CLINICAL IMAGE

Symptoms mimicking Sjögren syndrome in a heterozygous carrier of CFTR deltaF508 mutation

Marta Domżalska[1], Zbigniew Zdrojewski[1], Natalia Buda[1], Anna Masiak[1], Jolanta Szade[2], Grzegorz Romanowicz[3]

1 Department of Internal Medicine, Connective Tissue Diseases and Geriatrics, Medical University of Gdansk, Gdańsk, Poland
2 Department of Pathomorphology, Medical University of Gdansk, Gdańsk Poland
3 Department of Nuclear Medicine, Medical University of Gdansk, Gdańsk Poland

A 49-year-old female patient was admitted to our clinic due to the suspicion of Sjögren syndrome (SS). Symptoms of dry mouth and dry eye, with recurrent inflammation of the conjunctiva and cornea, accompanied by arthralgia, had been present for the past 3 years. The patient reported also periodic presence of painful sores in the mouth, constipations, and periodic dyspepsia. On admission, the general condition of the patient was good. There were no significant abnormalities on physical examination. The Schirmer test showed moderate dryness. Differential diagnosis included diseases associated with infiltration of the exocrine glands, diseases causing the formation of granuloma, lymphoma, hepatitis C virus infection, IgG4-related disease, and drugs that cause symptoms of dryness.

In laboratory testing, the results of the ANA HEp-2 test were positive (titer 1:640) but a Western blot study did not confirm the specificity of autoantibodies. Other results, including the levels of C-reactive protein, rheumatoid factor, protein electrophoresis, and complement components C3 and C4 were within reference ranges. An ultrasound examination of the major salivary glands revealed evidence of chronic inflammation (FIGURE 1A). ^{99m}Tc-pertechnetate standard scintigraphy of the salivary gland showed slight impairment of saliva secretion (FIGURE 1B). A histopathological evaluation of labial salivary glands showed no evidence of SS (FIGURE 1C).

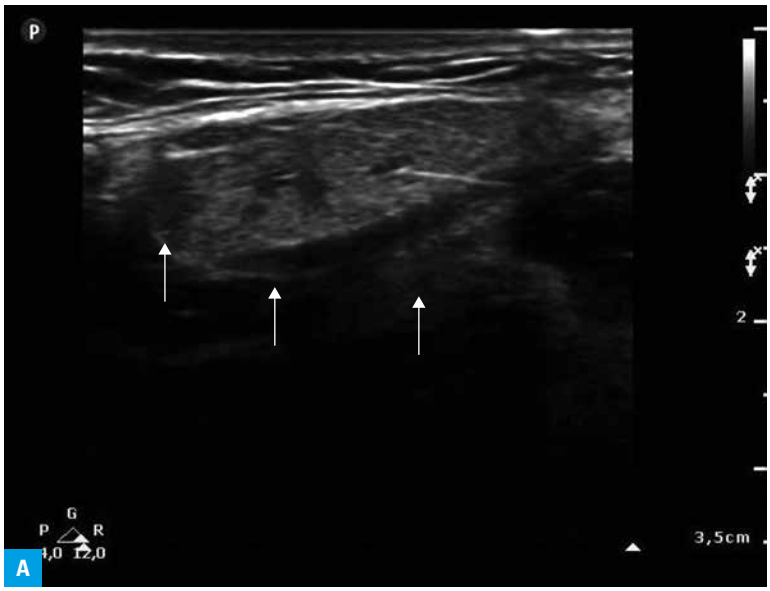
Discrete abnormalities were present both on ultrasound and scintigraphy, and although the symptoms were suggestive of SS, the patient did not fulfill either the 2002 American-European Consensus Group criteria or the 2012 American College of Rheumatology classification criteria for diagnosis of SS. During the diagnostic workup, we obtained additional information that the patient was a confirmed carrier of the *deltaF508* mutation in the *CFTR* gene. Both the patient and her husband underwent genetic testing several years earlier when 2 of 4 of their children were diagnosed with cystic fibrosis (CF). Considering the genetic changes, the sweat test was performed, yielding a result of 30.0 mmol/l (reference range, 0–60.0 mmol/l). Sicca syndrome mimicking SS in a heterozygous carrier of the *CFTR* mutation was recognized.

