CASE REPORT

RJME
Romanian Journal of Morphology & Embryology
http://www.rjme.ro/

# Silent sinus syndrome – report of a case

DANIELA DUMITRESCU[1)], BOGDAN FĂNUŢĂ[2)], ALEX EMILIAN STEPAN[3)], ADRIAN IOAN FRONIE[4)], CRISTIANA IULIA DUMITRESCU[5)], MARIUS CRISTIAN MÂRŢU[6)], PETRA ŞURLIN[7)], VALERIU ŞURLIN[8)], MIHAI POPESCU[9)]

[1)]*Department of Radiology, Emergency County Hospital, Craiova, Romania*
[2)]*Department of ENT, Emergency County Hospital, Craiova, Romania*
[3)]*Laboratory of Pathological Anatomy, Emergency County Hospital, Craiova, Romania*
[4)]*Department of Oro-Maxillo-Facial Surgery, Emergency County Hospital, Craiova, Romania*
[5)]*Department of Clinical Pharmacology, University of Medicine and Pharmacy of Craiova, Romania*
[6)]*Department of ENT, "Grigore T. Popa" University of Medicine and Pharmacy, Iassy, Romania*
[7)]*Department of Periodontology, University of Medicine and Pharmacy of Craiova, Romania*
[8)]*I[st] Clinic of Surgery, University of Medicine and Pharmacy of Craiova, Romania*
[9)]*Department of Radiology, Emergency County Hospital, Craiova, Romania*

## Abstract

*Introduction*: The "silent sinus syndrome" is a rare entity that was first described in 1964 and given this name 30 years later. Although it is well described both from clinically and radiologically point of view we consider that its rarity still makes it a subject for report. *Case presentation*: A 46-year-old patient was admitted for facial asymmetry, diplopia, unilateral left enophthalmos, and inferior displacement of the eye globe, and decreased occlusal pressure in left dentate region. CT scan revealed interior bulging of all left maxillary sinus walls with osteolysis and intense opacification, enlargement of the left middle meatus especially in the posterior part and lateralization of the uncinate process. Nasal endoscopy with 00 rigid scope visualized mild deviation to the right of the nasal septum, enlargement of the left middle meatus by the lateral deviation of the left intersinusal septum and uncinate process. Surgery was scheduled and performed a left maxillary sinus antrostomy. Histopathological examination on the biopsies revealed inflammation. A complete study was performed to assess the elements of inflammation. Postoperative course was simple. Follow-up visit at three and six months, showed significant regression of diplopia and improved facial aspect. *Conclusions*: Silent sinus syndrome is a well-defined clinical entity with characteristic imagistic findings. Surgical intervention that restores sinus drainage will interrupt the pathogenesis of the disease and lead to its progressive regression. Topographic associations and density of inflammatory elements analyzed in relation with neoforming vessels suggest their implication in reparatory angiogenesis characteristic to chronic inflammation. Modulating activity in the frame of inflammatory process, of the T-lymphocytes and especially of T-lymphocytes may represent a target for the therapeutic management. Surgery can and should be performed by an endoscopic approach.

***Keywords***: silent sinus syndrome, chronic inflammation, enophtalmos, antrostomy, endoscopic surgery.

## Introduction

The "silent sinus syndrome" is a rare entity that was first described in 1964 [1] and given this name 30 years later [2]. Numerous reports were made ever since in otorhinolaryngology, ophthalmology [1–10] and lately in radiology journals [11–13], so the clinical and radiological aspects of the syndrome are well defined. However, its pathogenesis is not completely understood, inflammation and obstruction of the maxillary sinus playing an important role [1–3].

We consider that its rarity and peculiar pathogenesis are still a subject for debate are advocates for a new case report, in which, beside clinical and imagistic aspects, we add a histological and immunohistochemical study of the inflammatory changes inside the sinus.

## Case report

A 46-year-old patient was admitted for facial asymmetry, diplopia, unilateral left enophthalmos, and inferior displacement of the eye globe and decreased occlusal pressure in the left dentate region (Figure 1). CT scan revealed: in coronal section, a completely opacified left maxillary sinus, retraction and thinning of the orbit floor of the left maxillary sinus, enlargement of the left middle meatus, lateralization and thinning of the left uncinate process (Figures 2A and 3A); in sagittal reconstruction, the retraction and thinning of the superior and posterior walls of the left maxillary sinus (Figure 2B); in axial section, the retraction and thinning of the posterior wall of the left maxillary sinus and enlargement of the pterygo-maxilarry fossa (Figure 4A). Nasal endoscopy with $0^0$ rigid scope visualized mild deviation to the right of the nasal septum, enlargement of the left middle meatus by the lateral deviation of the left intrasinusal septum and uncinate process, retraction of the superior and posterior walls of the left maxillary sinus and their thinning (Figures 2C and 3B). Surgery was scheduled and performed under endoscopic vision achieving a left maxillary sinus antrostomy to ensure its drainage (Figure 4B).

A complex histological examination was performed on the biopsies taken from the maxillary sinus that revealed inflammation.

We aimed for identification, density and distribution of inflammatory elements (lymphocytes, plasmocytes, macrophages) in relationship with angiogenesis, question vascular microdensity at the level of the sinusal mucosae with chronic non-specific inflammation.

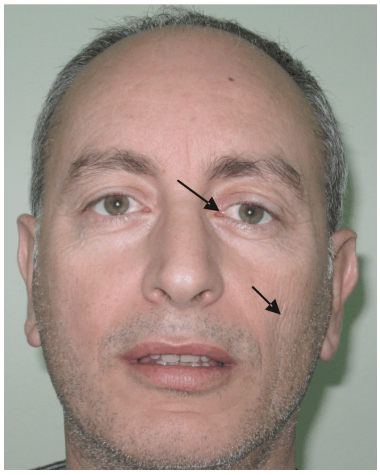

**Figure 1** – ***Left enophthalmos and hypoglobus. Wrinkles on the left genian region, noticed by the patients few months before diplopia (black arrows).***

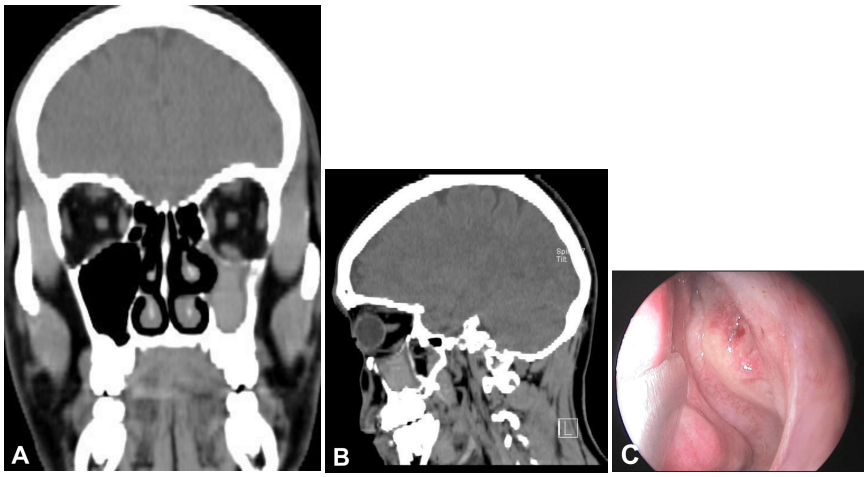


**Figure 2** – ***(A) CT-scan, coronal section. Retraction of the orbit floor of the left maxillary sinus and thinning; enlargement of the left middle meatus. Lateralization of the left uncinate process and its thinning. (B) CT-scan, sagittal reconstruction; retraction and thinning of the superior and posterior walls of the left maxillary sinus. (C) Nasal endoscopy. Enlargement of the middle left meatus, lateralization of the left uncinate process and thinning.***

