medicinska revija
medical review

UDK: 616.428-006.6-033.2

Knezevic M. et al. MD-Medical Data 2014;6(4): 357-361

Medicinska edukacija/ Medical education

THE SIGNIFICANCE OF FINDING METASTATIC NECK LYMPH NODES IN HEAD AND NECK MALIGNANT TUMORS TREATMENT

ZNAČAJ OTKRIVANJA MALIGNIH LIMFNIH ČVOROVA VRATA ZA LEČENJE MALIGNIH TUMORA GLAVE I VRATA

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Key words
lymph nodes in the neck, metastatic lymph nodes, metastases of unknown origin

Ključne reči
limfni čvorovi vrata, metastatski limfni čvorovi, metasrtaze nepoznatog porekla

Abstract

Neck lymph node metastases are the first symptom of 12% head and neck malignant tumors. In the case of a neck mass being alike cervical adenopathy, the differential diagnosis comprises three different etiologies: congenital, infectious and neoplastic. In adults, a potential neoplastic origin should be considered at first. The presumpted diagnosis should be confirmed by fine needle aspiration cytology, which enables a reliability of over 90%. The connection between neck lymph node location and the corresponding lymphatic drainage system indicates the most likely origin of the primary tumor. The location of the primary lesions, its T stage, histology and ploidy status, as well as the immune status of the patient have all been related to the risk of metastasis. In this regard, cervical metastases from an unknown primary tumor account for 5% of all cases of metastatic neck disease. The diagnosis requires random biopsies of the regions where a submucosal neoplasm gives rise to early dissemination. The location, histology, stage and detection of the primary tumor are the main prognostic factors in such situations.

INTRODUCTION

It has been estimated that about 12% of all head and neck tumors (1) manifest in the form of cervical adenopathies. However, the detection of a neck lymphatic node requires the exclusion of a possible infectious process in the corresponding lymphatic drainage region, as for example in those cases where adenopathy is the first manifestation of the disease.

The assessment of a neck node should be made within the context of the differential diagnosis required by cervical tumorations in general; in this sense, the maxillofacial surgeon must adopt a working protocol capable of yielding a prompt and reliable diagnosis.

The differential diagnosis of a neck tumor basically comprises three etiologies: congenital, infectious and neoplastic. In the specific case of a neck node, a congenital origin should be discharged, centering attention on the other two possibilities.

DIAGNOSIS

Anamnesis

The clinical diagnosis in the presence of a neck mass should begin with a thorough anamnesis, including the clinical history of the patient, toxic habits, antecedents of trauma or irradiation, uncontrolled food intake or recent travel to a tropical country. The time of appearance of the mass, its rate of growth and the presence of concomitant symptoms should also be evaluated.

The age of the patient is one of the main considerations in evaluating the etiology of a neck tumoration. Three age ranges have classically been established: pediatric (less than 15 years), young adults (16-40 years) and adults (over 40

years). Depending on the age group involved, the diagnosis of a neck tumoration centers on one etiology or another. Thus, in pediatric patients and young adults [2] adenopathies typically reflect the existence of congenital or infectious disorders with an increased prevalence in the second group of neoplastic lesions. In turn, among adults (over age 40) attention should first center on a possible neoplastic origin, with inflammatory pathology in the second place.

Physical examination

The physical examination should establish the precise location of the cervical mass, its size, the possible presence of other tumorations, and the existence of inflammation [3, 4]. The exploration should be carried out with the neck of the patient slightly flexed, and all the cervical lymph node chains are to be palpated systematically. The presence of pulses or vibrations in response to palpation of a tumor mass is indicative of a vascular origin of the adenopathy.

Examination should further include a thorough assessment of the maxillofacial territory in search of possible neoplastic or infectious causes for the neck node. A careful intraoral exploration is thus indicated, along with an Rx orthopantomographic study.

The age of the patient and the location of the tumoration generally serve to establish a differential diagnosis between adenopathy and other neck tumorations. Thus, in pediatric patients or young adults cervical tumorations located in the midline or below the sternocleidomastoid muscle, and involving rapid growth and signs of inflammation, are suggestive of congenital cervical masses.

