Autoimmune/Inflammatory Syndrome Induced by Adjuvant Associated with a Metal Implant in the Mouth; Explantation Was Followed by Recovery

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Autoimmune/inflammatory syndrome induced by adjuvant (ASIA), also known as Shoenfeld's syndrome, incorporates specific and non-specific autoimmune conditions that are induced following the exposure to an adjuvant. Adjuvants in predisposed individuals can cause an overt immune response and an autoimmune disease. Diagnosis of ASIA is based on major and minor criteria. Major criteria require exposure to an adjuvant, typical clinical manifestation (e.g., arthralgia, chronic fatigue, memory loss), improvement followed by the removal of the inciting agent, and typical biopsy of the involved organ. Minor criteria include antibodies against the suspicious agent, other clinical manifestation such as inflammatory bowel disease, specific human leukocyte antigen, and an evolvement of autoimmune disease. Patients must show at least two major criteria or one major and two minor criteria [1,2].

We present a case of a 38-year-old woman who had a dental metal crown implanted and later developed a systemic reaction to the metal used. This case is consistent with the criteria used to determine ASIA syndrome.

PATIENT DESCRIPTION

A 38-year-old woman, who had no health problems or illnesses, went through a dental procedure, in which a porcelain-fused-to-metal (PFM) crown was made on her lower right first molar, tooth number 46 [Figure 1A]. The metal component of the crown was a chrome and cobalt alloy (Cr-Co alloy).

One month later she started to complain about profound fatigue, xerostomia, sleeping disorders, depression, acne, hair loss, facial pain, headaches, tinnitus, dizziness, and heart palpitations. She also had symptoms of cognitive impairment manifested in words forgetfulness. She visited various specialists and numerous doctors complaining about these symptoms, including oral and maxillofacial specialists, ear nose and throat physicians, and neurologists, all of whom found nothing abnormal. Blood analysis was within normal limits.

The patient had no silicone implants, which have been shown to cause ASIA manifestations in a subpopulation of genetically susceptible women [1,3], but a brother had been diagnosed with Hashimoto's thyroiditis.

Since the patient's nonspecific complaints started adjacent to her dental procedure, we decided to remove her PFM crown. The treatment consisted of replacement of the crown, amalgam core, and metallic posts to a temporary acrylic crown, composite core and two D.T. translucent fiber posts, respectively [Figures 1B, 1C]. Five months after the procedure the patient was asked to complete a questionnaire. Most of her symptoms had disappeared. The patient still had episodes of xerostomia and tinnitus, but at much lower frequency and intensity.

The patient presented three of the major ASIA diagnostic criteria: the exposure to external stimuli (metal crown as an adjuvant), the appearance of typical clinical manifestations (fatigue, dry mouth, cognitive impairment, and sleeping disorder), and improvement followed by the removal of the inciting agent. Hence, the patient fulfilled the three major criteria for ASIA. Therefore, we suggested that a dental crown might be another trigger for ASIA.

COMMENT

The immunological effects of metals are immunomodulation, allergy, or autoimmunity. Metal induced inflammation may be involved in the pathology of various autoimmune and allergic diseases where abnormal fatigue, muscle pain, cognitive impairment, and other nonspecific symptoms are often present [4].

The metals present in dental alloys can produce inflammatory effects. The Cr-Co alloy is toxic compared with other materials. The alloy can corrode and release toxic elements by lowering the pH. Co-Cr alloys induce inflammatory responses through several inflammatory signaling pathways

including the NF-κB, ERK/p38/JNK MAPK, and JAK2/STAT3 pathways [5].

The extraction of the adjuvant metal can result in improvement of the patient's symptoms. The remarkable clinical course that finally resolved with the removal of the dental crown led us to consider ASIA syndrome.

The relative rarity of the events does suggest that in the pathogenesis of the disease, an individual's genetic predisposition plays an important role as well as environmental exposure to adjuvants [1]. Indeed, the patient had a genetic background of autoimmune disease since her brother had been diagnosed with Hashimoto's thyroiditis.

CONCLUSION

We presented a case in which the removal of a metal dental crown from a patient's mouth resolved most of the symptoms and helped the patient regain a quality of life. We suggest that physicians and patients be attentive to signs and symptoms compatible with ASIA syndrome and identify patients at a greater risk of autoimmune diseases following the exposure to adjuvants.

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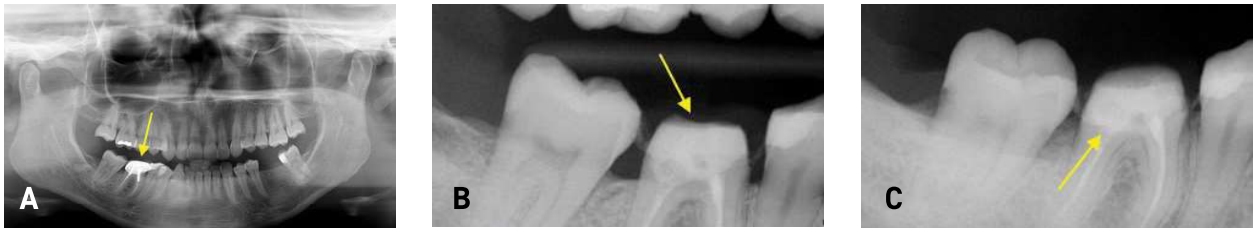
Figure 1. Patient's pre and post treatment X-rays
[A] Panoramic view of lower right first molar with a dental implant crown pre-treatment (arrow), **[B]** post-treatment bitewing X-ray of the right side, and **[C]** periapical X-ray lower right molars present the replacement of the metal crown to a new composite filling (arrow).



The greatest discovery of my generation is that a human being can alter his life by altering his attitudes of mind.
William James (1842–1910), American philosopher and psychologist

Capsule

In situ neutrophil efferocytosis shapes T cell immunity to influenza infection

Early recruitment of neutrophils from the blood to sites of tissue infection is a hallmark of innate immune responses. However, little is known about the mechanisms by which apoptotic neutrophils are cleared in infected tissues during resolution and the immunological consequences of in situ efferocytosis. Using intravital multiphoton microscopy, **Lim** et al. showed previously unrecognized motility patterns of interactions between neutrophils and tissue-resident phagocytes within the influenza-infected mouse airway. Newly infiltrated inflammatory monocytes become a chief pool of phagocytes and play a key role in the clearance of highly motile apoptotic neutrophils during the resolution phase. Apoptotic neutrophils further release epidermal growth factor and promote the differentiation of monocytes into tissue-resident antigen-presenting cells for activation of antiviral T cell effector functions. Collectively, these results suggest that the presence of in situ neutrophil resolution at the infected tissue is critical for optimal CD8+ T cell-mediated immune protection.

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