

NASAL SEPTUM PERFORATION OF LUPIC CAUSE ASSOCIATED WITH cANCA - CASE REPORT

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REZUMAT

Perforațiile septului nazal pot avea multiple cauze: traumatice, cancer, boli sistemice, infecțioase, toxice. În lupusul eritematos sistemic, perforația septului nazal este considerată o formă rară de manifestare a bolii. Prezentăm un caz de perforație asimptomatică de sept nazal la o femeie de 46 ani, diagnosticată cu lupus eritematos sistemic cu 2 ani anterior.

Cuvinte cheie: perforație de sept nazal, lupus eritematos sistemic, vasculită, ANCA

ABSTRACT

Nasal septum perforation can have multiple and various causes: traumatic causes, cancer, systemic diseases, infectious diseases, toxic causes. In systemic lupus erythematosus the nasal septum perforation is only sporadically reported being considered a rare clinical manifestation. We present a case of asymptotically nasal septum perforation in a 46-year-old woman, patient diagnosed with systemic lupus erythematosus two years previously. We carried out a set of investigations in order to appreciate the disease evolution, to confirm the presence of the nasal septum perforation and to exclude the other causes of nasal perforation. We determined the ANCA and we found a titer of 4.1 U/ml (normal value <6 U/ml) for p-ANCA and a high titer for c-ANCA. The association between systemic lupus erythematosus, nasal septal perforation and presence of c-ANCA has not yet been reported in any case related so far in the literature.

Key Words: nasal septum perforation, systemic lupus erythematosus, vasculitis, ANCA

INTRODUCTION

Nasal septum perforation can have multiple and various causes. In practice the most frequent of them are: traumatic causes, cancer, systemic diseases, infectious diseases, toxic causes.¹ It is very important to set up the causes of the nasal septum perforation in order to be able to decide the future therapy based on a rigorously taken anamnesis, on a minute clinical examination as well as on some targeted explorations depending on the clinical suspicion. In systemic lupus erythematosus the nasal septum perforation is only sporadically

reported being considered a rare clinical manifestation, which can be detected either during disease exacerbation or just at random after many years after diagnosis was made.¹ It is controversial whether the nasal septum perforation or ulcer is secondary to a simple inflammatory mucositis or a frank vasculitis of the mucous membranes.^{2,3,5}

Primary vasculitis can occur by itself without any obvious associated infection or other illness. Another type is represented by secondary vasculitis. Some of the illnesses that can cause secondary vasculitis are: systemic lupus erythematosus, rheumatoid arthritis, polymyalgia rheumatica, scleroderma, Wegener's granulomatosis, temporal arteritis, cryoglobulinemia, erythema nodosum, tumors, leukemia, lymphoma.^{2,3,5} The characteristic clinical appearance depends on the involved vascular segment, small vessels in Wegener's disease and microscopic polyangiitis, medium vessels in Churg-Strauss syndrome and panarteritis nodosa and large vessels in Horton's arteritis and Takayasu's arteritis.^{2,3,5} In 1989, at the First International ANCA Workshop, ANCA were established as useful markers

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for certain small vessel vasculitis.

Lupus patients may develop secondary vasculitis that is usually a lymphocytic proliferative vasculitis and perivasculitis with concentric fibrosis ("onion skin"). In lupus, there p-ANCA are an usual finding, the presence of c-ANCA being sporadically reported and strongly suggesting an associated small vessel vasculitis.^{4,5}

In this paper we report a case of systemic lupus erythematosus with nasal septum perforation associated with c-ANCA.

CASE REPORT

A 46-year-old woman, patient diagnosed with systemic lupus erythematosus two years previously, came in for a routine examination. The patient had no symptoms and was under treatment with 20 mg/day Prednisone, bisphosphonates (Fosamax), calcium, vitamin D. The clinical examination showed a typical look of „butterfly” facial rash and multiple scars on the skin as well as the presence of a visible nasal septum perforation at nasal cavity examination (Fig.1). All the other systems and organs were normal.



Figure 1. Visible nasal septum perforation

We carried out a set of investigations in order to appreciate the disease evolution: complete blood count, erythrocyte sedimentation rate, creatinine and electrolytes, immunologic tests (seric complement, antidsDNA and ANCA) urine tests (measuring the protein, detecting hematuria, leukocyturia). In our patient the antidsDNA had an increased level, 276 U/ml (nominal value <40 U/ml). We considered them in the clinical context, the patient being asymptomatic, and in correlation with the other analyses that were normal. We determined the ANCA and we found a titer of 4.1 U/ml (normal value <6 U/ml) for p-ANCA and a high titer for c-ANCA, 21 U/ml (nominal value <10 U/ml).

To confirm the presence of the nasal septum perforation the patient was referred to an otolaryngologist for evaluation. An anterior rhinoscopy exam was car-

ried out and a large anterior perforation, about 9 mm was found. A nasal septum biopsy was performed. The anatomical result excluded a neoplastic cause and Wegener's disease, revealing only an appearance of chronic inflammation.

Explorations were conducted to detect the corticotherapy complications: ophthalmologic consultation which excluded the cataract, the glycemia level which excluded the presence of steroid induced diabetes, osteodensitometry for controlling prolonged corticotherapy induced osteoporosis. Based on medical history, clinical examination and laboratory exploration we considered that our patient presented an asymptomatic nasal septum perforation as part of the systemic disease: systemic lupus erythematosus. Our patient was treated only with corticotherapy. After four years from diagnosis the patient's prognosis was good without complications.

