CASE REPORT

Rhinology, 47, 323-326, 2009

Synchronous myeloproliferative and inflammatory disease of the nasal cavity and paranasal sinuses: an interesting differential diagnostic problem*

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SUMMARY

The authors present a case of synchronous manifestation of a myeloproliferative – extramedullary plasmocytoma – and a chronic inflammatory disease of the nose and the paranasal sinuses. THey emphasise the importance of imaging techniques and immunohistochemistry in the differential diagnosis. They discuss on the basis of published articles the new classification, clinical manifestations, diagnostic and therapeutical approaches of this tumour belonging to the group of monoclonal gammopathies, which originates from an abnormal proliferation of mature B-lymphocytes, and is a rarity in the literature even nowadays.

Key words: extramedullary plasmocytoma, immunohistochemistry, monoclonal gammopathy, nasal cavity and paranasal sinuses

INTRODUCTION

Unilateral nasal discharge, bleeding and obstruction are mostly caused by certain tumours of the maxillo-ethmoidal region. The diagnosis of these masses is usually easy and unambiguous by imaging techniques, endoscopic and histopathological examinations. However, differential diagnostic problems may occur. In our case, the patients' rhinological symptoms were caused by a monoclonal-gammopathy, an extramedullary plasmocytoma (EMP) in the right nasal cavity. Nevertheless the radiological findings revealed also a soft tissue mass in the contralateral maxillary sinus, which had to be differentiated from the EMP.

Monoclonal gammopathies are characterized by the presence of a plasma cell clone, which are mature, well differentiated B-lymphocytes producing monoclonal proteins (M-protein, paraprotein). The abnormal proliferation of these cells results in the development of plasma cell tumours, which are still rarities in the literature [(1-6)]. The disease can take any of the following forms [(4)]:

1. Monoclonal gammopathy of undetermined significance (MGUS): This form is characterized by the presence of serum M-protein lower than 30g/L and less than 10% bone marrow clonal plasma cells. There is no evidence of organ or tissue impairment.

2. Smoldering/asymptomatic multiple myeloma (SMM): The presence of serum M-protein is equal or higher than 30 g/L, the proportion of bone marrow plasma cells is equal or greater than 10% with no symptoms of organ impairment.

3. Symptomatic multiple myeloma (MM): A neoplastic B-cell proliferation, during which the clonal lymphocytes, originating from one single cell, produce specific immunoglobulins.

a. Multiple Myeloma (Kahler's disease): a multiplex disease, affecting the bones, the kidneys and the bone marrow, and resulting in the weakening of the immune system and in metabolic disturbances. Diagnosis is mostly based on bone marrow biopsy (with a proportion of plasma cells greater than 10%), the results of laboratory and urine tests (Bence-Jones protein), X-ray examination and renal function tests belong to the minor criteria.

b. Solitary plasmocytoma of the bones: the monoclonal cell proliferation occurs within only one single bone of the skeleton.

c. Extramedullary plasmocytoma or *primary tissue plasmocytoma (EMP):* the first case of EMP was published at the beginning of the 20th century, as revealed by Shah et al. [(7)]. In case of positive histological results, further thorough tests – as mentioned above – are required to exclude organ or tissue impairment [(2-6,8)].

EMP occurs three times more frequently in men than in women – although in myltiple myeloma this ratio is equal. The appearance of symptoms has never been reported under the age of twenty, the disease develops mostly between 40-70 years

*Received for publication: February 21, 2008; accepted: August 5, 2008

Table 1. Incidence of extramedullary plasmocytoma in the upper airways and gastrointestinal tract according to histological data collected by Michaels and Hyams between 1940-1980 [11].

Localization	Number of cases (n=53)
Nasal cavity and paranasal sinuses	28 (52%)
Nasopharynx	10 (19%)
Pharynx (meso- and hypopharynx)	3 (6%)
Tonsils	3 (6%)
Larynx	9 (17%)

of age, with a mean of 60 years [1,2,7,9,10]. EMP represents 3-5% of all plasma cell neoplasms, and appears in 80-90% in the upper airways [3,7]. One of the biggest histological analyses in the literature, including the localisation of the disease, was carried out by Michaels and Hyams [11] between 1940 and 1980 (Table 1).

