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

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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). ⁹⁹mTc-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

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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


