Abstract

The association of clubbing with miscellaneous diseases and its diagnostic implications are such that its detection should prompt consideration of the underlying etiology. We encountered a 48-year-old woman with clubbed fingers and a cauliflower-like gingival swelling on the hard palate of the upper jaw. There were no conventionally well-known causes for clubbing. Histological examination of gum biopsy specimen revealed a diagnosis of inflammatory gingival hyperplasia. As an etiology of clubbed fingers, gingivitis was suggested, since clubbing was regressed in parallel with remission of the gingivitis after the treatment by extraction of anterior teeth. Possible involvement of an autoimmune process in the pathogenesis was also considered, because of concomitant elevation of serum anti-double strand DNA antibodies. We recommend examination of the oral cavity for search of an inflammatory disease in cases with clubbed fingers, particularly when other common causes are not apparent.

Case Presentation

A 48-year-old Japanese woman visited our university hospital, complaining of dysesthesia on the tip of all fingers of both hands for 3 months. She had been suffered from progressive gingival swelling of the upper jaw for 6 months and blurred vision of the left eye for one month. Until then, she had been well and not under any medication. Physical examination at presentation revealed clubbed fingers in both hands as assessed by the profile angle (185 degree), hyponychial angle (200 degree) that was proposed as a more reliable sign than the profile angle in the assessment of clubbing (2–3), and distal-interphalangeal depth ratio (1.3); in individuals without clubbing, the values for these indices do not exceed 176 degrees, 192 degrees, and 1.0, respectively (2). There were no other abnormal findings in skeleton and muscle including active synovitis. Examination of optic fundus revealed central retinal vein occlusion of the left eye. Oral examination revealed a cauliflower-like gingival thickening on the hard palate of the upper jaw (Fig. 1A, B). There was no struma. Physical examination was otherwise normal including the chest and abdomen.

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Received for publication March 14, 2005; Accepted for publication August 5, 2005
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Internal Medicine Vol. 44, No. 12 (December 2005) 1307
Laboratory examination results were normal except for an increased number of eosinophils (595/μl) and a positive reaction for anti-double strand DNA antibodies (dsDNA Ab) (ELISA) at 20.1 IU/ml (reference value <12 IU/ml). Urinalysis was normal including urinary sediments. Anti-nuclear antibodies and rheumatoid factor were negative. The levels of serum complements, immunoglobulin E and anti-cardiolipin-β1 glycoprotein 1 complex antibody (anti-CL-β1GP1) were normal. X-ray of fingers was normal except for soft tissue swelling of the distal phalangeal fingers. There were no hypertrophic changes of bones of extremities. Chest X-ray and computed tomography were negative for intrathoracic diseases.

Resection biopsy was performed from a tumorous portion of the upper jaw. The histopathological examination of the biopsy specimen revealed a granuloma lesion with an increased number of vessels and infiltration of eosinophils (Fig. 2A, B). These findings suggested a diagnosis of inflammatory gingival hyperplasia. In parallel with disappearance of inflammatory gingival hyperplasia after the treatment by extracting all of anterior teeth of the upper jaw (Fig. 1C), signs of clubbed fingers and blurred vision gradually regressed in 11 months (Fig. 3A, B). Meanwhile anti-ds DNA Ab decreased to a normal value in one month (2.1 IU/ml). Eosinophil counts in the peripheral blood were temporarily increased to 2,108/μl at 6 months after treatment. The clinical course is shown in Fig. 4.

**Discussion**

We encountered a Japanese woman who presented clubbed fingers and a cauliflower-like gingival swelling on the hard palate of the upper jaw. Well-known etiology of clubbing includes neoplastic or suppurative intrathoracic diseases, diffuse pulmonary diseases, cardiovascular diseases, hepatobiliary diseases, bowel inflammatory diseases and thyroid diseases (3–17). These diseases were not found in the present patient as judged by physical, laboratory and
Clubbed Fingers in Inflammatory Gingival Hyperplasia

Figure 2. Histopathological findings of inflammatory gingival hyperplasia. Hematoxylin and eosin stain: HE stain, ×50 (A), ×100 (B) (□). Resection biopsy was performed from a part of tumorous portion of the upper jaw. The histopathological examination of the biopsy specimen revealed a granuloma lesion with increased number of vessels and infiltration of eosinophils.