CASE REPORT

In July 2003 a 64-year-old woman appeared at our outpatient department with recurrent, frequent nasal bleeding and obstruction of the right nasal cavity. At the basis of the right nasal cavity a polypoid tissue, approximately 3x4 cm in size, was recognized from which histological sample was taken. The cytological picture was typical for localised plasmocytoma, with kappa light chain monoclonality (Figure 1). Immunohistochemistry showed proliferating plasma cell clones and CD38 positivity (Figure 2). The oto-rhino-laryngological physical examination was otherwise normal.

To exclude systemic manifestation of the disease, a bone marrow biopsy was carried out. The bone marrow contained normal cells with less than 10% of CD38+ plasma cells. The peripheral blood smear was normal. X-ray and ultrasonography, examinations were negative. Laboratory parameters were in the normal range.

On the basis of the examinations mentioned above we were able to exclude myeloma multiplex, with the only extramedullary focus shown to be in the nasal cavity.

On the endoscopic picture a tissue growth with a smooth surface was seen, that was covered with hyperaemic mucous membrane blocking the inferior nasal meatus almost completely. No discharge was present and the nasopharynx was free.

Computer Tomography (CT) scan of the paranasal sinuses (Figure 3a) surprisingly showed a tumour of soft tissue intensity in the left anterior ethmoid cells of the left maxillary sinus, and a second one in the region of the right inferior nasal meatus, suggesting the possibility of multifocal EMP. The bony margins appeared to be intact. In order to differentiate between plasmocytoma and chronic inflammation Magnetic Resonance (MR) examination was performed (Figure 3b) (neoplastic tissues often have higher proton density and relaxation time than the healthy tissues) [12].
As an exact diagnosis could not be settled by the radiological findings, sinoscopy and ethmoidotomy on the left side were carried out, and tissue samples were taken. Immunohistochemical polyclonality in the sample and the presence of follicles were characteristic for an inflammatory reaction; no sign of malignancy was seen.

Following repeated haematological and oncological consultation, we decided on surgery. From the Caldwell-Luc's approach and through the piriform aperture we partially amputated the inferior turbinate and removed the tumour extending on the inferior and lateral nasal wall together with the medial wall of the maxillary sinus and the mucosa of the nasal basis. The nasal septum and the bony nasal basis were spared. On the left side FESS (Functional Endoscopic Sinus Surgery) was carried out in order to ensure adequate drainage.

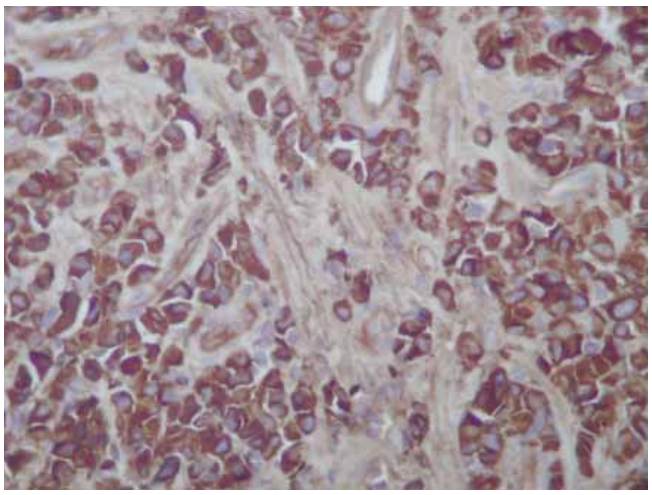

Figure 1. Kappa monoclonal light chain positivity (kappa-Dako-Autostainer, 440X).

