The simultaneous appearance of a nasal natural killer-cell lymphoma and acute myelogenous leukemia

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Introduction and aim: Sinonasal malignant neoplasms are uncommon, with an annual incidence of less than 1/100,000. About 80% of these are squamous cell carcinoma. Adenocarcinoma and adenoid cystic carcinoma are next in frequency. Lymphoma of the nasal cavity, paranasal sinuses and nasopharynx are rare, constituting less than 5% of all extranodal lymphomas.

Case report: A 47-year-old man was referred to our hospital because of severe headache and progressive facial pain. He also complained of right-sided visual acuity. He had a manifest exophthalmia with disturbed eye movements. Nasoscopy showed a large mass with atypical appearance. CT and MRI showed a bilateral ethmoid mass invading the frontal sinuses, the right orbit, the lamina cribrosa and the right frontal cerebral region, and growing posteriorly through the choana. The first biopsies were inconclusive, showing only necrotic cells and purulent inflammation with epithelial elements. A larger biopsy demonstrated a high-grade malignant tumour with necrosis. The differential diagnosis of undifferentiated sinonasal carcinoma, undifferentiated neuro-endocrine tumour or T-cell lymphoma was suggested. In the meantime our patient developed high fever and sudden-onset pancytopenia. Bone marrow puncture showed 65% blasts, leading to the diagnosis of AML type M2. He was immediately referred for chemotherapy, but died in intensive care before his first session. The biopsy of the sinonasal mass was diagnosed surprisingly as a natural killer cell lymphoma stage IVB.

Conclusions: Natural killer cell lymphoma is rare in Europe. The simultaneous appearance of a NK-cell lymphoma and acute myelogenous leukemia has, as far as we know, never been described in the English literature before.

Introduction

Tumours of the nasal cavity and paranasal sinuses are rare. In Asia and Africa they are more common. The annual incidence of nasal tumours in the United States is less than 1 per 100,000 people. The incidence in males is 1.5 to twice that in females. Sinonasal malignancies are predominantly seen in the fifth to sixth decade of life. More than 50% of sinonasal tumours originate from the maxillary sinus.

Squamous cell carcinoma is the most common histological subtype, with an incidence of 80%, followed by adenocarcinoma and adenoid cystic carcinoma (approximately 10%).¹³ Lymphoproliferative diseases of the nasal cavity, paranasal sinuses and nasopharynx are uncommon, constituting less than the 5% of all extranodal lymphomas.⁴

Risk factors are exposure to wood dust, nickel, mustard gas and chemical products used in the furniture-making, leather and textile industries. The initial manifestations of sinonasal tumours are usually unilateral epistaxis and nasal obstruction. Other presenting symptoms are unilateral facial cheek and nasal swelling or pain, diplopia or blurred vision, headache, nasal discharge or repeated infection, unilateral proptosis and cranial neuropathies.¹³

Case report

A 47-year-old man presented at the emergency department with severe headache, progressive right-sided facial pain and a seriously swollen right eye. He was otherwise in good general condition, and his history was unremarkable. He was referred to our ENT department because of suspicion of a subperiostal abscess.

The patient had a severe right-sided exophthalmia and displacement of the eye in the temporal and inferior directions, with disturbed movements in an almost immobile eye. Vision on the right decreased progressively in a few days. He had been suffering from chronic sinusitis for many years. Sinus endoscopy revealed, however, a huge tumour mass with a pale, atypical appearance. Twenty years previously, he had worked with tropical wood for 3 years.

Blood analysis showed a raised CRP (8.0 mg/dL). The red blood count (5.25 × 10^6/µL), white blood count (7.7 × 10^3/µL) and platelets (288 × 10^3/µL) were within the normal range.

A biopsy of the mass was taken. Because of a preseptal abscess in the upper eyelid, a puncture for partial decompression of the eye was performed. Histological examination showed purulent cells and Streptococcus pneumoniae. The patient was hospitalised for intravenous antibiotic therapy.

An urgent computed tomography (CT) was made after injection of an iodinated contrast agent. This showed a strongly enhancing mass in the ethmoid bilaterally, expanding through the frontal sinuses and sphenoid (see Figure 1). The mass extended intracranially through the posterior wall of the frontal sinus, with expansion in the frontal cerebral lobe and perilesional oedema in the brain. The severe exophthalmia was obvious.

Magnetic Resonance Imaging (MRI) took place the next day to differentiate the mass better. In the nose, there was a bi-ethmoidal mass with an anteroposterior diameter of 7.5 cm, a craniocaudal diameter of 8.4 cm and a laterolateral diameter of 6 cm. The tumour expanded through the frontal sinuses and invaded intracranially through the lamina cribrosa and the posterior wall of the frontal sinus (see Figure 2). Retro-obstructive maxillary and sphenoidal sinus opacification was seen. Meningeal invasion was noted on the right. Intracerebral oedema was seen, which was even better appreciated in the T2-weighted images. They showed the invasion through the lamina papyracea on the right. The tumour invaded the orbit and caused lateral deviation of the medial rectus muscle.

