Epidemiologic Systematic Review/Meta-Analysis and a Consensus Guideline from the Brazilian Society of Rheumatology (Hepatic, Gastrointestinal and Pancreatic). *Advances in Rheumatology*, **62**, 35. https://doi.org/10.1186/s42358-022-00267-y

[12] Vivino, F.B. (2017) Sjogren's Syndrome: Clinical Aspects. *Clinical Immunology*, **182**, 48-54. https://doi.org/10.1016/j.clim.2017.04.005

[13] Siso-Almirall, A., Meijer, J.M., Brito-Zeron, P., *et al*. (2021) Practical Guidelines for the Early Diagnosis of Sjogren's Syndrome in Primary Healthcare. *Clinical and Experimental Rheumatology*, **39**, 197-205. https://doi.org/10.55563/clinexprheumatol/pal3z7

[14] Sandrine, J.J. and Guillaume, C. (2020) Current Status of Imaging of Sjogren's Syndrome. *Best Practice & Research Clinical Rheumatology*, **34**, Article ID: 101592. https://doi.org/10.1016/j.berh.2020.101592

[15] Shilpa, S. (2020) Sjogren's Syndrome. *International Journal of Nursing Education and Research*, **8**, 114-116. https://doi.org/10.5958/2454-2660.2020.00024.1

[16] Sam Shiny, T. and George Rinu, J. (2020) Sjogren's Syndrome: An Overview. *International Journal of Nursing Education and Research*, **8**, 539-542. https://doi.org/10.5958/2454-2660.2020.00120.9

[17] Zandonella, C., *et al*. (2019) Hyperechoic Bands Detected by Salivary Gland Ultrasonography Are Related to Salivary Impairment in Established Sjogren's Syndrome. *Clinical and Experimental Rheumatology*, **37**, S146-S152.

[18] Rusthen, S., *et al*. (2019) Dysbiotic Salivary Microbiota in Dry Mouth and Primary Sjögren's Syndrome Patients. *PLOS ONE*, **14**, e218319. https://doi.org/10.1371/journal.pone.0218319

[19] Rodriguez, M.F., Asnal, C., Gobbi, C.A., *et al*. (2022) Primary Sjogren Syndrome and Development of Another Autoimmune Rheumatic Disease during the Follow-Up. *Advances in Rheumatology*, **62**, 19. https://doi.org/10.1186/s42358-022-00250-7

[20] Berman, N., Vivino, F., Baker, J., *et al*. (2019) Risk Factors for Caries Development in Primary Sjogren Syndrome. *Oral Surgery*, *Oral Medicine*, *Oral Pathology and Oral Radiology*, **128**, 117-122. https://doi.org/10.1016/j.oooo.2019.04.011

[21] Utomo, S.W. and Putri, J.F. (2020) Infections as Risk Factor of Sjögren's Syndrome. *Open Access Rheumatology*: *Research and Reviews*, **12**, 257-266. https://doi.org/10.2147/OARRR.S276727

[22] Trevisani, V., Pugliesi, A., Pasoto, S.G., *et al*. (2022) Recommendations for Evaluation and Diagnosis of Extra-Glandular Manifestations of Primary Sjogren Syndrome: Results of an Epidemiologic Systematic Review/Meta-Analysis and a Consensus Guideline from the Brazilian Society of Rheumatology (Articular, Pulmonary and Renal). *Advances in Rheumatology*, **62**, 18. https://doi.org/10.1186/s42358-022-00248-1

[23] Tu, R., *et al*. (2022) Renal Tubular Acidosis and Nephrogenic Diabetes Insipidus Caused by Sjögren's Syndrome with Hypokalemic Periodic Paralysis as the First Symptom: A Case Report. *Revue Neurologique*, **178**, 861-864. https://doi.org/10.1016/j.neurol.2022.02.458

[24] Jooha, L.J., Jae, P.Y., Misun, P., *et al*. (2021) Longitudinal Analysis of Symptom-Based Clustering in Patients with Primary Sjogren's Syndrome: A Prospective Cohort Study with a 5-Year Follow-Up Period. *Journal of Translational Medicine*, **19**, 394. https://doi.org/10.1186/s12967-021-03051-6

[25] Ciro, M., Jordi, S. and Marco, I. (2021) Comment on: Comorbidities (Excluding Lymphoma) in Sjögren's Syndrome. *Rheumatology* (*Oxford*, *England*), **60**, e453-e454. https://doi.org/10.1093/rheumatology/keab602

[26] Onorina, B., Piero, R., *et al*. (2021) Association between Minor Salivary Gland Biopsy during Sjögren's Syndrome and Serologic Biomarkers: A Systematic Review and Meta-Analysis. *Frontiers in Immunology*, **12**, Article ID: 686457. https://doi.org/10.3389/fimmu.2021.686457

[27] Ainat, K., Jonathan, K., Moran, C., *et al*. (2022) Acinar Atrophy, Fibrosis and Fatty Changes Are Significantly More Common than Sjogren's Syndrome in Minor Salivary Gland Biopsies. *Medicina*, **58**, 175. https://doi.org/10.3390/medicina58020175