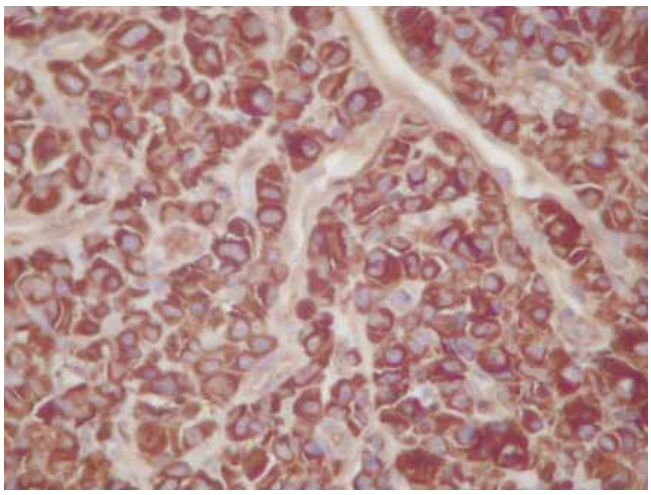

Figure 2. Immunohistochemistry: Intranuclear Mib1 positivity marks the proliferating plasma cells, and as endogen control respiratory cells can be seen (Mib1-Dako-Autostainer, 224X).

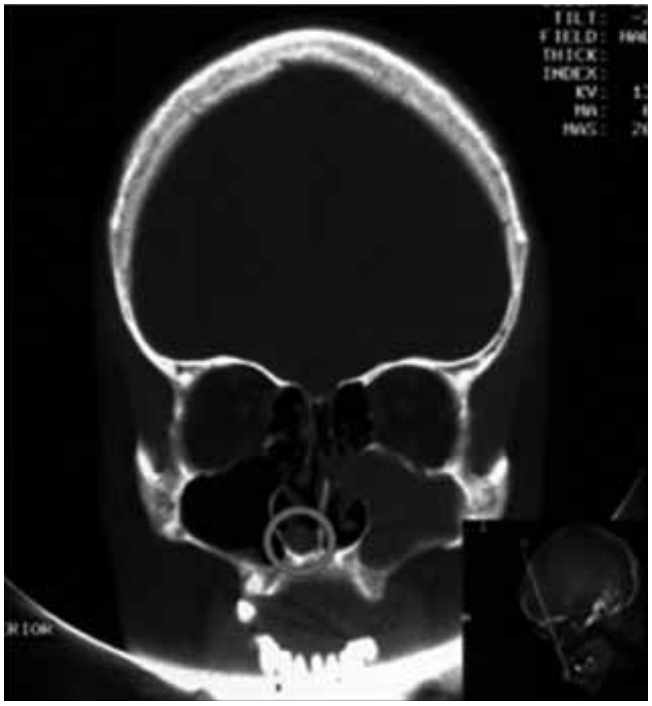

Figure 3a. Preoperative CT scan (EMP is marked by a circle).

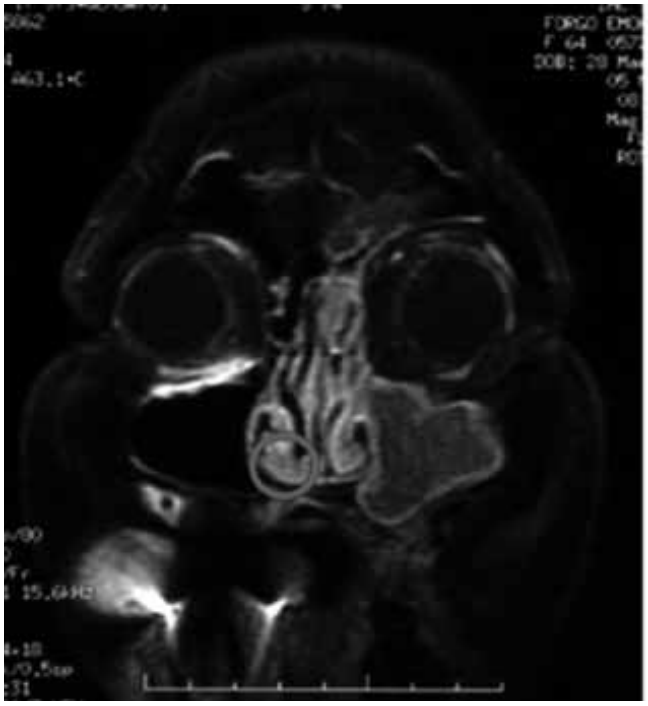

Figure 3b. Preoperative MR scan (EMP is marked by a circle).

