Pseudoactinomycotic radiate granules in the maxillary sinus. A case report

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Background. Pseudoactinomycotic radiate granules are biologically inactive formations simulating true actinomycotic granules. They occur mainly in the female genital tract. Here we describe a previously unreported case of these granules in a maxillary sinus.

Methods and Results. A 74-year old man underwent maxillectomy for a carcinoma of the right alveolar ridge. In the tumor-free sinus mucosa, a deposit of condensed mucus, cell debris and eosinophilic granules, surrounded by leukocytes, were seen. These Gram-positive granules were refractile, not bi-refringent and revealed radiate pattern with peripheral club-like thickening. Alcian blue staining was negative, PAS reaction was present at the periphery. Ziehl-Neelsen, Grocott and Kongo red reactions tested negatively. In the mucoid surroundings, strong IgM, moderate IgG, weak IgA and IgG4, but no IgD immunoreactivity was present.

Conclusions. PAMRAGs in the maxillary sinus have not been described so far. Despite their extremely rare occurrence, they must be taken into consideration in histopathological differential diagnosis of actinomycosis of that anatomic location.

Key words: maxillary sinus, pseudoactinomycotic granules, Splendor-Hoeppli phenomenon

INTRODUCTION

Pseudoactinomycotic radiate granules (PAMRAGs) are eosinophilic formations composed of club-like rods simulating actinomycotic granules. In human beings, they occur mostly in the female genital tract where they are typically, but not exclusively, associated with the use of intrauterine contraceptive device (IUCD) (ref.1-3). In extragenital locations, they were described in colloid cysts of the third ventricle of the CNS (ref.4) and inspissated bronchial mucus5. Genesis of the PAMRAGs remains obscure. In IUCD users, they might represent particles of that device or organic deposits precipitated on its fragments. In extragenital locations, they could be an antigen-antibody complex (also called as Splendor-Hoeppli phenomenon). However, non-immune mechanisms are also supposed to be responsible for the formation of these granules. Here we report a case of PAMRAGs in the maxillary sinus and discuss the nature and comment on their clinical relevance. To the best of our knowledge, this is the first description of these granules at that site.

CASE REPORT

A 74-year old man was diagnosed with a T2N3MX squamous cell carcinoma of the alveolar ridge of his right upper jaw. The treatment consisted of a partial maxillectomy, comprehensive I-V neck dissection and subsequent radiotherapy. Histopathologic analysis of the surgical specimen revealed no presence of a carcinoma in the maxillary sinus, the mucosa of which showed focally regressive inflammatory changes with sparsely distributed polymorphonuclear leukocytes. Condensed mucus contained cell debris and widely spreading, usually spheric eosinophilic radiate granules surrounded by leukocytes (Fig. 1). Less often, some hyphal-like granules were present (Fig. 2). The PAMRAGs were refractile but not birefringent. In Gram staining, they revealed peripheral club-like thickening (Fig. 3). Alcian blue staining was negative, weak PAS reaction was stronger at the periphery. Ziehl-Neelsen, Grocott and Kongo red reactions tested negatively. In the mucoid substance, precipitates revealing strong IgM, moderate IgG, weak IgA and IgG4, but no IgD immunoreactivity, were present. The granules showed conspicuous CD68 positivity, which was faint in their surroundings.

DISCUSSION

Pathomorphology of PAMRAGs closely resembles that of true actinomycotic granules. However, there are some distinct features enabling their differentiation. The latter are non-refractile formations with an eosinophilic granular dense centre and peripheral Gram, Ziehl-Neelsen and PAS-positive, thin (circa 1 μm) branching
Fig. 1. A pseudoactinomytic granule in a pool of mucus is surrounded by leukocytes and cellular debris (HE, ×400).
Inset: At high magnification (×1000), distinct radiate pattern of a PAMRAG is evident.

Fig. 2. A hyphal-like PAMRAG in mucoid substance (HE, ×400).

Fig. 3. Strongly Gram-positive radiating granules reveal peripheral clubbing (arrows) (×400).
filaments. On the contrary, central core lacking refractile
PAMRAGs show thick (> 10 μm) irregular non-branching
club-like peripheral projections. They occasionally reveal
histochemical profile similar to that in true actinomycotic
granules 

[2,3,6-7]. In these cases the differential diagnosis is
based on the presence of actinomycotic filaments, high-
lighted by Gomori reaction.

The nature and morphogenesis of PAMRAGs has
not been satisfactorily elucidated yet. In many extra-
genital locations, primarily in veterinary fields, radiat-
ing eosinophilic deposits (occasionally referred to as
Splendor-Hoeppli phenomenon) were found to surround
certain bacteria, fungi and parasites in inorganic mate-
rials. By some authors these granules were considered
to be a non-specific reaction to these agents and disinte-
grated surrounding reactive cells 

[3,9]. Smith et al. 