The clinically observed mass in the nose was confirmed to be a stage T4b nasal tumour by imaging studies, according to the American Joint Committee on Cancer staging criteria. The result of the first nasal biopsy was inconclusive: necrotic and purulent inflammation with epithelial elements. The immunohistochemistry remained doubtful with regard to the exact nature of the process. In view of the location of the mass and given that the patient worked in the tropical wood industry, the preferred differential diagnosis was a spinocellular carcinoma versus an adenocarcinoma.

Because of the urgency of the situation, new biopsies were taken. These showed an undifferentiated high-grade malignant tumour with extensive tumour necrosis. Differential diagnoses were undifferentiated carcinoma or olfactory neuroblastoma, but an undifferentiated neuro-endocrine tumour, a malignant melanoma or a T/NK-cell lymphoma still had to be excluded. Further immunohistochemistry suggested a lymphoma.
The simultaneous appearance of a nasal NK-cell lymphoma and AML

A bone marrow biopsy was performed for the purposes of further staging. A day later, our patient had a high fever despite antibiotic therapy. The CRP rose to 14.7 mg/dL. He developed a pancytopenia (RBC 4.03 × 10^6/µL, WBC 2.5 × 10^3/µL, platelets 230 × 10^3/µL), with disturbed coagulation and liver tests. The bone marrow aspirate showed 65% blasts, which were morphologically biphenotypical, but with expression of MPO and negative TdT, resulting in the diagnosis of acute myelogenous leukemia (AML). Bone marrow biopsy confirmed this diagnosis.

Septic shock syndrome complicated with ARDS resulted in the transfer of the patient to intensive care for immediate chemotherapy. Unfortunately, he died due to cardiac arrest before the first administration.

Discussion

This patient was diagnosed with two concurrent haematological malignancies. Post mortem, the nasal biopsies showed a NK-cell lymphoma, stage T4b. At the same time, the patient developed AML.

A natural killer cell is a cytolytic cell capable of targeting tumour cells and bacteria- or virus-infected cells. It develops in the bone marrow from a bipotential T/NK progenitor cell. CD56 is a unique marker for NK cells.1,4,6

NK-cell malignancies are rare, with racial predisposition for Asians and South Americans.4,5 These tumours represent less than 1% of all lymphomas in Western countries.6,7 Lymphoproliferative diseases of the nasal cavity, paranasal sinuses and nasopharynx are uncommon, constituting less than the 5% of all extranodal lymphomas. Most lymphomas are diffuse large B-cell lymphomas.6 An association with Epstein-Barr virus (EBV) has been described.4,8

The WHO classification divides NK-cell lymphomas into two histological categories: extranodal NK-cell lymphoma, nasal type, which is divided clinically into nasal and non-nasal lymphomas, and aggressive NK-cell leukemia/lymphoma.4,5 Patients with an extranodal NK-cell lymphoma, nasal type, are between 50 and 60 years old. Nasal NK-cell lymphomas occur in the nose, paranasal sinuses and the upper airways. The primary sites of a non-nasal NK-cell lymphoma are the skin, the gastrointestinal tract, the salivary glands, spleen, testis and soft tissues.4,6 Patients with an aggressive NK-cell lymphoma leukemia are younger: between 30 and 40 years old. Men and women are equally affected. The outcome is poor, with a median survival of 2 months.4,5

The symptoms of a nasal NK-cell lymphoma are local, as in all malignancies of the sinuses: nasal obstruction, nasal tumour mass, facial swelling and discharge, epistaxis, proptosis, impairment of extraocular movement, visual disturbances, headaches.1,4,6,7

Cytogenetic abnormalities are common in extranodal NK-cell lymphomas of the nasal type: in 91% of the nasal NK-cell lymphoma a loss of heterozygosity at chromosome 6q is found.8 Our patient also had numerous genetic aberrations, such as a deletion of the 6q.

The therapy for a nasal NK-cell lymphoma is a combination of radio- and chemotherapy. The prognosis is poor, with a median survival rate of less than one year.4,5

Figure 2

On this coronal MR image, after the intravenous injection of gadolinium, the bilateral ethmoid and right-sided orbital tumour extension is clear to see, as is the large intracranial extension of the tumour to the right, with heterogeneous and strong enhancement.
Our patient had a NK-cell lymphoma, a very rare disease, and at the same time he developed another disease, AML. The possibility that both haematological diseases were related could be excluded.

The NK-cell lymphoma could be an extramedullar localisation of the AML, or a chloroma. This possibility was excluded by further immunohistochemistry.

The development of a secondary AML is rare. AML is considered secondary if it appears after the first chemotherapy for a malignancy such as a breast carcinoma, Hodgkin and Non-Hodgkin lymphoma in adults or childhood acute lymphoblastic leukemia (ALL). None of these possibilities were the case in our patient. Nasal NK-cell lymphomas are also localised; distant metastases are infrequent. Marrow involvement occurs in less than 10% of patients. Very rarely an extranodal NK-cell lymphoma ends in a terminal leukaemia, but this is an ALL.

We can consider the rather rare haematological malignancies as two different entities appearing coincidentally in one person. To the best of our knowledge, a similar case has never been described before in the English literature.

Conclusion

A sinonasal mass can present as a periorbital mass. Our case report showed a natural killer cell lymphoma, which is rare in Europe. The simultaneous appearance of a NK-cell lymphoma and acute myelogenous leukemia has, as far as we know, never described in the English literature until now.

References


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