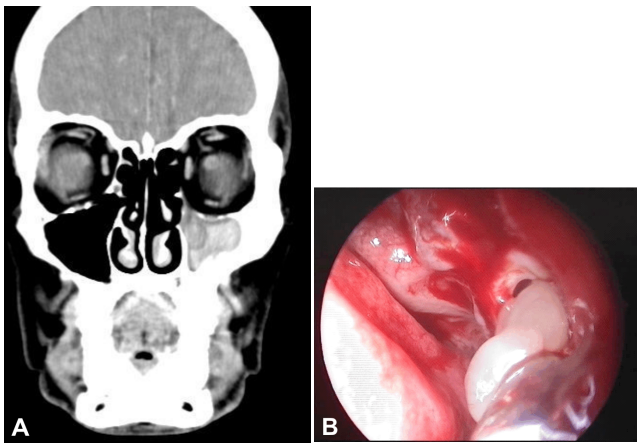


**Figure 3** – ***(A) CT-scan, coronal section. Completely opacified left maxillary sinus. (B) Nasal endoscopy. Secretions at the ostium of the left maxillary sinus.***

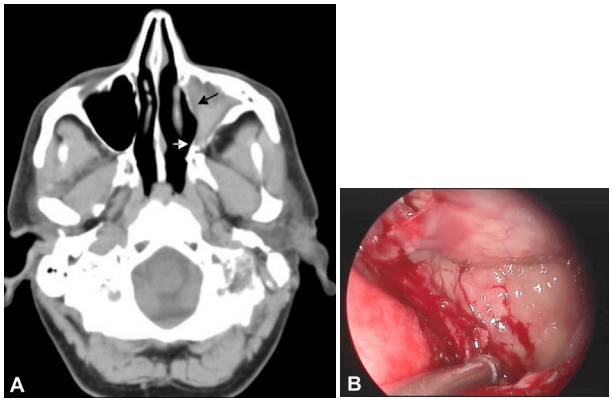


**Figure 4** – ***(A) CT-scan, axial section. Retraction of the posterior wall of the left maxillary sinus and thinning with enlargement of the pterygomaxillary fossae. (B) Nasal endoscopy. Retraction of the superior and posterior walls of the left maxillary sinus and their thinning.***

## Materials and Methods

The study included a case of chronic nonspecific inflammatory lesions of sinus mucosa, diagnosed in the Laboratory of Pathological Anatomy, Emergency County Hospital, Craiova, Romania.

Biological material was represented by biopsy specimens, which were fixed in 10% buffered neutral formalin, processed for paraffin embedding and Hematoxylin–Eosin (HE) staining.

Morphological parameters were investigated and immunohistochemical analysis was performed on serial sections, the panel of antibodies used being shown in Table 1.

For immunohistochemical analysis, we used simple reactions. After antigen retrieval, endogenous enzyme blocking, and unspecific sites' blocking, the sections were incubated overnight with primary antibodies. The next day, for CD45, CD20, CD8, CD138, CD31, the sections were incubated with biotinylated species-specific secondary antibodies and amplified with the LSAB 2 System–HRP (code K0675, Dako). In case of CD4, CD68 it was used the polymeric amplification (Histofine polymer-HRP, Nichirei, Japan). The reactions were visualized with 3,3'-diaminobenzidine tetrahydrochloride (DAB, Dako, code 3467).

We used external positive controls and respectively negative controls, by omitting the primary antibodies.

For the quantification of CD31, we assessed the microvascular density (MVD) by "hot spot" method, which was

the average number of stained blood vessels in three microscopic fields (MF) with the richest vasculature [14]. Areas were identified at 10× MF, and quantification was performed at 20× MF.

The quantification was performed only for small/ medium caliber vessels susceptible to be the result of angiogenesis.

The same method was used for quantification of inflammatory elements. In addition, we used a grading system of inflammatory elements according to Table 2.

**Table 1 –** ***The panel of used antibodies***

| Antibody | Clone/Source | Dilution | Antigen retrieval | External positive control |
|---|---|---|---|---|
| *CD45 (leukocyte common antigen)* | Clone RP2/18, Leica Biosystems | 1:100 | Tris-EDTA, pH 9 | Tonsil |
| *CD20cy* | Clone L26, Dako | 1:150 | Citrate, pH 6 | Tonsil |
| *CD8* | Clone 1A5, Leica Biosystems | 1:40 | Citrate, pH 6 | Tonsil |
| *CD4* | Clone 4B12, Leica Biosystems | 1:100 | Tris-EDTA, pH 9 | Tonsil |
| *CD138* | Clone MI15, Leica Biosystems | RU | Citrate, pH 6 | Tonsil |
| *CD68* | Clone 514H12, Leica Biosystems | 1:100 | Tris-EDTA, pH 9 | Tonsil |
| *CD31* | Clone 1A10, Leica Biosystems | 1:100 | Citrate, pH 6 | Tonsil |

**Table 2 –** ***Inflammatory infiltrate grading***

| Rare diffuse or perivascular inflammatory elements | Moderate diffuse or perivascular inflammatory elements | Massive diffuse or perivascular inflammatory elements |
|---|---|---|
| Grade 1 | Grade 2 | Grade 3 |

## Statistical analysis and image acquisition

For the statistical analysis, it was created an electronic database and the results were compared using the Student's *t*-test (SPSS, Inc., Chicago, IL, USA). All central tendencies were reported as average ± standard deviation (SD). Results were considered significant for *p*-values <0.05. The acquisition of the images was done on a Nikon Eclipse E600 microscope and with the software package Lucia 5.

## Results

Histopathological analysis indicated mononulear inflammatory infiltrate, predominantly intraepithelial lymphoplasmocytary, in the lamina propria and in the seromucosal glands, as though moderate collagenous sclerosis; areas of basal epithelial hyperplasia and capillaries of small and irregular caliber were also observed in the glandular acini (Figure 5, A and B)

Immunoexpression of the analyzed markers was identified in all slices. CD45 immunomarking was observed in the membrane and cytoplasm of the B- and T-lymphocytes and had an increased intensity, compared to the markings of monocytes/histiocytes. Distribution of CD45+ elements was predominantly diffuse intra- and subepithelial (grade 3), with focal periglandular and perivascular accumulations (grade 2) (Figure 2, A and B). Density of CD45+ was between 4–16/microscopic field 400× (MF), with an average of 8.6±3.64/MF.