DISCUSSIONS

The systemic lupus erythematosus is considered an inflammatory disease with a self-immune mechanism affecting a large number of systems and organs and which is characterized by unexpecting exacerbations and remissions.^{2,5} Due to the protean clinical manifestations that could mime any other disease, lupus is considered the greatest "imitator".^{2,3}

The clinical manifestations may vary in time fact which generates difficulties in diagnosing, reason for which the American Rheumatology Association (ARA) issued 11 symptoms and signs that could help us in differentiating lupus of other diseases and that represent the diagnostic criteria for systemic lupus erythematosus:^{2,4}

1. Malar rash;
2. Discoid rash;
3. Photosensitivity;
4. Oral or nasal ulcers;
5. Nonerosive arthritis;
6. Serositis (pleuritis or pericarditis);
7. Renal disorders;
8. Neurologic disorders (seizures or psychosis);
9. Hematologic disorders (hemolytic anemia or leukopenia or lymphopenia or thrombocytopenia);
10. Immunologic disorders (anti-dsDNA or anti-Sm or antiphospholipid antibodies);
11. Antinuclear antibodies.

Four of the 11 ARA criteria are necessary and sufficient at a given moment in order to diagnose the patient as having SLE.^{2,4} There are also situations the patients present only two or three ARA criteria for lupus but if she/he has anti-nuclear antibodies present

or the cutaneous or renal biopsy is suggestive for lupus then the diagnosis can be made.^{2,3} Also, it can happen that a patient with obvious clinical symptoms and signs of lupus has no antinuclear antibodies, fact which does not rule out the lupus diagnosis.^{2,3} Our patient, at the moment of diagnosing, showed eight out of eleven criteria for lupus.

Many authors consider the appearing of nasal septum perforation in lupus a rare clinical manifestation as a proof it is included much later within the diagnosing criteria of lupus.^{2,4} There are very few data in the literature regarding the frequency of nasal septum perforation appearing in each detected disease, including lupus. It can be detected on clinical examination or at rhinoscopy, just by chance, after many years after the disease has been diagnosed or sometimes during or after an exacerbation of the lupus.^{2,6}

In other authors' opinion the nasal septum perforation is a clinical manifestation considered usual in lupus but subdiagnosed because it is asymptomatic and it develops independent of the lupus treatment. For this reason, Vignes and co-workers consider that all the patients diagnosed with lupus or any other systemic disease should be submitted to the examination of the nasal cavity even if they are asymptomatic.^{4,6-8} Most of the authors who published data on nasal septum perforation consider that nasal septum biopsy has no significant contribution for the diagnosis and that it would be recommended only to exclude a neoplastic cause.⁴⁻⁸

We considered necessary to carry out the nasal septum biopsy for our patient as a consequence of detecting c-ANCA in a significant titer. ANCA are associated with a number of vasculitis including Wegener's disease, Churg-Strauss disease, microscopic polyangiitis and idiopathic necrotizing and crescentic glomerulonephritis.^{2,3,5,9} Wegener's disease is the only vasculitis in which c-ANCA are associated with septal nasal perforation.^{2,3,5,9} In our case it is important to elucidate if Wegener's disease is associated or not with systemic lupus erythematosus.¹⁰ Our patient doesn't meet the diagnosis criteria for Wegener's granulomatosis. She doesn't have haematuria or abnormal chest X-Ray and also she doesn't have granulomatous inflammation on biopsy. The presence of two or more of these criteria in a patient with vasculitis supports the diagnosis of Wegener's granulomatosis.

In 1994, Kallenberg et al. as well as Hagen et al., in 1993 showed that ANCA could be present both in lupus and in other collagen diseases as a result of the presence of the associated vasculitis.^{9,11,12} In lupus, vasculitis is determined by a series of unknown antigens that lead to the development of immune complexes.^{2,4,9,11,12} In a cohort of 566 patients with systemic

lupus erythematosus, Galeazzi and co-workers showed that ANCA were detectable and were associated with particular clinical manifestations. They could not elucidate at that time whether "ANCA plays a direct pathogenic role in the vascular damage of systemic lupus erythematosus or represents an epiphenomenon or a marker of disease activity".^{2,5,12}

Some authors consider the appearing of these antibodies in lupus could be explained by more hypotheses: either they are not typical antibodies (at immunofluorescence there are perinuclear but at ELISA testing they are negative MPO) or falsely positive c-ANCA antibodies. The role of C-ANCA in reinforcing the diagnosis of collagen diseases is limited enough compared to the special importance of detecting them in Wegener disease.^{9,11,13}

The guidelines regarding the patient testing for revealing antinuclear antibodies recommend initially testing by indirect immunofluorescence and later a more specific ELISA method that will outdistance the two types of antibodies in: c-ANCA (anti PR3) and in p-ANCA (anti MPO, anti lactoferrin, etc.).¹³

CONCLUSIONS

We presented this case as a consequence of the clinical rareness of a nasal septum perforation in systemic lupus erythematosus as well as of the association with the presence of c-ANCA, as we could not find any similar case related so far in the literature. The characteristic features presented by our patient are in agreement with the data in the literature regarding the asymptomatic aspect of the disease, occasional detection, as well as the decreased contribution of nasal septum biopsy in setting the diagnosis.

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