[8,9] and von Lichtenberg et al. 

[11] noticed similarities in the histochem-
istry of schistoma eggs and associated Splendor-Hoeppli
phenomenon. They represented the phenomenon rep-
resented an immune-host reaction to antigenic products
of cephalic glands of that parasite, resulting in the formation
of an antigen-antibody complex precipitating around the
eggshells. That opinion was in concert with an ultrastruc-
tural study demonstrating that the substance of a fungi-
associated Splendor-Hoeppli phenomenon was composed
of cytoplasmic and nuclear debris derived from reactive
cells and amorphous granular material considered to be
antigen-antibody complex

[12].

In the female genital tract, neither specific staining
nor ultrastructural analysis could demonstrate presence of
any infection agents in the PAMRAGs 

[ref.2,3,6-7]. O’Brien et al. initially believed that the PAMRAGs represented
particles of plastic IUCP dissociated in the endometrium
owing to cyclically changing environment of the endo-
metrial cavity

[13]. In their later study the authors analyzed
ultrastructure of copper IUCP-associated pseudoactino-
mycotic granules identified in histologic sections of an
uterine curettage taken from a female patient

[2]. Neither biological nor artificial materials could be found in the
granules, which - as well as their immediate vicinity 

- contained various chemical elements, primarily copper.
Therefore it was concluded that the PAMRAGs were
precipitates of the latter element, which could have been a
derivative of metallic component of the IUCD or en-
dogenous copper, which is abundant in lipofuscin.
The authors also questioned their previous view on the plas-
tic character of the PAMRAGs. Striepecke et al.

[7] studied pseudoactinomycotic granules found in 14 of 123 uterine
curettage specimens in women using copper compounded
IUCD. In the granules, empty areas were seen. The authors
considered them to be negative imprints of IUCD-
associated metallic particles. In one case, the surface of the
removed IUCD was covered with an amorphous hya-
line mass, revealing radial pattern. This finding suggested
that the pseudogranules were organic deposits on copper
fragments detached from the IUCD.

The fact, that pseudomycotic granules can occur in
tissues free of any artificial materials, raises the question
of their endogenous, presumably cellular origin.

Paedberg et al.

[3] found marginal IgG (but not IgD, IgA and IgM) positivity in pseudoactinomycotic granules pre-

cent in a bacteria-free uterine curettage specimen taken
from an IUCP user. At the border of the pseudogran-
ules, granulocytes and signs of intensified phagocytosis
were present. The authors concluded that the PAMRAGs
consisted chiefly of products of disintegration of mac-
rophages and immunoglobulin with added debris and
fibrin. In our case, in which neither infectious agents nor any non-biological particles could be demonstrated, the
PAMRAGs showed positive CD68 reaction and were sur-
rounded by leukocytes and immunoglobulin precipitates.
These findings suggest that immunological mechanisms,
similar to those hypothesized in the Splendor-Hoeppli
phenomenon, were involved in the pathogenesis of the
granules composed of PAS positive mucus and leukocytic
debris.

On the other side, Bhagavan et al.

[1] studied 6 cases of genital tract PAMRAGs, three of which were not as-
associated with the IUCD. In all samples, histochemical
analysis identified lipids, calcium, neutral glycoproteins,
but no fibrin, immunoglobulins or complement. The au-

tors concluded that the PAMRAGs were not formed by
an immune process, but derived from host leukocytes ag-
gregated in a non-specific response to IUCD or bacteria
present in that location.

Powers et al.

[4] analyzed 3 cases of colloid cysts origi-
nating in the third ventricle. They contained eosinophilic,
hyphal-like structures. The light microscopy, histochem-
istry and ultrastructure corresponded with the PAMRAGs
and failed to demonstrate presence of any bacterial, acti-
nomycotic or fungal agents. Special stains suggested that
these hyphal-like structures represented admixture of the
material of degenerating nuclei and cytoplasmatic mem-
branes of the lining epithelial cells.

The PAMRAGs are biologically non-active forma-
tions. Their only clinical relevance thus resides in that
they might be misdiagnosed as a true actinomycosis. That
infection, showing usually low pathogenicity is seldom in
the cervicofacial region and exceptionally rare in the pa-
ranasal sinuses

[14,15]. However, in the latter locations it may
take a very invasive course, causing even intracranial com-
lications. Therefore, especially immunodeficient patients
diagnosed with paranasal sinus actinomycosis should be
started on a long-term antibiotic therapy postoperatively,
which would be unnecessary in cases of PAMRAGs.

CONCLUSIONS

PAMRAGs are harmless pathomorphological for-
formations, the nature of which remains unclear. They are
encountered mostly in the female genital tract. In the
paranasal sinuses, their occurrence is extremely rare.
Nonetheless, also in this location they must be taken into
consideration in the histopathological differential diag-
nosis of actinomycosis to avoid unnecessary antibiotic
therapy.

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