CD20cy immunoreaction was identified in the apical cytoplasm of B-lymphocytes. CD20+ lymphocytes presented a week diffuse subepithelial distribution, periglandular and perivascular (grade 1) (Figure 2, C and D). Density of CD20+ elements was between 1–4/microscopic field 400× (MF), with an average of 2.2±0.96/MF.

CD4 markings were identified at the membrane of T-helper lymphocytes (ThLy). T-helper lymphocytes presented both massively diffuse (grade 3) and perivascular moderate (grade 2) arrangement (Figure 7, A and B). Density of CD4+ was between 3–12/microscopic field 400× (MF), with an average of 7.8±2.9/MF. CD8 immunoreaction was identified in the apical cytoplasm and membrane of the cytotoxic (TcLy) with week periglandular, intra- and subepithelial diffuse disposition (grade 1), and moderate perivascular arrangement (grade 2) (Figure 7, C and D). Density of CD8+ was between 1–8/ microscopic field 400× (MF), with an average value of 5.3±2.19/MF.

CD138 immunoreaction was identified in the cytoplasm and the membrane of the plasmocytes, as though at the level of basal and intermediate level of the lining epithelia. These showed a moderate perivascular arrangement (grade 2). We observed also a focal periglandular preferential disposition of the CD138+ elements. Density of CD138+ elements was between 2–11/microscopic fields (MF), with an average value of 5.8±2.45/MF. CD68 markings were presented in cytoplasm and membrane of the macrophages, which showed a moderate diffuse and perivascular disposition (grade 2), being also focally distributed around the high caliber vessels, periglandular and in the intermediate and basal layer of the covering epithelia. Density of CD68+ elements was between 2–8/microcopic field 400× (MF), with an average value 6.6±1.8/MF (Figure 8).

CD31 immunoreaction was identified at the level of endothelial cells, which lined the blood vessels of variable caliber. Subepithelial and glandular acini vessels were predominantly of small/medium size caliber, with irregular lumen, some of them with unicellular aspect, and presented a microvascular density (MVD) CD31+ between 2–6/microscopic field 400× (MF), with an average value of 3.4±1.3/MF. On the contrary, the marking in the deep lamina propria belonged to blood vessels of higher caliber, and the reaction was usually discontinuous (Figure 9).

In this study, at the level of the inflammatory infiltrate, we noticed the net predominance of T-lymphocytes compared to B-lymphocytes (T-lymphocytes/B-lymphocyte ratio was 3.9), plasmocytes (T-lymphocytes/plasma cells = 1.4) and macrophages (T-lymphocytes/macrophages = 1.3) (Figure 10).

All analyzed inflammatory elements showed close relationship with neoformation capillaries, T-lymphocytes and macrophages having the highest median density. In

case of T-lymphocytes, T-helper lymphocytes presented a superior average density in relationship with Tc-lymphocytes (1.47 ratio), with no differences compared to neoforming capillaries. We did not noticed any statistical correlations of the MVD with the density of the analyzed inflammatory elements ($p>0.05$, Student's $t$-test).

All elements of inflammation showed also a close relationship with glandular compartment of the lesions, and basal and intermediate layers of the lining epithelia excepting CD4+ T-helper lymphocytes.

Postoperative course was simple. Follow-up visit at three and six months, showed significant regression of diplopia and improved facial aspect. Nasal endoscopy confirmed complete local healing and the patency of the antrostomy. Patient was very satisfied with his facial appearance.

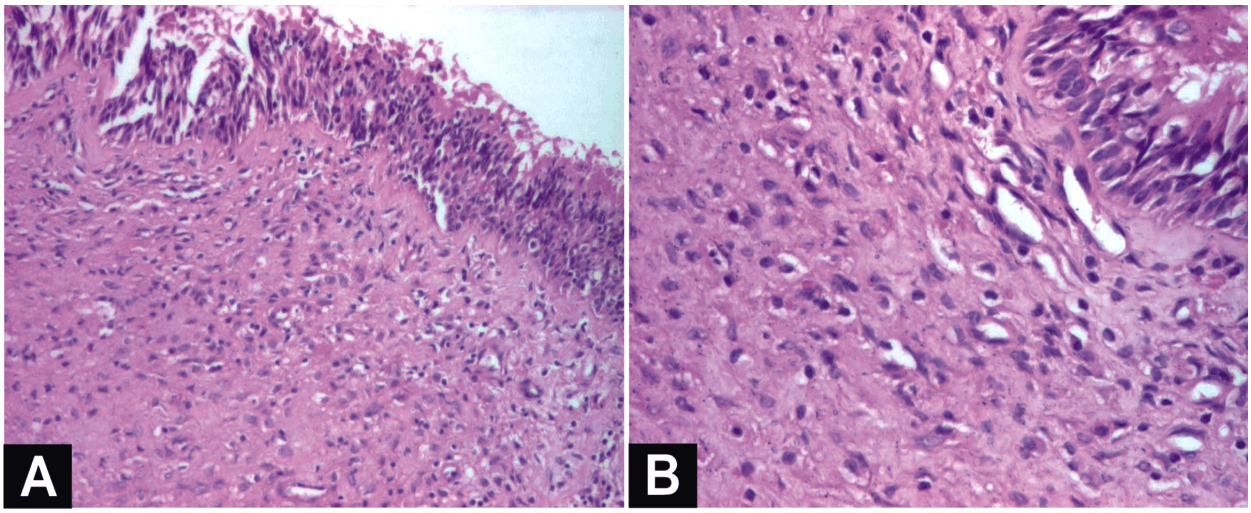


**Figure 5** – ***(A) Sinus mucosa with chronic inflammatory infiltrate, HE staining, ×100. (B) Small and irregular subepithelial vessels, HE staining, ×200.***

