CASE REPORTS

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Intravascular Lymphoma of the Inferior Turbinate: An Unusual Rhinologic Presentation of a Rare Neoplasm

ABSTRACT

Objective: To present a unique case of intravascular lymphoma of the inferior turbinate because of its rarity, unusual clinical presentation and difficulty in establishing a diagnosis.

Design: Case Report

Setting: A tertiary hospital

Patient: A 66-year-old male admitted to the hospital due to intermittent high grade fever of six months duration.

Result: The patient presented with fever of unknown origin, and exhaustive laboratory, ancillary procedures and biopsies to rule in/out infectious, autoimmune and oncologic causes were performed to arrive at a diagnosis. Nasal endoscopy revealed an enlarged, hypertrophied and violaceous right inferior turbinate with watery to mucoid discharge and septal deviation to the right confirmed by CT scans of the paranasal sinuses. Functional Endoscopic Sinus Surgery (FESS), septoplasty and turbinoplasty with biopsy revealed intravascular lymphoma. Chemotherapy was deferred due to the deteriorating medical condition and the patient expired seven months after the initial onset of symptoms.

Conclusion: Patients who present with fever of unknown origin should undergo a thorough otorhinolaryngologic examination to exclude primary ENT conditions and ensure proper management. Given its rarity and multiplicity of presentation, it is extremely difficult to make a diagnosis of intravascular lymphoma. A high index of suspicion of intravascular lymphoma is necessary so that timely acquisition of tissue biopsy of any lesion involved will make a definite diagnosis.

Keywords: *Intravascular lymphoma, Fever, Fever of Unknown Origin*

FEVER OF Unknown Origin (FUO) is defined as continuous fever of at least three weeks duration with daily temperature elevation above 101ºF or 38°C remaining undiagnosed after one week of intensive study in the hospital. It is also defined as temperature >100ºF persisting for at least three weeks in whom history, physical examination, CBC, urinalysis, chest x-ray fail to indicate a diagnosis. [1] It has always been a challenging task to look for the focus of fever. Given a case of FUO the possibility of malignancy, infection and autoimmune & connective tissue diseases must be investigated. This process usually entails extensive laboratory and ancillary procedures before finally reaching the definite diagnosis.

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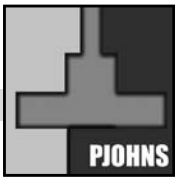

CASE REPORT

Our patient presented with a 6-month history of intermittent high-grade fever (temp 39-40C), chills, anorexia and weight loss. He had been admitted previously for the same complaint, when a complete blood count, urinalysis, blood culture, chest x-ray and 2D echo had failed to identify the source of the fever. He was discharged after a week with an impression of Fever of Unknown Origin (FUO), but persistence of fever, accompanied by generalized body weakness and dehydration, led to the present admission.

On physical examination, the patient was conscious, coherent and ambulatory. Aside from a fever of 38.8°C all other findings were essentially normal. The patient was evaluated by a multidisciplinary team composed of an internist, infectious disease specialist, rheumatologist and nephrologist and eventually a neurologist and an otorhinolaryngologist. Serial complete blood counts (CBC) showed anemia with normal differential count. Erythrocyte Sedimentation Rate (ESR) was elevated at 70mm/h. Prothombin time and Activated Partial Thromboplastin time were normal. Ultrasonograms showed normal sized spleen, liver and pancreas, small gallbladder cholesterolosis and bilateral diffuse parenchymal renal disease, with a double upper collecting system on the left.

Urine cultures, blood aerobic and mycobacterium tuberculosis cultures yielded no growth. A malarial smear was negative. With persistent anemia despite multiple blood transfusions, a bone marrow aspiration biopsy was taken, which showed normocellular marrow. Bacterial and fungal culture and sensitivity studies of the aspirate failed to grow any organism. Antinuclear antibody, anti-neutrophil cytoplasmic antibody, pANCA and cANCA were all negative.

The patient developed dyspnea, bipedal edema, electrolyte imbalances and elevated levels of serum creatinine, and subsequent acute renal failure probably secondary to decreased effective circulating volume, controlled with colloid infusions and diuretics.

