Rheumatoid Arthritis and Coexisting Parkinson’s Disease a Report of 5 Cases

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ABSTRACT

It is a commonly seen condition that the hand deformities which are seen in Parkinson disease (PD) mistakenly diagnosed as Rheumatoid arthritis (RA) so PD and RA have been associated with each other in the literature. Looking for the another view, in autoimmune diseases, such as RA, there is a chronically high concentrations of inflammatory mediators product over long periods of time and it has been hypothesized that these patients may be at increased risk for neurodegenerative diseases such as PD. To contribute to a few recently published reports, we describe five patients, over 65 years old, with a primary diagnosis of RA and coexisting PD and we discuss possible pathogenetic link between RA and PD. The coexisting cases in this report are most probably incidental but the prevalence of coexisting of RA and PD may be higher than that of regularly thought. The present report is draw attention to the possibility of coexisting and to keep in mind the possibility of developing neurodegenerative disorders due to the chronic inflammation in the course of patients with RA.

Key words: Rheumatoid arthritis, Parkinson disease, deformity

INTRODUCTION

Rheumatoid arthritis (RA) is a chronic polyarthritis with cartilage degeneration, bone erosion, and joint deformations that can be seen clearly in hands. RA affects 0.5-1.0 % of adults in developed countries. Prevalence rises with age and is highest in women older than 65 years (1).

Parkinson’s disease (PD); is a chronic and progressive neurodegenerative disorder characterized by bradykinesia, rigidity, tremor, and postural instability. Pathological hallmarks of PD are destruction of dopaminergic neurons in the basal ganglia, especially the substantia nigra (SN). Prevalence of PD clearly increases with age (2).
Hand deformities are characteristic features of RA. Hand deformities in PD were first described in 1864 and since that time studies have pointed out the importance of the hand deformities causing the misdiagnosis of RA and unnecessary medical treatment (1,3).

Although PD can cause deformities mimicking RA; patients with autoimmune diseases, such as RA, produce chronically high concentrations of inflammatory mediators over long periods of time and it has been hypothesized that these patients may be at increased risk for neurodegenerative diseases such as PD (4). Some reports recently described patients with primary diagnosis of RA and coexisting PD (5,6). Ertan et al. have been evaluated extra pyramidal rigidity in patients with RA and described about 24 % of the RA patients with rigidity (6). On the other hand, Rugbjerg et al observed a decrease in the risk of PD by 30% among RA patients (4).

Therefore, there seems to be a conflicting evidence on the coexistence of RA and PD. In this report, 5 cases with a primary diagnosis of RA coexisting PD are described and a possible pathogenetic link between RA and PD are discussed. The aim of the present report is to draw attention to the possibility of coexistence of RA and PD.

CASE 1
A 69-year-old male patient is admitted with the complaints of pain, swelling, deformities and tremor in hands. His complaints started 5 years ago with symmetric elbow, wrist, and hand joints arthritis. He has been complaining of tremor in hands and gait abnormality with posture alterations for 3 years. Limitation and tenderness on bilateral wrist movements, bilateral ulnar deviation, and flexion deformities with swelling of hand joints are observed. In the neurological examination; bradykinesia, resting tremor and marked rigidity in the form of cogwheel in the upper extremities are present. Levels of acute phase reactants (APR) and Rheumatoid factor (RF) are higher than normal levels. Anti-cyclic citrullinated peptide antibodies (anti-CCP) are positive. In hand radiograms, erosions and periarticular osteoporosis are present. The patient is diagnosed as RA (7). The initial treatment with non-steroidal anti-inflammatory drugs (NSAIDs) and disease modifying anti-rheumatic drugs (DMARDs) is applied. Then the patient is referred to the neurology clinic. He is diagnosed as PD according to the United Kingdom Parkinson’s Disease Society (UK PDS) Brain Bank Clinical Diagnostic Criteria (8).

CASE 2
A 72-year-old female patient who is admitted to the hospital with a 9 years history of RA and she has been taking NSAIDs and DMARDs since that time. She began to experience the resting tremor and slowness of movements in 2004 and since that time, she has been taking several drugs for PD. In the physical examination, extension of both elbows and hand joints is limited. Bilateral ulnar deviation is present. In the neurological examination; bradykinesia, resting tremor, and minimal rigidity in the right upper extremity are found. Laboratory findings and hands radiography are consistent with RA. The patient is diagnosed as RA (7) and PD (8) and medication is modified.