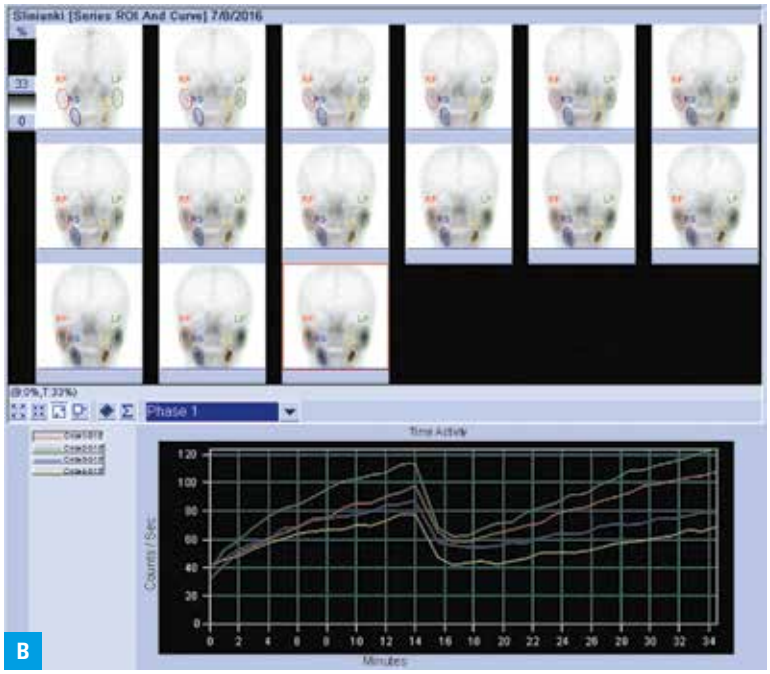
SS is a chronic autoimmune disease characterized by the presence of lymphocytic infiltrates in the exocrine glands, which results in xerophthalmia and xerostomia. CF is an autosomal recessive genetic disorder that affects mainly the respiratory and gastrointestinal tracts. Previous studies have shown that the heterozygosity of *CFTR* mutations is associated with an increased risk of poor pulmonary function and chronic pancreatitis.[1] Congenital bilateral absence of the vas deferens, acute recurrent or chronic pancreatitis, and disseminated bronchiectasis are classified as *CFTR*-related disorders (CFTR-RD).[2]

To our knowledge, the relationship between the heterozygosity for *CFTR* mutations and the presence of sicca syndrome has not been described so far. We put forward a hypothesis that *CFTR* gene heterozygosity may be associated with symptoms mimicking SS and may be another CFTR-RD.

Data from the literature support the above hypothesis. It was found that *CFTR* is involved in epithelial fluid transport in the exocrine glands. Moreover, it was demonstrated that the expression of *CFTR* in rabbits with induced autoimmune dacryoadenitis is changed.[3] As a chloride selective channel, it may influence the qualitative

Correspondence to:
Marta Domżalska, MD, Klinika Chorób Wewnętrznych, Chorób Tkanki Łącznej i Geriatrii Uniwersyteckie Centrum Kliniczne w Gdańsku,
ul. Dębinki 7, 80-952 Gdańsk, Poland,
phone: +48 58 349 28 32;
e-mail: marta.domzalska@gmail.com
Received: August 18, 2016.
Revision accepted: October 21, 2016.
Published online: November 28, 2016.
Conflict of interests: none declared.
Pol Arch Med Wewn. 2016; 126 (11): 895-896
doi:10.20452/pamw.3654
Copyright by Medycyna Praktyczna, Kraków 2016