In contrast, a unilateral cervical tumoration in an adult patient located in the trajectory of the lymph node chains, with rapid growth, a size of over 2 cm and no signs of inflammation are indicative of a neoplastic lesion; measures required to identify the primary tumor must therefore be adopted. If adenopathies are bilateral and smaller, and are detected in a young adult, the underlying cause is typically inflammatory.

The findings of the physical examination, the location of the tumor, and the case history of the patient will yield a probable diagnosis, though complementary explorations are still needed to establish a definitive diagnosis [5, 6].

Complementary explorations

Fine needle aspiration cytology (FNAC) is the first procedure indicated after physical examination, and in most cases it suffices to identify the underlying etiology [7]. The technique involves the use of a fine gauge needle to puncture the tumoration and extract a sufficient number of cells to secure a rapid histological diagnosis of the lesion, with only minimal patient discomfort. The performance of multiple aspirations, a correct puncture technique, and the expertise of the cytologist are essential considerations for ensuring the máximum Information possible. In this context, fine needle aspiration offers a sensitivity of 97% and a specificity of 95% -with inter-cytologist variations that can reach approximately 8% [8].

The largest margin of error corresponds to the differential diagnosis between lymphoma and thyroid papillary carcinoma, while the reliability of the technique matches 100% in cases of malignant epithelial lesions. A biopsy with the Vim-Silverman needle is contraindicated due to the risk of tumor cells seeding along the trajectory of the needle. Fine needle aspiration has been found to be particularly useful in the diagnosis of thyroid nodules [9, 10], and in the etiological assessment of cyst lesions. It is also of help in the lymph node staging of oncological patients, for the planning of different treatment modalities.

The ability of fine needle aspiration cytology to differentiate between carcinomas and lymphomas generally allows open biopsies to be avoided, and facilitates the implementation of prompt and adequate treatment [11].

Negative fine needle aspiration findings, particularly in adults with risk factors, do not allow us to discard the presence of malignancy; repeat fine needle aspirations are required in such cases, together with complementary tests to rule out a neoplastic origin.

In this sense, imaging diagnostic techniques allow us to visualize the initial lesion and the presence of other adenopathies, and help assess their size, adhesion to tissue planes or structures, and so on. Likewise, when no definitive diagnosis of the adenopathy has been established, or in the event of discrepancies between the clinical picture and aspiration findings, than imaging techniques may yield additional information.

Computed axial tomography (CAT) or magnetic resonance imaging (MRI) -both of which have relative advantages and inconveniences- are the imaging techniques of first choice while the rest of explorations are usually reserved for more concrete situations.

Computed axial tomography [12, 13] provides a differential diagnosis between solid and cyst masses, and establishes the location and extent of the lesion, the presence of calcifications, and its relations to neighboring structures. Data can also be obtained to establish a possible glandular origin, and imaging with contrast injection serves to delimit blood flow. Cervical metastases are defined by adenopathies 1,5 cm in size or larger, adenopathies with evidence of central necrosis, a group of three or more adenopathies with a length of 8-15 mm, and the loss of tissue plane definition.

Magnetic resonance imaging [14-16] provides as much (if not more) Information as CAT. T2-weighted sequencing can localize incipient mucosal lesions in cases of metastases of unknown origin. Contrast injection delimits major vessel involvement, and in some cases the technique can replace arteriography. Image resolution is generally greater than with CAT in lesions at the base of the skull and in the upper third of the neck, and multilane imaging can be performed. An inconvenience of MRI is the possibility of artifacts caused by patient salivation or pulsatile vessel movements. Moreover, the exploration is more costly and longer than with CAT, and has a series of contraindications.

Echography is useful in distinguishing between solid and cyst masses. In those cases where a differential diagnosis is required between an inflammatory or metastatic lymph node in the context of patient staging, ultrasound is useful in guiding the needle in fine needle aspiration cytology. Echo-Doppler exploration can in turn detect vascular masses and carotid involvement.

Angiography [17, 18] has gradually increased in importance with the resolution of its technical problems. It is particularly indicated in patients with neck tumorations suspected of having a paraganglioma, but is also useful in the diagnosis of arteriovenous malformations, and in the evaluation of cervical tumor vascularization and the possible effects of tumors or traumatisms upon the carotid artery. Selective preoperative embolization can be carried out in the event of hyper vascularized masses, and in combination with CAT the technique can assess collateral arterial circulation in situations of infernal carotid ligation.

