Atypical localization of rheumatoid nodule: case report

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ACTA REUMATOL PORT. 2015;40:81-84

ABSTRACT

Rheumatoid nodules can be seen in about 30% of patients with rheumatoid arthritis. They are occasionally localized subcutaneously, but they can rarely be seen in visceral organs. Their appearance can be confused with many clinical conditions when they have atypical localizations. To exclude the presence of a malignancy, these lesions should always be investigated. We aimed to discuss a patient with rheumatoid nodule localized in close neighbourhood of hyoid bone, presumed as a malignancy.

Keywords: Hyoid bone; Malignancy; Rheumatoid nodule; Mass.

INTRODUCTION

Rheumatoid arthritis (RA) is a chronic autoimmune disease with unknown aetiology, which is characterized by peripheral symmetrical polyarthritis, typically with joint and bone erosion that leads to deformity and destruction[1]. Most common extra-articular involvement in patients with RA are subcutaneous rheumatoid nodules[2]. Subcutaneous nodules are usually seen on the extensor surface of the proximal ulna and in areas subjected to pressure such as sacrum, Achilles tendon, occipital area and hand tendons. Visceral rheumatoid nodules are detected in areas such as lung, heart, larynx and vocal cords[3].

The prevalence of laryngeal involvement in RA ranges from 13 to 75% in various clinical studies, and between 45 and 88% in post-mortem studies[4,5]. Laryngoscopic examination can demonstrate mucosal oedema, hyperaemia, swelling of the arytenoids, intrinsic laryngeal muscle myositis, epiglottitis, crycoarytenoid joint (CJ) involvement, reduction in mobility of the vocal cords and vocal cord rheumatoid nodules[4-7]. If an atypically localized space-occupying lesion detected in patients with complaints like throat ache, hoarseness; primarily malignancy and benign laryngeal lesions are considered, a rheumatoid nodule may not come to mind[8]. This can cause confusion, misdiagnosis and exposure of patients to unnecessary tests. In this case we aimed to discuss the case of a patient with a rheumatoid nodule localized in close neighbourhood of the hyoid bone, that had presumed malignancy and to performe a review of the literature.

CASE REPORT

Forty-nine years old female patient with a diagnosis of RA for 25 years, admitted to our clinic due to an increase in complaints of wide-spread joint pain and morning stiffness. After diagnosis, the patient had been treated with hydroxychloroquine, sulfasalazine, leflunomide and corticosteroid during short periods. She had not been receiving any treatment in last 2 years and had dificulties in performing everyday activities due to the weakness, fatigue and pain. She referred dysphagia in swallowing, sore throat and hoarseness for four months. She did not describe mouth and eye dryness, rashes, aphthous lesions, diarrhea, abdominal pain or an infection recently. She had no previous history of surgery or major trauma and hadn't been used any other drugs for a systemic disease.

On physical examination the patient's body temperature was 36,1ºC; blood pressure 120/70 mmHg; heart rate 80 beats per minute. Examination of locomotor

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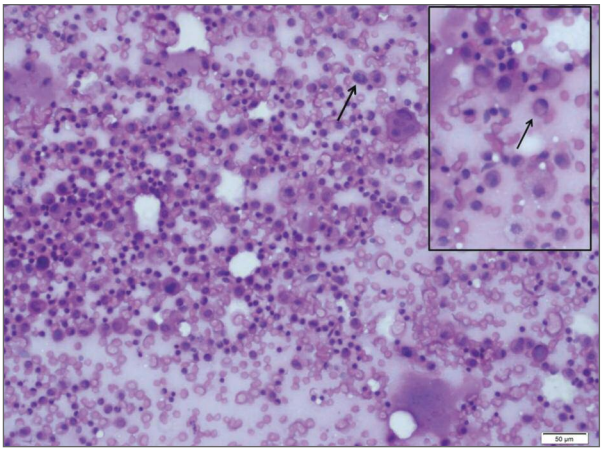

FIGURE 1. Hypercellular smear shows a predominantly isolated single dispersed cell population. Cytoplasm is mostly finely vacuolated or " histiocyte-like". Some cells have eccentric nuclei and abundant eosinophilic cytoplasm, mitotic figure (arrow). Sparse multinucleated cells were also observed. There is an isonucleosis in some cells and a signet ring-like cell (arrow, inset) (Hematoxylin&Eosin X200)

system revealed tenderness in the joints of the hands and feet, bilateral swelling of the 1st and 2nd metacarpal joint and bilateral Z deformity of the thumb. In neck palpation, a hard mobile 2x2 cm lymphadenopathy was discovered on the left side, about the level of C3. Rheumatoid nodules were present on the right olecranon. No further changes were observed on examination.