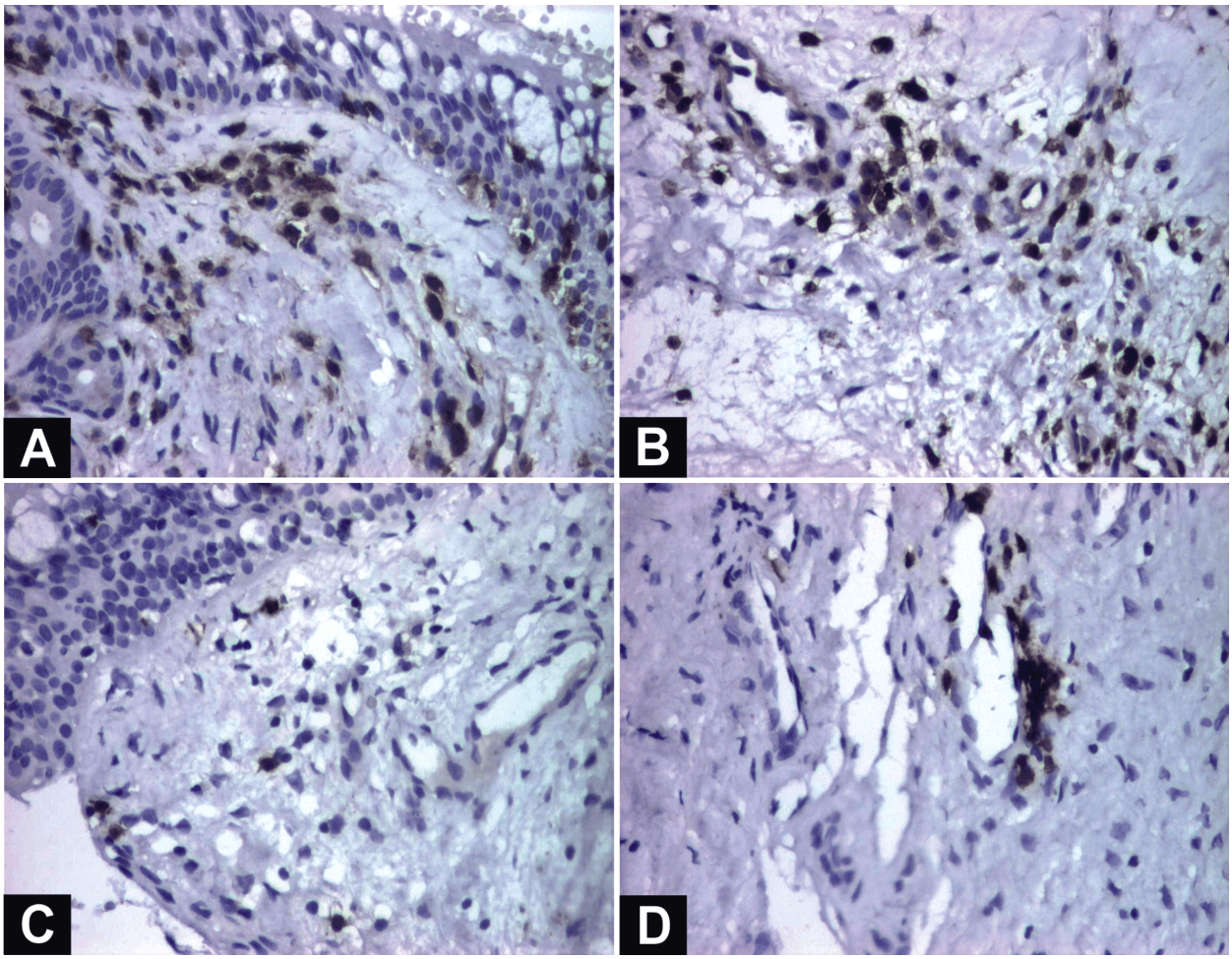


**Figure 6** – ***(A) Diffuse subepithelial lymphocytes, CD45 immunostaining, ×200. (B) Focal perivascular lymphocytes, CD45 immunostaining, ×200. (C) Rare subepithelial B-lymphocytes, CD20cy immunostaining, ×200. (D) B-lymphocytes with perivascular disposal, CD20cy immunostaining, ×200.***

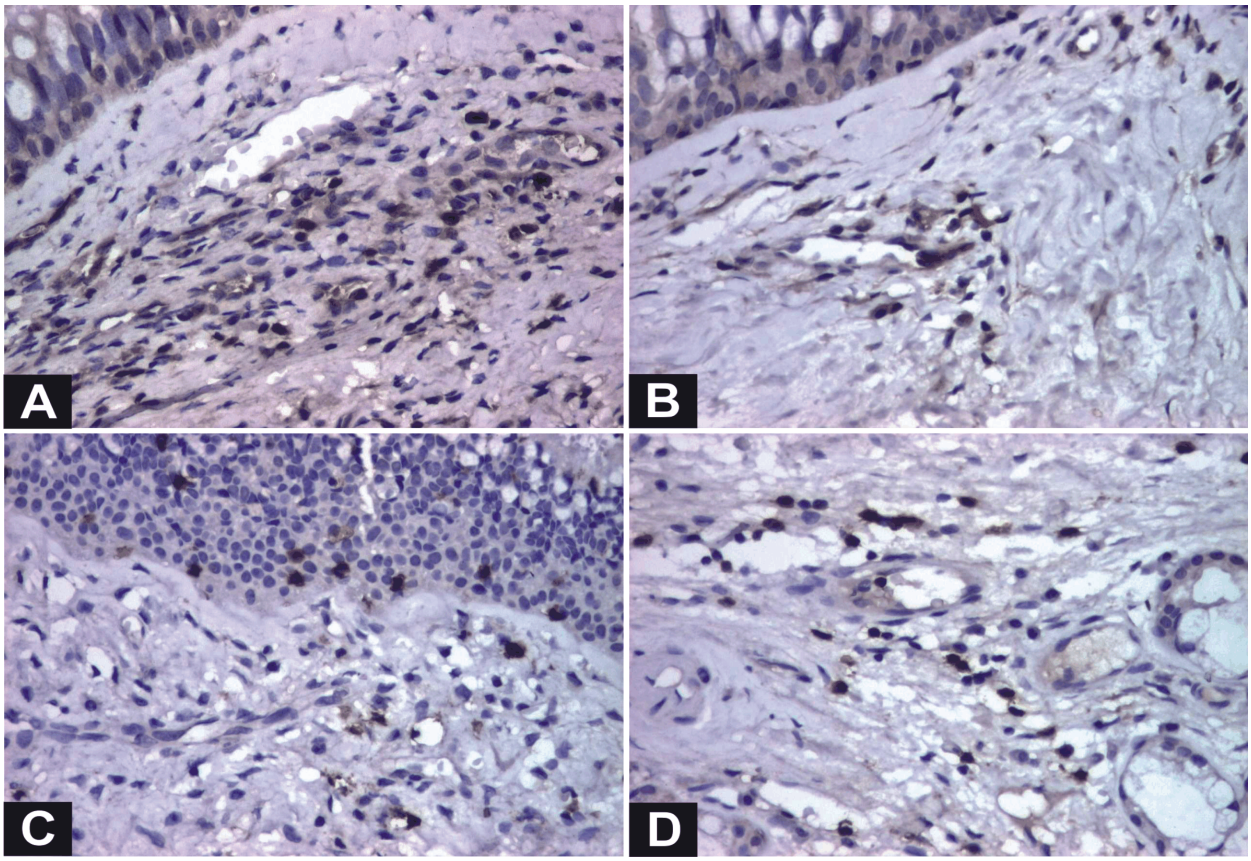


**Figure 7** – ***(A) LyTh with massive diffuse subepithelial disposal, CD4 immunostaining, ×200. (B) Focal perivascular LyTh, CD4 immunostaining, ×200. (C) Rare diffuse intra- and subepithelial LyTc, CD8 immunostaining, ×200. (D) Perivascular LyTc, CD8 immunostaining, ×200.***