Histopathological examination revealed, that the tumour from the right nasal cavity appeared to be EMP. Early postoperative period and wound healing was normal. Endoscopic and histological control was carried out every three months. After one year on the endoscopic picture normal mucosa was seen all over the nasal cavity as well as in the paranasal sinuses. The patient did not receive any chemo-radio therapy.

DISCUSSION

The occurrence of EMP is usually a nodular or peduncular growth with pinkish-reddish colour, always covered with normal mucosa [1,11]. The disease has characteristic symptoms like nasal bleeding, nasal discharge, and nasal obstruction. The patient may report difficulties with swallowing and discomfort in the throat. In the advanced stage of maxillo-ethmoidal or scull base localization, eye dislocation on facial palsy may also occur [2-4,7,10]. Nearly 20% of EMPs can metastasise into the loco-regional lymph nodes; excision and/or irradiation of these lymph nodes together with the primary neoplasm is obligatory [1,8]. One fifth of EMPs may become generalised, or transform to myeloma multiplex, although this mostly happens after 10 or 20 years. Such a long follow-up period is however rare, so the real incidence of transformation is unknown [1,4,8].

Plasmocytoma should be differentiated from the following syndromes: diffuse large B-cell lymphoma, carcinoma, acute myeloid leukaemia, plasmocytosis and monoclonal gammopathies of unknown origin [9].

To help differentiation, immunohistochemistry with detecting monoclonal antibodies might be useful [11,13], like in our case (Figure 2). On the microscopic picture plasma cells were seen in large groups or in linear formation, meshed by connective tissue and small vessels. Cytoplasm of the cells is eosinophilic or basophilic while the nuclei are round, eccentric, with the chromatin situated in a wheel-like shape or attached to the nuclear membrane [6,11]. Mitosis is rarely seen; few duplex nuclei are sometimes visible. A large number of atypical nuclei may be a sign of malignancy. Amyloid deposits are infrequent and have no prognostic importance [5].

Treatment of EMP is primarily radiotherapy as the tissue is radio-sensitive [13]. If there is evidence for lymph node metastasis, irradiation of these is also necessary. Table 2 shows the frequency of loco-regional recurrence after irradiation therapy.

Concerning surgical therapy opinions are divided. Some authors suggest that surgery should be the first line of treatment [1,6,14], while others deny it [3,8,10]. In the disseminated form of the disease surgery is not helpful. In these cases chemotherapy is the first line of treatment [3-5,7,10]. A solitary tumour in a surgically good localization can be treated adequately with radical excision [6]. In our presented case the small, well-delineated tumour was in an easy to reach location,

Table 2. Frequency of loco-regional recurrence after irradiation therapy of extramedullary plasmocytoma according to Dimopoulos et al. [8].

Form of recurrence	Recurrence ratio (n=128)
Local recurrence	7 %
Regional lymph node metastasis	7 %
Multiple Myeloma	15 %
Multiplex extramedullary recurrence	13 %

so an adequate surgical excision could be carried out. If surgery is ineffective, chemo-radio therapy can be used as second line treatment.

Chemotherapy may be used as adjuvant therapy in case of well-localized tumours or if recurrent or residual EMP is present after irradiation [4]. It can even reduce the frequency of transformation to myeloma multiplex [3,10].

In an elderly woman the presenting clinical symptoms suggested a right-sided paranasal sinus tumour, however the subsequent examinations confirmed a maxillo-ethmoidal lesion on the left side. This turned out to be associated with routine chronic inflammatory disease but it drew the focus of attention away from the seemingly less serious but potentially malignant haematological disorder of the right nasal cavity. Notwithstanding the thorough radiological examinations and laboratory tests, immunohistochemistry was the only method that confirmed the presence of a myeloproliferative disease. We think this case represents an interesting clinical, radiological and pathological differential diagnostic problem in the field of oto-rhino-laryngology. Adequate diagnosis of EMP and the individual therapy planning should be a joint task of the haematologist, the pathologist, the oncologist and the surgeon.

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