The basic laboratory tests including complete blood count, erythrocyte sedimentation rate (ESR), blood biochemistry findings, rheumatoid factor (RF), liver function tests and urinary analysis were within normal limits. Disease activity score (DAS-28) was calculated as 4.41. Upon detection of thyroid-stimulating hormone (TSH): 5.65 uIU/ml (0.35-5.50), FT3: 2.24 pg/ml (2.3-4.2), FT4: 1.2 ng/dL (0.88-1.72) thyroid ultrasonography (USG) and thyroid antibody tests were planned. In USG slight coarsening was observed in the parenchyma of the thyroid gland but no nodules detected. A mass lesion about 13x9.33 mm was located posterior to the hyoid bone. The lesion was heterogeneous, hypoechoic and its borders were indistinguishable. In differential diagnosis necrotic lymph node and complicated cystic lesion was considered. Magnetic resonance imaging (MRI) examination, thyroid scintigraphy and fine-needle aspiration biopsy (FNA) was planned. Diffuse hyperplasia was found in thyroid scintigraphy. Thyroid autoantibodies were negative.

In neck MRI lingular tonsil volumes had increased. A tissue that had the same signal characteristics as thyroid gland was discovered at the right of hyoid bone, between strep muscles. The patient was referred to the endocrinology clinic and an USG guided FNA biopsy was performed to the mass. The cytological examination of the obtained smears revealed a large number of isolated atypical cells with eosinophilic, vacuolated or clear cytoplasm, "histiocytic" cells, some of them were suggestive for signet-ring cells, in a amorphous eosinophilic material background (Figure 1). Mitotic figure and anisonucleosis was observed in some cells. A small number of multinucleated giant cell histiocytes were also seen. Cytomorphological findings were primarily considered as a neoplasm with a cystic component and metastatic carcinomas (signet ring or renal cell carcinoma) were also suspected. Clinical, radiological examination and excision of mass for definitive diagnosis was recommended.

The biopsy results were discussed at the Otolaryngology, Urology and General Surgery clinics. There were no malignancy findings in gastroscopy and colonoscopy. No pathological findings were detected in computed tomography (CT) of all abdomen and high-resolution CT of lung. Ear, nose and throat (ENT) Clinic performed a biopsy with flexible laryngoscopy. In pathological examination a cell organization that may accompany inflammatory cystic neoplasm was observed. Total excision of the mass was recommended. Pathological examination of the excisional biopsy showed features of a rheumatoid nodule (Figures 2 and 3). The patient's medical treatment was planned and scheduled a follow-up in our rheumatic diseases clinic.

DISCUSSION

Rheumatoid nodules are seen in approximately 30% of RA patients. They can be detected on the compression exposed areas like elbows, forearms, fingers, tendons, sacrum, heel bone and visceral organs (liver, kidney, lung, heart), larynx, pharynx, trachea, vocal cords, penis, vulva and breast[3,7,9-13]. Most nodules are asymptomatic, but those located under pressure areas such as periosteum or tendons, can be painful[2,3]. Nodules are more common in RA patients who have RF and anti-cyclic citrullinated peptide (anti-CCP) positivity, bone erosions and extra articular manifestations.

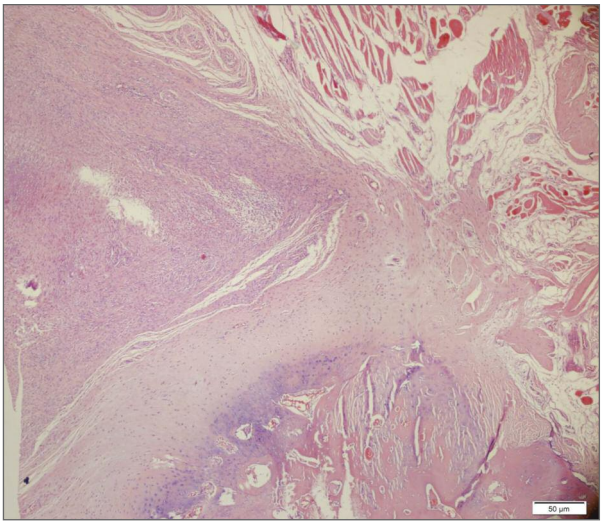

FIGURE 2. The mass-forming diffuse cellular infiltration nearby hyoid bone and muscle tissue (Hematoxylin&Eosin X40)