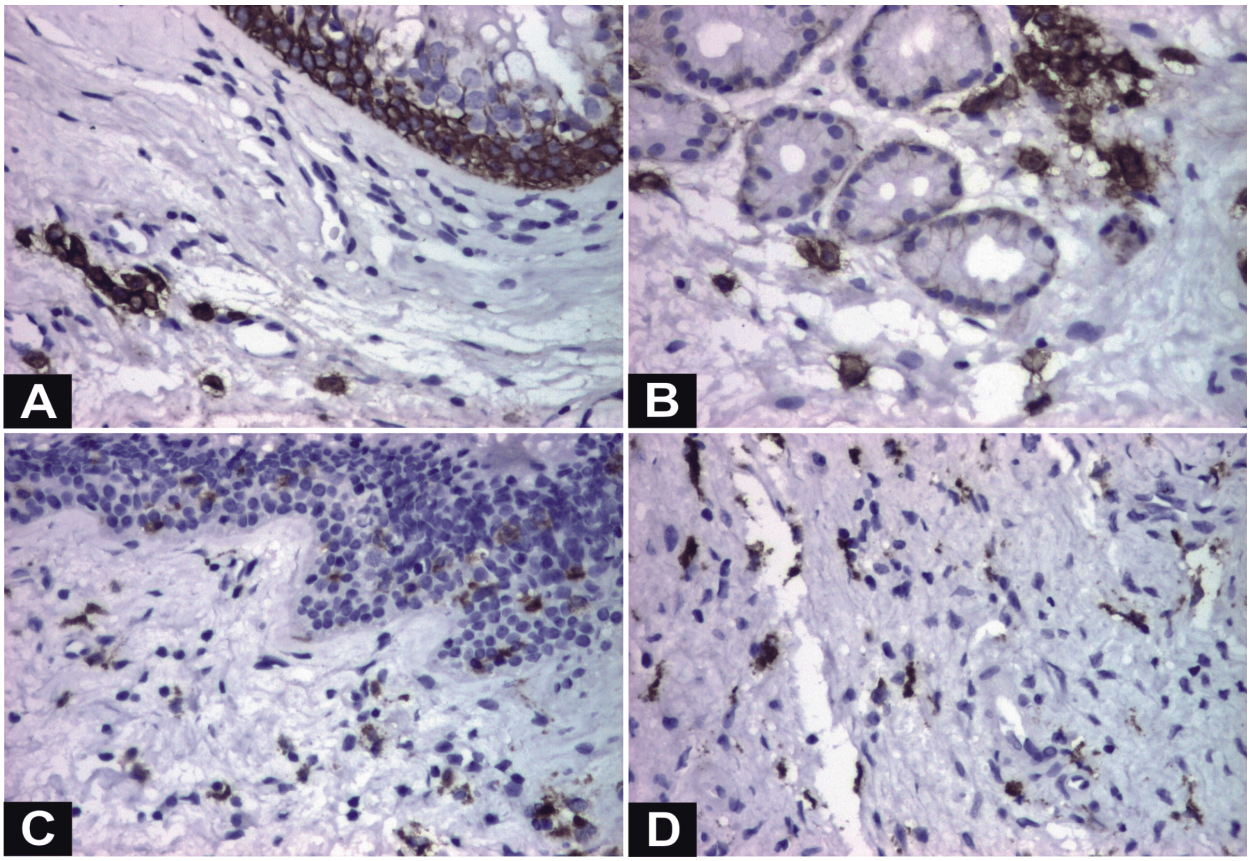


**Figure 8** – ***(A) Moderate perivascular plasma cells, CD138 immunostaining, ×200. (B) Focal glandular plasma cells, CD138 immunostaining, ×200. (C) Intra- and subepithelial macrophages, CD68 immunostaining, ×200. (D) Perivascular macrophages, CD68 immunostaining, ×200.***

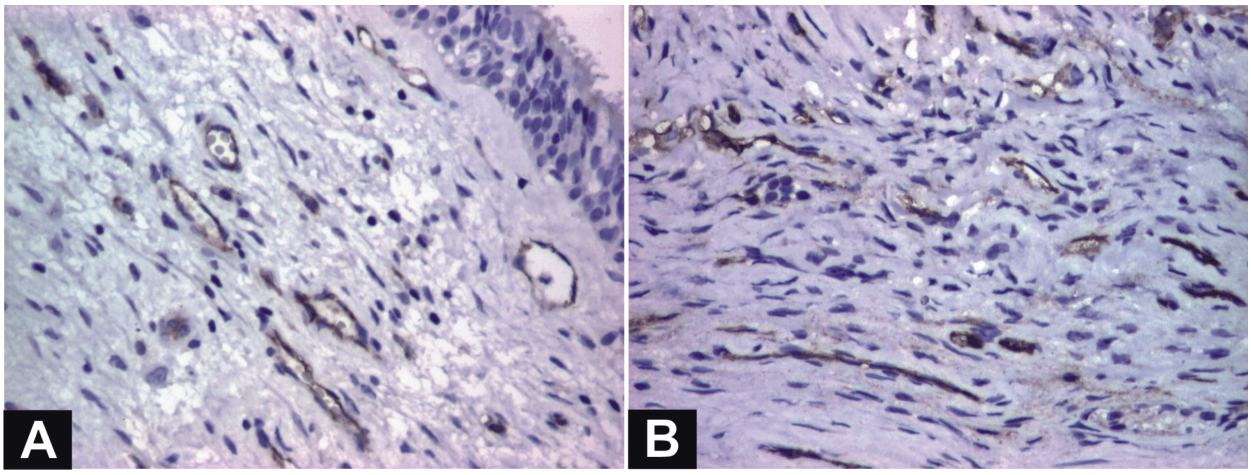


**Figure 9 –** ***(A) Subepithelial capillaries, CD31 immunostaining, ×200. (B) Small, irregular capillaries, CD31 immunostaining, ×200.***

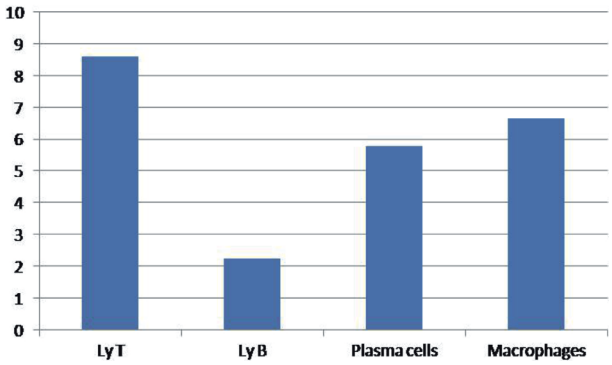


**Figure 10 –** ***Average values distribution of the inflammatory elements.***

## Discussion

Since its first mentioning in the literature, numerous cases have been documented and reported. The largest series of cases belongs to Kass *et al.* [3].

The silent sinus syndrome is defined as an implosion of the antrum and chronic maxillary sinus atelectasis and manifests with painless enophthalmos and inward retraction of the ipsilateral maxillary sinus walls [4, 5].

The disease may be congenital or acquired. Some authors still believe that the silent sinus syndrome may be related to a congenital underdevelopment of the maxillary sinus, because there is not a clear imagistic distinction from a hypoplastic maxillary sinus. However, the acquired condition seems to be more probable [2].