CASE 3
A 76-year-old woman who had had complaints of symmetric wrist and hand arthritis, morning stiffness and rheumatoid nodules (RN) was diagnosed as having RA about 40 years ago. She has been taking NSAIDs and DMARDs for last 6 years. In the physical examination; ulnar deviation, swan neck, and Z deformities of the thumbs are found (figure 1). In the neurological examination, bradykinesia, rigidity, and postural instability, which were recently started, are determined. APR are slightly higher than in normal levels, RF is positive. The patient is referred to the neurology clinic because of the possibility of coexisting PD. She is diagnosed as PD (8) and levodopa-benserazid is administered.

CASE 4
A 66-year-old female patient was diagnosed as RA eleven years ago and has been taking NSAIDs and DMARDs since that time. Extension of bilateral elbow joints is limited. Radial deviation on hand joints and wrist tenderness are present. In the neurological examination hypophonia, bradykinesia and marked rigidity in the form of cogwheel are determined. APR and RF levels are higher than normal levels. In hand radiographies periarticular osteopenia, cysts, erosions and narrowing in joint spaces are observed. She is diagnosed as PD (8) in the neurology clinic and medication is started.
CASE 5

A 80-year-old female patient presents with 15-year-history of RA and 2-month-history of tremor in hands and bradykinesia. In physical examination, bilaterally ulnar deviations, bilaterally rheumatoid nodules at the elbows and symmetrical minimal rigidity in upper extremities are found. PD is diagnosed (8) and benserazid began.

DISCUSSION

In the literature, PD and RA have been associated with each other for many years owing to the cases of hand deformities that are seen in PD but mistakenly diagnosed as RA. The absence of local signs of inflammation and typical involvement which can also be seen in hand radiographies rule out the diagnosis of RA in patients with PD (3). In the above-mentioned cases, there were signs of joint inflammation such as higher levels of APR and RF. Our cases met the diagnostic criteria of RA. Therefore, the deformities were not attributed to PD. These patients were also fulfilled the diagnostic criteria of PD. Based on the data, the present cases are acceptable as coexistence of RA and PD.

The co-existence of RA and PD was mentioned previously by a few authors (5,6). Kogure et al witnessed a 52-year-old woman with RA that had started to suffer from PD (5). In Ertan et al., the frequency of PD among RA patients was found as 2.3 % (6). On the other hand, Rugbjerg et al. showed no overall association between autoimmune diseases and PD by a population-based case-control study. The authors also observed a decrease in the risk of PD by 30% among RA patients (4). The present paper has not designed as a population based study and we did not screen for PD in our RA population. The 5 cases with coexisting RA and PD were incidentally found and our database involving the RA population of 473 patients was searched in terms of a possible coexistence of RA and PD and no other patients were found.

The possible relationship between RA and PD in terms of etiology is probably complex, multifactorial, and controversial. Ertan et al. suggested a possible explanation about the existence of cogwheel rigidity among patients with RA through the changes occur in joint mechanics and alterations in muscle tone in addition to the involvement of the dopaminergic system in RA (6). Inflammation is one of the key etiopathogenetic factors in RA and possible hypothetic process in PD (1,9). Inflammatory mediators are chronically produced in RA and these mediators may cause or contribute to the degeneration of the neurons. The key role of TNF in RA is clear but the mechanisms by which TNF moderates the neuroinflammatory and neurotoxic effects that lead to nigrostriatal degeneration have not been well understood yet. TNF levels in the brain of healthy adults are generally very low and produced mainly by neurons. In contrast, TNF levels have been found to be higher in the SN of postmortem brains of patients with PD. Studies also suggest that dopaminergic neurons in SN are utterly sensitive to TNF (1,10). A review recently published that adhesion molecules, TNF, interleukin-1β and -6, nitric oxide (NO) are found to be elevated in PD patients and these substances amplify and mediate the irreversible destruction of dopaminergic neurons in the SN (11).

The reported patients have been taking several kinds of NSAIDs. NSAIDs are often used in the treatment of RA (1) and regular use of NSAIDs is controversial that NSAIDs inhibit neurodegeneration and protect against the development of PD. Recently studies shows that the use of NSAIDs was not associated with a substantially altered risk of developing PD except ibuprofen taking (12). On the other hand Rugbjerg et al., indicate that their result about the decreased risk for PD in patients with RA might be explained by the protective effect of the long-term NSAID treatment (4).

The etiologic link regarding the coexistence of RA and PD is speculative according to the recent data. Therefore, the coexisting cases in this report may be considered as
incidental. However, taken together with the previous studies showing higher prevalences, physicians should be more careful when unexplained symptoms which may be related to a coexisting disease are observed in patients with diagnoses of RA or PD.

REFERENCES