Open surgical biopsy is in turn indicated when imaging techniques and cytology fail to etiologically diagnose the neck node. This generally occurs in patients with lymphomas, where despite fine needle aspiration positivity additional biopsy is needed for histological labeling of the tumor [4, 11, 19, 20].

In those cases where biopsy implies an extensive cervical approach, a preoperative pathological diagnosis should be established, with cervical lymph node removal in the course of the same surgical procedure in those cases where a melanoma or carcinoma is diagnosed. In contrast, if an adenocarcinoma or lymphoma is identified, the surgical wound should be closed and subsequent action evaluated [21].

NEOPLASTIC DISEASES

Neoplastic pathology of the neck comprises two clearly differentiated etiologies: metastatic disease and lymphomas.

Malignant lymphomas are lymphatic neoplasms affecting the lymphoreticular system. They account for 5% of all neoplasms globally -a figure that increases to 55% among the pediatric population. The diagnosis is histological, and the processes are in turn divided into Hodgkin and non-Hodgkin lymphomas. Hodgkin lymphomas account for 60% of all lymphomas. As to patient age at presentation, a bimodal curve is observed, with a first peak at around 75-30 years of age, and a second peak at about age 50. Certain male predominance has been established. The primary symptom is the appearance of progressively growing lymph nodes without signs of inflammation. Fever, nocturnal sweating, weight loss and pruritus are occasionally observed. The adenopathies are located in the neck in 60-80% of cases, in the mediastinum in 60%, and in the abdominal cavity in 25%. In young patients, and following a thorough clinical examination, a biopsy is required to confirm a suspected lymphoma in the presence of a progressively growing neck tumoration without inflammation, since carcinomas are unusual in this particular age group.

Neck lymph node metastases are the first symptom in 12% of malignant tumors of the head and neck. The appearance of lymphatic metastases is de-pendent upon the histological grade of the tumor, the initial size of the lesion and the abundance of lymphatic capillaries within dependent territories. Unilateral lesions spread to lymph nodes on the same side, while lesions in proximity to the midline, those affecting the lateral margin of the tongue, and lesions in the nasopharynx can disseminate to both sides.

Metastatic adenopathy is to be suspected in an adult presenting an asymmetrical cervical mass measuring over 2 cm in diameter, with pain in response to palpation, relatively rapid growth in the past 3-4 months, and a history of smoking and alcohol intake. The diagnosis is confirmed by fine needle aspiration of the neck node. A thorough clinical study should be conducted, including careful examination to detect cutaneous lesions in the facial region, scalp and neck. Further-more, the oral cavity, nasopharynx, hypopharynx and larynx should he examined in search of the primary origin of the tumoration. The patient study is in turn completed by imaging assessments (MRI or CAT) of the maxillofacial zone. Despite these explorations, however, the primary cause of the adenopathy remains unestablished in 5% of cases (corresponding to metastases of unknown origin).

A series of factors predisposing to cervical metastases have been postulated, including:

1. Tumor location: Lesions in the floor of the mouth more frequently give rise to bilateral metastases, while tumors of the piriform sinuses and oral cavity show an increased tendency to develop occult metastases.

2. Tumor stage: The probability of lymphatic spread increases with primary tumor size.

3. Histological grade: A marked lack of tumor cell differentiation and the existence of perivascular and lymphatic invasion imply an increased risk of metastasis [21].

4. Tumor cell ploidy: Recent studies have demonstrated increased aggressiveness -and hence a greater tendency to metastasize- in tumors with a high percentage of diploid DNA [22].

5. Patient immune status: Host immune function appears to play an important role in the phase of tumor spread [23].

On the other hand, the following factors have been considered to indicate a poor prognosis:

A. Lymph node positivity: Survival among patients with positive nodes decreases 50%. This correlation to decreased survival is also observed when analyzing patients with clinically positive nodes versus those without palpable adenopathies [24].

B. Number of affected nodes: Survival has been shown to decrease among patients with multiple positive nodes versus those with only one affected node -particularly when four or more nodes are involved. Not all series confirm this, however [25].