Pathogenesis of the disease relies on the hypothesis that the obstruction of the ostium of the maxillary sinus initiates a sequence of events that finally lead to the inward retraction of the walls. Accumulation of mucus inside the cavity of the sinus and stagnation will elicit a local inflammation that will induce osteolysis and weakening of the walls [3, 6–9]. In the mean time, in the condition of a sealed cavity and absence of ventilation, gas and mucus absorption will create a negative pressure [1, 3, 4, 6–8, 10, 15, 16], that will progressively pull the sinuses' walls inside. Increased orbital volume and retraction of the orbital floor lead to unilateral spontaneous enophthalmos and hypoglobus, a characteristic of the disease.

In addition to the orbital floor being pulled downward, there may be bone remodeling and thinning due to increased osteoclastic activity. Typically, the periosteum is not affected. This mechanism is very similar to that causing tympanic membrane retraction observed in patients with chronic Eustachian tube obstruction [10].

There are many arguments for this theory. All of these phenomena, like chronic inflammation, osteolysis of the orbital floor and the existence of a negative intrasinusal pressure, were documented in experimental models and patients with silent sinus syndrome [3, 6–9]. Bossolesi *et al.*, an experienced team in treatment of silent sinus found always a non-specific chronic inflammatory aspect on biopsies taken from maxillary sinus mucosa but a viable microorganism was not identified on microbiological cultures [17]. This is also consistent with our findings.

Angiogenesis is the process of forming new blood vessels from the preexisting ones, manifesting pre- and postnatally, with role in development, growth and tissular repair [18]. The process consists in initiation, activation, invasion and migration of endothelial cells consecutive to proteolytic degradation of extracellular matrix, maturation of endothelial cells and coalescence to form tubular structures in which blood is circulating [18].

In physiologic conditions, it is the result of the balance between the proangiogenic factors and antiangiogenic, mechanism by which endothelial cells are maintained in dormant status and the process is self-limiting in time [19]. In chronic inflammation, angiogenesis is involved in constitution of granulation tissue and tissular repair. Between the angiogenesis and chronic inflammatory infiltrate there are co-dependent mechanisms that ensure reciprocal stimulation, some authors proposing modulating therapies of angiogenesis with anti-inflammatory effect or modulating the signals of inflammatory elements with angiogenetic effect [20, 21]. Therefore, the inflammatory elements may secrete numerous proangiogenic factors that, on their turn, stimulate the maintaining of inflammatory population.

Chronic rhinosinusitis has a partially known pathogenesis in which are involved immunity defects and

activation of numerous inflammatory elements [22, 23]. Infiltration with cells like T-lymphocytes, B-lymphocytes and macrophages is a feature of upper respiratory tract infections [24].

T-lymphocytes are essential for the initiation and progression pf inflammation, with role of secretion of numerous cytokines and chemokines [25].

At the same time, T-lymphocytes are capable of providing growth factors as VEGF (vascular endothelial growth factor) to the inflammation sites, and one of the roles of VEGF is to stimulate the differentiation of T-lymphocyte towards pro-inflammatory activity [26].

In our study, T-lymphocytes showed a moderate perivascular distribution, with the predominance of CD4+ T-helper lymphocytes and a supraunitary CD4+/CD8+ ratio. Data from the literature indicate that chronic rhinosinusitis with an elevated percent of T-helper lymphocytes are inflammatory active processes, independent of allergies or presence of antimicrobial antigens, and drop of CD4+ lymphocytes, indicate especially in the presence of polyps, diseases that are difficult to control therapeutically [27]. Nowadays it is known that rhinosinusistis with nasal polyps are inflammations characterized by the preferential accumulation of T-helper lymphocytes and eosinophils [23, 24, 28, 29].

In this study, we observed a close relationship of the T-lymphocytes with the glandular compartment, and in case of Tc-lymphocytes also with the lining epithelia. The aspect was highlighted in other studies that indicated in chronic rhinosinusitis, massive presence of Tc lymphocytes at the level of the epithelia, as good as in the glandular compartment, with role in the stimulation of glandular production, question removal of antigens [24].

It is known that the T-helper lymphocytes have a role in stimulating B-lymphocyte to differentiate in antibodies producing plasmocytes [24].

In a complex immunohistochemical and molecular recent study, upon chronic polypous rhinosinusitis, Hulse *et al.* stress out the role of B-lymphocytes and plasmocytes in maintaining the inflammatory population and production of different types of antibodies [22].

In our study, B-lymphocytes had a week representation in all lesional compartments, including at a perivascular level. On the contrary, plasmocytes were well represented at a glandular and perivascular level. In this sense, it is proven that the plasmocytes in the spine cord express over 30 proangiogenic factors, and their supernatant may induce angiogenesis *in vitro* [30]. In the same time, the plasmocytes represent inflammatory elements that are present in chronic rhinosinusitis, the quantity being appreciable in case of associating polyps [31].

Macrophages are key elements of chronic inflammation, with role in phagocytosis of pathogenic agents, cellular detritus and some components of the extracellular matrix [32].

In the frame of inflammatory process, the activation of macrophages is followed by the releasing of numerous proangiogenic factors as cytokines and VEGF [33]. In cases of chronic obstructive rhinosinusitis it was signaled the increase of number of macrophages [24]. Even in our study, the density of macrophages was well represented in all compartments including perivascular.

Iatrogenic damage during endoscopic sinus surgery was claimed to be cause of a silent sinus syndrome in a child [13]. Hourany *et al.* also considered that a nasal trauma followed by surgical trauma in childhood were likely the factors responsible for later insidious development of silent sinus syndrome [34]. During rhinotomy and reconstructive surgery of the septum, an osteotomy that normally pass through the nasal process of the maxilla, if it is extended more posteriorly, may enter and damage the maxillary sinus. In time, scar contracture and maxillary sinus hypoventilation, might then have resulted in the sinus atelectasis, hypoglobus, and enophthalmos, exactly like in a silent sinus syndrome [34]. Existence of a chronic maxillary sinusitis was excluded based on the absence of symptoms, but in our opinion it may not be entirely true.

In the most recent review, Rose *et al.* found that, as well as the orbital floor being drawn downwards, there were abnormal concavities in the medial and posterolateral walls of all the maxilla that could be assessed on CT scanning [5]. They also describe an iatrogenic version of the disease occurring after orbital decompression [35]. These relatively acute changes have led them to use the term "imploding antrum syndrome".

Similar processes may occur within an opacified hypoplastic maxillary sinus, an entity with imaging findings similar to that of the silent sinus syndrome and often used interchangeably with the silent sinus syndrome in the literature [4, 7]. This may be a form of silent sinus syndrome, less severe because smaller sinus volume, shorter and thicker walls not allowing important inward retraction.

This theory does not explain the fact that there is a very high prevalence of maxillary sinus obstruction but a rare incidence of silent sinus syndrome and an exclusive involvement of the maxillary sinus [36]. Therefore, other local factors must also be involved in the pathogenesis, still unknown.