He also experienced nasal congestion more on the right nasal cavity. Nasal endoscopy showed enlarged, hypertrophic and violaceous right inferior turbinate with watery to mucoid nasal discharge and septal deviation to the right. CT scans of the paranasal sinuses showed a hypertrophied right turbinate or polyps, right maxillary and ethmoid sinusitis, with obstructed right osteomeatal unit (Figures 1A and 1B). Antibiotics were started and he subsequently underwent Endoscopic Sinus Surgery (ESS), septoplasty and turbinoplasty with biopsy. Culture and sensitivity of the nasal discharge showed growth of *Enterobacter cloacae* and *Staphylococcus aureus.*

The patient later developed altered sensorium and an erythematous rash over the chest (Figure 2). The attending neurologist detected nuchal resistance, right-sided weakness and bilateral Babinski reflex which led to an impression of probable CNS tumor to consider lymphoma (leptomeningeal or parenchymal).

Histopathologic diagnosis of nasal lesion was angiotropic or intravascular large cell lymphoma, positive for CD20 (B-cell marker) (Figure 3A, 3B and 3C).

Chemotherapy was offered, but not consented to by relatives due to the deteriorating condition of the patient, who expired seven months after the onset of fever.

DISCUSSION

Intravascular lymphoma (IVL) is a rare and aggressive form of extra nodal diffuse B-cell lymphoma. To oncologists, intravascular lymphoma is the "great imitator" because it is very difficult to diagnose.[2] It can occur in any organ of the body with clinical presentations mimicking other diseases. The absence of malignant lymphoid cells in lymph nodes and reticuloendothelial system is a hallmark of the disease. It is characterized by the presence of large to intermediate size lymphoid cells only in the lumina of blood vessels without obvious tumor mass or leukemia.[3]

The disease was first reported in the literature in 1959 by Pfleger and Tappeiner in Germany and was described as *angioendotheliomatosis proliferans systemasata*,[4] as the authors then believed that the neoplastic cells were derived from endothelium.[2] But in 1980s immunophenotyping demonstrated that the neoplastic cell of origin is the lymphocyte.[5]

IVL has an estimated incidence of less than one person per million. It has been described in patients ranging from 34-90 years of age, with a median age of 70 years. It occurs equally in women and men.[3]

Pathogenic mechanisms have been proposed for the intravascular localization of IVL that relate to defective adhesion mechanism, in which tumor cells express CD44 antigen, the hermes-3-antibody-defined lymphocytic homing receptor for endothelial cells[6,7] but lack CD18 surface glycoprotein, which aids in lymphocyte extravasation.[7] Despite the large number of intravascular tumor cells, these cells are often not seen in peripheral blood smears.[3]

The majority of cases can be grouped into a few discrete presentations: fever of unknown origin (FUO), central nervous system involvement and cutaneous involvement.[8] Beyond these major presentations, there are single case reports of IVL presenting primarily in almost every organ system.[2] Anemia, elevated lactate dehydrogenase (LDH) and erythrocyte sedimentation rate (ESR) are the most common laboratory abnormalities seen in IVL.

Diagnosis is made through surgical biopsy of a suspected site of involvement.[2] However, the absence of any anatomic abnormality like lymphadenopathy often delays the diagnosis. In majority of cases, diagnosis is made only after a routine post mortem tissue examination.

The standard treatment of intravascular lymphoma if detected early is chemotherapy, however, relapses are common and the condition is usually terminal. Treatment options currently available are irradiation,

high dose corticosteroids and anthracycline-based chemotherapy. The anti-CD20 monoclonal antibody Rituximab is widely used for the treatment of IVL with skin and solid organ manifestation. Unfortunately, studies have shown that even with chemotherapy, prognosis is poor with a median survival of approximately five months.[9]

In summary, intravascular lymphoma is very rare malignant disease of extranodal Large B cell variety. Difficulty in diagnosis is evident due to the inherent diverse clinical presentations mimicking different diseases. Part of a thorough examination should include detailed evaluation of the ears, nose and throat in order to search for the early initial manifestation and subsequent histopathologic evaluation of any anatomic involvement. To our knowledge, this is the first and only reported case of intravascular lymphoma of the inferior turbinate, a rare type of lymphoma presenting in a very unusual manner.

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