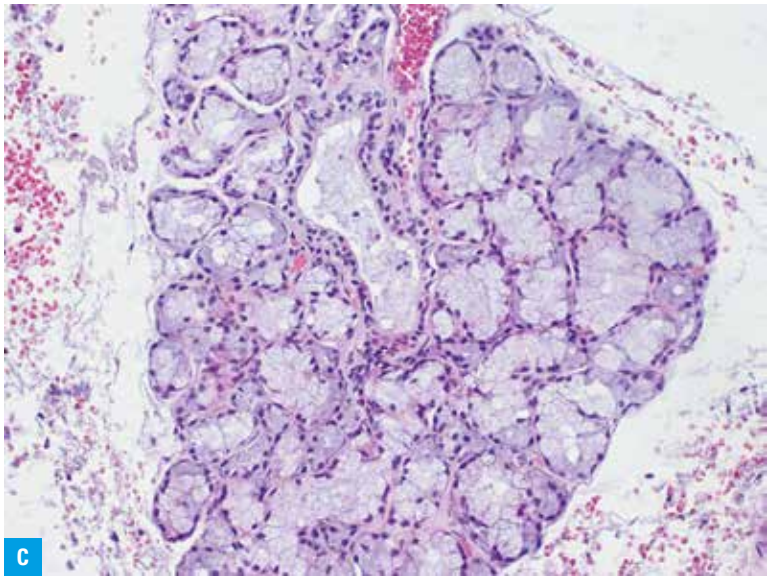


FIGURE 1 **A** – the parotid gland with mild unspecific inhomogeneity on ultrasound; **B** – standard salivary gland scintigraphy. Dynamic imaging was performed with the use of dual-head gamma camera (Symbia T6, SIEMENS Helthineers, Hoffman Estates, Illinois, United States) with the LEAP collimator. Dynamic acquisition in 64 × 64 pixel matrix of the anterior view started following an intravenous injection of 185 Mbq (5 mCi) ^{99m}Tc-pertechnetate at the speed of 1 frame per 30 seconds for 35 minutes. At 14 minutes after the injection, freshly squeezed lemon juice was administered orally to boost tracer excretion (via a tube to prevent moving). The analysis of the study included a visual assessment of the image as well as generation of time-activity curves (T-AC) from the region of interest (ROI) of all the 4 salivary glands (right and left submandibular as well as right and left parotid). All ROIs were drawn manually. The visual analysis of the scintigraphy image showed a relatively normal uptake in all glands. However, the T-AC analysis showed a slight delay of the first phase as well as a relatively slower than expected reaction to the secretory stimulus, which is consistent with slight impairment of the saliva secretion. The function of all glands in T-AC was relatively symmetrical. **C** – a histopathological evaluation of minor salivary glands. Labial salivary glands with scanty lymphocytic infiltrates, which does not fulfill the criteria for Sjögren syndrome (focus score >1; refers to a cluster of 50 or more lymphocytes per 4 mm2). Magnification, × 20.

composition of tears. The *CFTR* mutation may also increase the production of proinflammatory cytokines.[4]

Despite substantial progress in the field of genetic testing in Poland, our case, along with another single report,[5] emphasizes the need for further development of genetic diagnostic workup in patients with symptoms that cannot be assigned to a specific disease entity or in whom the disease course is atypical.

REFERENCES

1 Griesenbach U, Geddes DM, Alton EW. The pathogenic consequences of a single mutated CFTR gene. Thorax. 1999; 54: 19-23.

2 Bombieri C, Claustres M, De Boeck K, et al. Recommendations for the classification of diseases as CFTR-related disorders. J Cyst Fibros. 2011; 10: 86-102.

3 Nandoskar P, Wang Y, Wei R, et al. Changes of chloride channels in the lacrimal glands of a rabbit model of Sjögren's syndrome. Cornea. 2012; 31: 273-279.

4 Mrugacz M. Ocular surface changes in patients with cystic fibrosis. In: Leatte PN ed. Cystic fibrosis: etiology, diagnosis and treatments. New York: Nova Science Publishers; 2009: 217-230.

5 Wypasek E, Potaczek DP, Stąpor R, et al. First report of the genetic background of Marfan syndrome in Polish patients. Pol Arch Med Wewn. 2013; 123: 646-647.