[28] Bagga, A. and Sinha, A. (2020) Renal Tubular Acidosis. *Indian Journal of Pediatrics*, **87**, 733-744. https://doi.org/10.1007/s12098-020-03318-8

[29] Aiyegbusi, O., Mcgregor, L., Mcgeoch, L., *et al*. (2021) Renal Disease in Primary Sjögren's Syndrome. *Rheumatology and Therapy*, **8**, 63-80. https://doi.org/10.1007/s40744-020-00264-x

[30] Yayla, M.E., Şahin Eroğlu, D., Uslu, Y.E., *et al*. (2022) Indications and Risk Factors for Hospitalization in Patients with Primary Sjögren Syndrome: Experience from a Tertiary Center in Turkey. *Clinical Rheumatology*, **41**, 1457-1463. https://doi.org/10.1007/s10067-022-06053-x

[31] 刘正钊, 胡伟新, 章海涛, 等. 原发性干燥综合征肾损害的临床病理特征及预后[J]. 肾脏病与透析肾移植杂志, 2010, 19(3): 225-229.

[32] 郑法雷, 赵素梅, 李雪梅, 等. 范可尼综合征的临床特点与生化异常[J]. 中华内科杂志, 2000, 39(11): 14-17.

[33] 周雷, 周玲丽, 徐春兰, 等. 12 例肾小管酸中毒患者误诊原因分析与护理[J]. 中国实用护理杂志, 2005, 21(9): 22-23.

[34] 宋捷, 刘正钊, 胡伟新, 等. 75 例干燥综合征肾脏损害患者远期预后及影响因素分析[J]. 肾脏病与透析肾移植杂志, 2014, 23(1): 18-22.

[35] 雷鸣, 刘春晓, 曾国华, 等. 含钙性肾结石患者尿液代谢异常、远端肾小管性酸中毒的检测及意义[J]. 山东医药, 2010, 50(10): 74-75.

[36] 穆妮热·阿塔吾拉, 郭艳英. 低钾血症病因与发病机制的研究进展[J]. 中国医药科学, 2022, 12(18): 39-43.

[37] 李东宝, 华琦. 低钾血症的临床处理[J]. 内科急危重症杂志, 2005, 11(2): 87-89.

[38] Phuyal, P. and Nagalli, S. (2022) Hypokalemic Periodic Paralysis.

[39] Louis-Jean, S., Ching, P.R. and Wallingford, A. (2020) Distal Renal Tubular Acidosis in Sjogren's Syndrome: A Case Report. *Cureus*, **12**, e10962. https://doi.org/10.7759/cureus.10962

[40] George, V., John, W.D., Isaac, P., *et al*. (2019) Distal Renal Tubular Acidosis and Severe Hypokalemia: A Case Report and Review of the Literature. *Journal of Medical Case Reports*, **13**, 103. https://doi.org/10.1186/s13256-019-2056-1

[41] Chalkia, A., Giannou, P., Thomas, K., *et al*. (2021) Distal Renal Tubular Acidosis and Nephrocalcinosis as Initial Manifestation of Primary Sjogren's Syndrome. *Saudi Journal of Kidney Diseases and Transplantation*, **32**, 1470-1474.

[42] Tarn, J., Lendrem, D., Mcmeekin, P., *et al*. (2022) Primary Sjögren's Syndrome: Longitudinal Real-World, Observational Data on Health-Related Quality of Life. *Journal of Internal Medicine*, **291**, 849-855. https://doi.org/10.1111/joim.13451

[43] Goules, A.V., Argyropoulou, O.D., Pezoulas, V.C., *et al.* (2020) Primary Sjgren's Syndrome of Early and Late Onset: Distinct Clinical Phenotypes and Lymphoma Development. *Frontiers in Immunology*, **11**, Article ID: 594096. https://doi.org/10.3389/fimmu.2020.594096

[44] Agata, S., Marta, M., Maciej, S., *et al.* (2021) Differences in Clinical Phenotypes of Primary Sjögren's Syndrome Depending on Early or Late Onset. *Advances in Clinical and Experimental Medicine*: *Official Organ Wroclaw Medical University*, **30**, 1141-1146. https://doi.org/10.17219/acem/140178

[45] Sebastian, A., Madej, M., Sebastian, M., *et al.* (2021) Differences in Clinical Phenotypes of Primary Sjogren's Syndrome Depending on Early or Late Onset. *Advances in Clinical and Experimental Medicine*, **30**, 1141-1146. https://doi.org/10.17219/acem/140178

[46] Kawada, T. (2022) Smoking, Obesity, and Risk of Primary Sjögren Syndrome. *The Journal of Rheumatology*, **49**, 231-234. https://doi.org/10.3899/jrheum.210808

[47] Del Papa, N., Minniti, A., Maglione, W., *et al.* (2021) Instruments for Outcome Evaluation of Specific Domains in Primary Sjögren's Syndrome. *Biomolecules*, **11**, 953. https://doi.org/10.3390/biom11070953

[48] Francois, H. and Mariette, X. (2020) Renal Involvement in Sjogren's Syndrome. *Nephrologie & Therapeutique*, **16**, 440-452. https://doi.org/10.1016/j.nephro.2020.10.002