Figure 3. Clubbed fingers after extracting anterior teeth of the upper jaw. Three (A) and 11 months (B) after the treatment. Values for the three indices for clubbed fingers were decreased after extracting anterior teeth of the upper jaw (before, 3 and 11 months after the treatment, respectively); the profile angle (185 to 160, 160 degree), the hyponychial angle (200 to 175, 175 degree) and the distal-interphalangeal depth ratio (1.3 to 1.1, 1.0).
Radiographical examination. The gingival thickening on the hard palate of the upper jaw was histologically diagnosed as inflammatory gingival hyperplasia. With treatment by extracting all of anterior teeth of the upper jaw, inflammatory gingival hyperplasia disappeared and then clubbing regressed. This clinical course in combination with concurrence of the clubbing and the gingivitis would suggest inflammatory gingival hyperplasia as an etiology of the clubbing in the present case.

Etiology of clubbed fingers includes bowel inflammatory diseases such as Crohn’s disease and ulcerative colitis (10, 11, 13). Inflammatory or neoplastic diseases of esophagus and nasopharynx have also been reported to have association with clubbed fingers (2–4, 18, 19). Thus, it is possible that diseases in any part of the alimentary tract would have association with clubbed fingers. Oral inflammatory diseases such as inflammatory gingival hyperplasia should be added to a list of etiology of clubbing.

Essential pathogenesis of clubbed fingers is thickening of the nail bed connective tissue. Morphological changes at the microscopic level include the presence of primitive fibroblasts, increased numbers of eosinophils and lymphocytes and increased caliber and numbers of vessels (1, 3, 20). Genetic predisposition, vagally mediated neural mechanisms, and the direct effect of tissue hypoxia or of circulating vaso-dilators that elude metabolism in the lung through right-to-left shunting have all been proposed to explain the morphological changes (20). However, it has not been possible to formulate a comprehensive theory of a pathogenesis applicable to all of the clinical circumstances (1, 3, 20).

Evidence for immunological involvement includes positive autoimmune antibodies and immune complex (21, 22). A case of lupus erythematosus has been reported as the etiology of clubbing (22). In the present case, laboratory examination revealed positive anti-double strand DNA antibodies at 20.1 IU/ml, which is more significant than anti-single strand DNA antibodies. The combination of clubbing, occlusion of central vein thrombosis and positive anti-double strand DNA antibody may suggest underlying autoimmune diseases. However, a diagnosis of lupus erythematosus was unlikely in the present case, because there were no typical findings including cytopenia, positive anti-nuclear antibodies, anti-phospholipid antibodies such as anti-CL-β₂GP1 and abnormal urinary sediments. As the gingivitis went into remission, the symptoms and signs of clubbed fingers were gradually regressed and anti-double strand DNA antibodies decreased to a normal range. Although there was no decrease of serum complements suggesting involvement of immune complex, concomitant elevation of anti-double strand DNA antibodies with clubbing and inflammatory gingival hyperplasia would lead one to consider an underlying autoimmune process in the present case. Inflammatory gingival hyperplasia has also been suggested to be induced by autoimmune or allergic process (23–27).

Of note in the laboratory data of the present case was eosinophilia in the peripheral blood, which was more prominent while gingival hyperplasia was regressed after the resection of teeth. Inflammatory gingival hyperplasia results from chronic inflammation of the gingival tissues such as periodontitis (23). The infiltration of eosinophils and plasma cells is seen occasionally (23). The peripheral eosinophilia in the present case may reflect a marked infiltration of eosinophils in the gingival lesion, and enhanced by tissue repair in the wound healing after the resection of teeth (28).

In summary, inflammatory gingival hyperplasia was suggested as an underlying cause of clubbing in the present case. The autoimmune process in the pathogenesis was considered. We recommend examination of the oral cavity for search of an inflammatory disease, particularly when other common causes for clubbing are not likely present.

References