A patient with silent sinus syndrome is usually an adult in the third to the fifth decades of life presenting to the ENT or ophthalmologist with spontaneous, painless, and occasionally progressive enophthalmos and hypoglobus causing eye of facial asymmetry [3, 4] with or without diplopia [10].

Symptoms related to sinusitis may or may not be present [1, 6, 7]. There is no gender or racial predilection [37].

In the medical history of the patient, there are no contributory aspects. Generally, the patients are denying preexisting sinus disease and orbitofacial trauma.

On physical examination upper lid retraction, deepened upper lid sulcus, malar depression, facial asymmetry, and diplopia may be found. Extraocular motility and the rest of the eye examination are usually normal [1, 2, 3, 6, 10, 15, 16]. In our case, the diplopia and enophthalmos were preceded by the appearance of some wrinkles on the left nasogenian region.

The diagnosis of SSS is initially made clinically and then confirmed radiologically. The imaging findings of the silent sinus syndrome are characteristic. The sinus is usually fully developed and opacified [3, 6, 10]. The adjacent middle meatus is correspondingly enlarged

with varying degrees of lateral retraction of the middle turbinate). The most characteristic imaging feature of the silent sinus syndrome is the inward retraction of the sinus walls into the sinus lumen with associated decrease in sinus volume [1, 2, 3, 6, 10, 16].

Illner *et al.* found that in all of the patients included in their study, the medial, posterolateral wall, and orbital floor were involved [11]. The eye or facial asymmetry identified by the patient is provoked by the downward retraction of the orbital floor into the maxillary sinus. The orbital floor (maxillary roof) is always retracted and commonly thinned. The other walls may be thinned, normal, or slightly thickened. The maxillary infundibulum is always occluded and the sinus is opacified. The uncinate process is retracted against the inferomedial aspect of the orbital wall [15]. All of the aforementioned aspects were seen on the CT scans in coronal, axial and sagittal reconstructions in our case.

The maxillary infundibulum is occluded. Occlusion is usually caused by lateral retraction of the uncinate process with apposition of the uncinate process against the inferomedial aspect of the orbital wall [3, 6, 15].

The diagnosis of silent sinus syndrome can be made clinically, but it should be differentiated from other causes of spontaneous enophthalmos such as Parry–Romberg syndrome, linear scleroderma [37] and other rare conditions, such as Horner's syndrome, progressive lipodystrophy, and facial hemiatrophy [17].

Optimal management of the SSS should be grounded on pathogenesis of the disease. The initial management in this syndrome should be conservative. Superimposed sinusitis should be first treated with antibiotics [36].

If medical treatment is inadequate, surgery should be applied. The objective is to restore the normal sinus drainage and to interrupt the pathogenesis of the disease. By creating an outlet for mucous drainage from the obstructed sinus, surgical intervention to improve sinus aeration stops the progression of maxillary sinus contraction [1, 2, 3, 6, 10, 14, 37–39].

The intervention is performed endoscopically and creates a nasal antral window or a maxillary antrostomy [1, 3, 4, 6, 10, 15, 16].

The silent sinus syndrome can be definitively treated but after surgery, the volume of the sinus may remain unchanged, improve slightly, or be restored to a near-normal configuration over time [10, 15, 16].

In patients with diplopia or severe cosmetic deformity, repair of the orbital floor with placement of a subperiosteal implant can be performed at the same time or after functional endoscopic sinus surgery [1, 3, 4, 6, 10, 15, 16]. Bossolesi *et al.* considers that an implant is not always required when endoscopic functional sinus surgery is done, as the reexpansion of the sinus (as evidenced by the imaging) stops the progression of orbit displacement. This means that, especially in less severe cases, an expectative attitude may be adopted with the possibility of a secondary repair if still required [17]. Medpor, titanium, autologous bone or another material may be fashioned into a subperiosteal implant, which is placed on the orbital floor. This aids in the repositioning of the globe with improvement of enophthalmos and eyelid position [37–39].

## Conclusions

Silent sinus syndrome is a well-defined clinical entity with characteristic imagistic findings. Topographic associations and density of inflammatory elements analyzed in relation with neoforming vessels suggest their implication in reparatory angiogenesis characteristic to chronic inflammation. Modulating activity in the frame of inflammatory process, of the T-lymphocytes and especially of T-lymphocytes may represent a target for the therapeutic management. Surgical intervention that restores sinus drainage will interrupt the pathogenesis of the disease and lead to its progressive regression. Surgery can and should be performed by an endoscopic approach.

**Conflict of interests**

The authors declare that they have no conflict of interests.

**Author contribution**

All authors made equal contribution to the paper, equal to that of the first author.

## References

[1] Soparkar CNS, Patrinely JR, Cuaycong MJ, Dailey RA, Kersten RC, Rubin PAD, Linberg JV, Howard GR, Donovan DT, Matoba AY, Holds JB. The silent sinus syndrome. A cause of spontaneous enophthalmos. Ophthalmology, 1994, 101(4): 772–778.

[2] Montgomery WW. Mucocele of the maxillary sinus causing enophthalmos. Eye Ear Nose Throat Mon, 1964, 43:41–44.

[3] Kass ES, Salman S, Rubin PAD, Weber AL, Montgomery WW. Chronic maxillary atelectasis. Ann Otol Rhinol Laryngol, 1997, 106(2):109–116.

[4] Soparkar CN, Patrinely JR, Davidson JK. Silent sinus syndrome: new perspectives? Ophthalmology, 2004, 111(2):414–415; author reply 415–416.

[5] Rose GE, Sandy C, Hallberg L, Moseley I. Clinical and radiologic characteristics of the imploding antrum, or "silent sinus" syndrome. Ophthalmology, 2003, 110(4):811–818. Erratum in: Ophthalmology, 2003, 110(8):1475.

[6] Boyd JH, Yaffee K, Holds J. Maxillary sinus atelectasis with enophthalmos. Ann Otol Rhinol Laryngol, 1998, 107(1):34–39.

[7] Kass ES, Salman S, Montgomery WW. Manometric study of complete ostial occlusion in chronic maxillary atelectasis. Laryngoscope, 1996, 106(10):1255–1258.

[8] Davidson JK, Soparkar CNS, Williams JB, Patrinely JR. Negative sinus pressure and normal predisease imaging in the silent sinus syndrome. Arch Ophthalmol, 1999, 117(12): 1653–1654.

[9] Scharf KE, Lawson W, Shapiro JM, Gannon PJ. Pressure measurements in the normal and occluded rabbit maxillary sinus. Laryngoscope, 1995, 105(6):570–574.

[10] Gillman GS, Schaitkin BM, May M. Asymptomatic enophthalmos: the silent sinus syndrome. Am J Rhinol, 1999, 13(6): 459–462.

[11] Illner A, Davidson HC, Harnsberger HR, Hoffman J. The silent sinus syndrome: clinical and radiographic findings. AJR Am J Roentgenol, 2002, 178(2):503–506.

[12] Gaudino S, Di Lella GM, Piludu F, Martucci M, Schiarelli C, Africa E, Salvolini L, Colosimo C. CT and MRI diagnosis of silent sinus syndrome. Radiol Med, 2013, 118(2):265–275.