C. Location of adenopathy: Patients with positive nodes at inferior jugular and supraclavicular level have a poorer prognosis than when other locations are involved.

D. Bilateral adenopathies: Tumors of the oral cavity, oropharynx and hypopharynx with bilateral metastases imply a poorer prognosis. Bilateral dissemination is only observed in 5% of head and neck tumors, however -particularly those of the base of the tongue, floor of the mouth, hypopharynx and supraglottic larynx. The appearance of contralateral metastases in a posterior phase has not been shown to imply a poorer prognosis than simultaneous bilateral presentations.

E. Fixed adenopathies: This factor interacts with others such as the number of affected nodes, their size and extra capsular invasion, since they generally manifest simultaneously. In 30% of cases of lymph node fixation, no extra capsular spread is observed, however. Fixation to neighboring

structures implies a two-fold greater recurrence rate than in patients with mobile adenopathies. Fixation is moreover a sign of non-operability, while fixation to large vessels suggests the need for radical treatment with possible pre-operative patient management.

F. Extra capsular invasion: This has been found to be the main factor influencing patient survival, and is also associated to an increased recurrence rate. Extra capsular tumor spread is intimately linked to the size of the adenopathy. In this sense, while 75% of those nodes measuring over 3 cm present extra capsular invasion, 14% of those only 1 cm in size also show extra capsular involvement. Survival in such cases is 15% at three years, versus 33% among patients with positive nodes but no extra capsular infiltration.

Despite the diagnosis of metastatic adenopathy, a thorough clinical study and CAT or MRI imaging the primary tumor remains unidentified, then the metastasis is said to be of unknown origin. Randomized biopsies are required in such cases of the nasopharynx, base of the tongue, tonsils and piriform sinuses, as these are regarded as the most likely sites of origin of such metastatic spread. The rationale for such biopsies is based on the theory ofa submucosal origin of the primary neoplasm, where metastasis occurs at a very early stage. In pa¬tients with supraclavicular or low jugular adenopathies, the study must be complemented by bronchoscopy and esophagoscopy. Nevertheless, it has been estimated that only 20% of these supraclavicular adenopathies originate from the aero digestive tract -the rest being circumscribed to the maxillofacial region.

The most common location of adenopathies of unknown origin is the jugulodigastric zone (50-70%), followed in order of frequency by the submaxillary and middle jugular regions, Approximately 45% are detected in stage N3, followed by stage N2 in 40%, and stage N1 in only 15% of cases. In terms of the histopathological diagnosis, squamous carcinoma is the most frequent presentation (60%), followed by adenocarcinoma (22%) and a lesser prevalence of other tumor types, such as melanomas and anaplastic carcinomas.

The management of metastases of unknown origin is a matter of debate, and the lack of randomized series precludes the drawing of firm conclusions. In any case, the choice of treatment is dependent upon the histology, stage and location of the lesions involved [26].

Sažetak

Metastaze u limfnim čvorovima su prvi simptom malignih tumora u regiji glave i vrata u 12% slučajeva. U slučaju izraštaja na vratu koji podseća na cervikalnu adenopatiju, diferencijalnom dijagnozom se mogu pronaći tri uzročnika: kongenitalni, infektivni i neoplastični. Kod odraslih, kao uzročnika promene prvo treba razmotriti neoplastični proces. Pretpostavljenu dijagnozu treba potvrditi citološkom analizom uzorka dobijenog iglenom biopsijom, čija je pouzdanost preko 90%. Povezanost lokacije limfnog čvora i limfatičnog drenažnog sistema ukazuje na najverovatnije mesto porekla primarnog tumora. Sa rizikom od metastaza se povezuju lokacija primarnog tumora, njegov T stadijum, histološki tip, stepen ploidije kao i imunološki status pacijenta. Prema tim kriterijumima, metastaze na vratu koje potiču od tumora nepoznate primarne lokacije čine 5% metastaza na vratu. Za dijagnozu je potrebna biopsija nasumično odabranog submukoznog regiona neoplastične promene gde ona može da otpočne ranu diseminaciju. Lokacija metastatskog limfnog čvora, histološki tip tumora, stadijum bolesti i lokacija primarnog tumora su prognostički faktori u ovim slučajevima.

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■ The paper was received on 23.10.2014. Accepted on 01.11.2014.