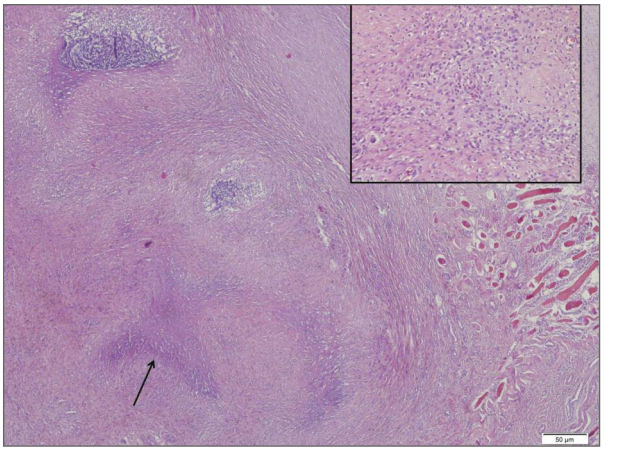

FIGURE 3. Rheumatoid nodule: nodular lesion infiltrating the striated muscle; fibrin deposition and necrobiosis is seen in centre of nodule surrounded by histiocytes, proliferated vascular endothelial cells, lymphocytes, plasma cells and occasional giant cells (Hematoxylin&Eosin X40, inset X100)

Nodules are generally seen in long-term disease[3]. Also, increased rheumatoid nodule formation has been reported with methotrexate treatment[14].

The pathogenesis of rheumatoid nodules is not clearly understood. However, has been hypothesized that trauma to pressure points on the body, with subsequent small haemorrhages, results in accumulation of RF complexes at the site of the injury. RF complexes have a chemotactic role in immune response by activating local monocytes and developing local vasculitis. Involvement of T and B-lymphocytes increases the immune response[15]. This explains the formation of rheumatoid nodules also in the internal organs and in the skin that are exposed to micro traumas, like our case.

Laryngeal manifestations of RA involve CJ arthritis, rheumatoid nodules, and rarely amyloidosis as well as secondary Sjogren's syndrome affecting the larynx[4-6]. The larynx and vocal cord rheumatoid nodules have been reported in literature[7,9,11]. However, there is only a single case report like our patient that has a rheumatoid nodule localized in close neighbourhood of the hyoid bone. Gomez-Rivera et al.[10] detected a mass lesion adjacent to the hyoid using CT in a patient presenting with sensitivity at the base of tongue. After failing to diagnose with FNA biopsy, the excision of was compatible with a rheumatoid nodule on pathological examination. In our case, rheumatoid nodule was located in the posterior left para-median of hyoid bone.

Larynx rheumatoid nodules may present with many symptoms. Dyspnoea, stridor, hoarseness, fullness in the throat and pain in swallowing are some of them[5,12,13]. In patients with RA if one of these findings suggesting larynx involvement are present, radiographs may be used for showing most common involvement erosive CJ arthritis. However CT is considered the method of choice. The main findings that include CJ thickening or erosions, arytenoid subluxation and asymmetry of the glottis or aryepiglottic folds can be better displayed by CT[4,16]. We primarily examined our patient with a neck MRI, because of suspected cystic or necrotic lymph node component of the mass lesion. Other imaging methods were also used in the differential diagnosis by clinical suspicion during follow-up.

As our patient, FNA can be applied to mass lesions for the differential diagnosis. The histologic progression of rheumatoid nodules occurs in three stages: an acute inflammatory stage, a granulomatous stage, and finally a necrotic stage[17-19]. In the last stage the pathological examination shows, a central necrotic area, which is surrounded by a palisading mononuclear cell infiltrate and a zone of vascular connective tissue. Lymphocytes and plasma cells are present peripherally around the palisading layer[15,18,19]. FNA of rheumatoid nodules are not commonly applied and the cytological features of such nodules may not be as well characterized as the histologic features. The age and size of the nodule affects the composition of the aspirated

material. Particularly atypical spindle cells with hyperchromatic and large nuclei found in biopsy materials, may suggest neoplasms in diagnosis[17].

In our case, signet ring-like macrophages and histiocytic or cells with clear cytoplasm, some cells with hyperchromatic nuclei and atypical cells were seen in ultrasound-guided FNA biopsy material of the mass near hyoid bone. Those findings led to suspect of metastases from kidney or gastrointestinal tract, malignant and benign laryngeal lesions as differential diagnosis. Like our case; patients that had biopsy findings mixed with squamous cell carcinoma have been reported in the literature[10,20].

In the presence of laryngeal masses; laryngocele, amyloidosis, papillomas and inflammatory processes like tuberculosis from benign lesions; squamous cell carcinoma, adenoid cystic carcinoma, lymphoma, and sarcoma from malignancies, should primarily be considered in the differential diagnosis[10].

Steroid use has been associated with improvement in symptoms in laryngeal rheumatoid nodules. Large symptomatic nodules can be excised with laryngoscopy. Also there are cases that have benefited from colchicine treatment[4,9].

Viscerally localized rheumatoid nodules may be confused with many clinical conditions especially with malignancies due to biopsy findings and mass like appearance. Clinicians should be aware of rheumatoid nodules as a potential cause of laryngeal masses, mainly in advanced long-standing RA.

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