[13] Bas A, Tutar O, Samanci C, Kepek F. Silent sinus syndrome: CT and MRI findings. BMJ Case Rep, 2012 Dec 5.

[14] Weidner N, Carroll PR, Flax J, Blumenfeld W, Folkman J. Tumor angiogenesis correlates with metastasis in invasive prostate carcinoma. Am J Pathol, 1993, 143(2):401–409.

[15] Hunt SM, Tami TA. Sinusitis-induced enophthalmos: the silent sinus syndrome. Ear Nose Throat J, 2000, 79(8):576, 579–581, 584.

[16] Wan MK, Francis IC, Carter PR, Griffits R, van Rooijen ML, Coroneo MT. The spectrum of presentation of silent sinus syndrome. J Neuroophthalmol, 2000, 20(3):207–212.

[17] Bossolesi P, Autelitano L, Brusati R, Castelnuovo P. The silent sinus syndrome: diagnosis and surgical treatment. Rhinology, 2008, 46(4):308–316.
[18] Folkman J. What is the evidence that tumors are angiogenesis dependent? J Natl Cancer Inst, 1990, 82(1):4–6.
[19] Raica M, Cîmpean AM, Gaje PN, Ribatti D. Angiogeneza şi limfangiogeneza tumorală, Colecţia Academica, Ed. Victor Babeş, Timişoara, 2010.
[20] Chidlow JH Jr, Shukla D, Grisham MB, Kevil CG. Pathogenic angiogenesis in IBD and experimental colitis: new ideas and therapeutic avenues. Am J Physiol Gastrointest Liver Physiol, 2007, 293(1):G5–G18.
[21] Jackson JR, Seed MP, Kircher CH, Willoughby DA, Winkler JD. The codependence of angiogenesis and chronic inflammation. FASEB J, 1997, 11(6):457–465.
[22] Hulse KE, Norton JE, Suh L, Zhong Q, Mahdavinia M, Simon P, Kern RC, Conley DB, Chandra RK, Tan BK, Peters AT, Grammer LC 3rd, Harris KE, Carter RG, Kato A, Schleimer RP. Chronic rhinosinusitis with nasal polyps is characterized by B-cell inflammation and EBV-induced protein 2 expression. J Allergy Clin Immunol, 2013, 131(4):1075–1083, 1083.e1–1083.e7.
[23] Tan BK, Schleimer RP, Kern RC. Perspectives on the etiology of chronic rhinosinusitis. Curr Opin Otolaryngol Head Neck Surg, 2010, 18(1):21–26.
[24] Grevers G, Klemens A, Menauer F, Sturm C. Involvement of inferior turbinate mucosa in chronic sinusitis – localization of T-cell subset. Allergy, 2000, 55(12):1155–1162.
[25] Anderton SM, Wraith DC. Selection and fine-tuning of the autoimmune T-cell repertoire. Nat Rev Immunol, 2002, 2(7): 487–498.
[26] Mor F, Quintana FJ, Cohen IR. Angiogenesis-inflammation cross-talk: vascular endothelial growth factor is secreted by activated T cells and induces Th1 polarization. J Immunol, 2004, 172(7):4618–4623.
[27] Pant H, Hughes A, Schembri M, Miljkovic D, Krumbiegel D. CD4(+) and CD8(+) regulatory T cells in chronic rhinosinusitis mucosa. Am J Rhinol Allergy, 2014, 28(2):e83–e89.
[28] Van Zele T, Claeys S, Gevaert P, Van Maele G, Holtappels G, Van Cauwenberge P, Bachert C. Differentiation of chronic sinus diseases by measurement of inflammatory mediators. Allergy, 2006, 61(11):1280–1289.
[29] Bachert C, Van Bruaene N, Toskala E, Zhang N, Olze H, Scadding G, Van Drunen CM, Mullol J, Cardell L, Gevaert P, Van Zele T, Claeys S, Halldén C, Kostamo K, Foerster U, Kowalski M, Bieniek K, Olszewska-Ziaber A, Nizankowska-Mogilnicka E, Szczeklik A, Swierczynska M, Arcimowicz M, Lund V, Fokkens W, Zuberbier T, Akdis C, Canonica G, Van Cauwenberge P, Burney P, Bousquet J. Important research questions in allergy and related diseases: 3-chronic rhinosinusitis and nasal polyposis – a GALEN study. Allergy, 2009, 64(4):520–533.
[30] Hose D, Moreaux J, Meissner T, Seckinger A, Goldschmidt H, Benner A, Mahtouk K, Hillengass J, Rème T, De Vos J, Hundemer M, Condomines M, Bertsch U, Rossi JF, Jauch A, Klein B, Möhler T. Induction of angiogenesis by normal and malignant plasma cells. Blood, 2009, 114(1):128–143.
[31] Arjomandi H, Gilde J, Zhu S, Delaney S, Hochstim C, Mazhar K, Wrobel B, Markarian A, Masood R, Rice D. Relationship of eosinophils and plasma cells to biofilm in chronic rhinosinusitis. Am J Rhinol Allergy, 2013, 27(4):e85–e90.
[32] Nucera S, Biziato D, De Palma M. The interplay between macrophages and angiogenesis in development, tissue injury and regeneration. Int J Dev Biol, 2011, 55(4–5):495–503.
[33] Lingen MW. Role of leukocytes and endothelial cells in the development of angiogenesis in inflammation and wound healing. Arch Pathol Lab Med, 2001, 125(1):67–71.
[34] Hourany R, Aygun N, Della Santina CC, Zinreich SJ. Silent sinus syndrome: an acquired condition. AJNR Am J Neuroradiol, 2005, 26(9):2390–2392.
[35] Rose GE, Lund VJ. Clinical features and treatment of late enophthalmos after orbital decompression: a condition suggesting cause for idiopathic "imploding antrum" (silent sinus) syndrome. Ophthalmology, 2003, 110(4):819–826.
[36] Waqar S, Dhir L, Irvine F. Silent sinus syndrome: a cause of unexplained enophthalmos. Can J Ophthalmol, 2010, 45(5): 547–548.
[37] Levine SB, Mitra S. Maxillary sinus involution after endoscopic sinus surgery in a child: a case report. Am J Rhinol, 2000, 14(1):7–11.
[38] Hobbs CGL, Saunders MW, Potts MJ. Spontaneous enophthalmos: silent sinus syndrome. J Laryngol Otol, 2004, 118(4):310–312.
[39] Gill HS, Silkiss RZ. Diagnosis and management of the silent sinus syndrome. Eyenet, 2011, 37–38.

***Corresponding author***
Valeriu Şurlin, Associate Professor, MD, PhD, Attending Surgeon, I[st] Clinic of Surgery, University of Medicine and Pharmacy of Craiova, 2 Petru Rareş Street, 200349 Craiova, Dolj County, Romania; Phone +40740–182 346, e-mail: vsurlin@gmail.com

*Received: October 12, 2014*

*Accepted: March 21, 2015*