Management of neck masses in adults

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Abstract. Initial management of a neck mass in adults is a frequently encountered problem in ENT practice. The differential diagnosis with regards to clinical presentation, localization, imaging studies and cytology and/or histology is reviewed. An algorithm is provided to help the practioner.

Introduction

Differential diagnosis and initial management of a neck mass in adults is a frequently encountered problem in ENT practice.

Inflammatory and infectious diseases, such as cat scratch disease, are common in young adults. Congenital masses, such as branchial anomalies and thyroglossal ducts cysts, must be considered in the differential diagnosis. Neoplasms, benign or malignant are more likely to present in older adults.

It is difficult to make accurate statements about the percentage of masses that fall into one or other disease group (Table 1) as there are too many variables in the published data and regarding the age group. However, one of the most important underlying considerations in an adult presenting with a lump in the neck, is that the mass may represent a metastatic lymph node from a primary cancer often situated in the upper aerodigestive tract. To avoid delay in the treatment it is important to rapidly find the primary site – preferably without an open biopsy.

Fine-needle aspiration (FNA) and contrast-enhanced computed tomographic scanning are the best techniques for the evaluation of these masses.

When the complete evaluation, including serologic studies and search for a possible primary tumour, does not prove the benign or inflammatory nature of the neck mass, endoscopy under general anaesthesia, excisional biopsy with frozen section and subsequent neck dissection if relevant, random-biopsy of the base of tongue and diagnostic tonsillectomy should be considered.

Clinical picture

When confronted to a neck mass in an adult patient, a relevant medical history should be obtained and a thorough ENT examination should be performed.[1,2]

The physical characteristics of the mass are important: indurated tumour with an irregular surface, rock-hard or fixed masses suggest a carcinoma. Multiple soft, rubbery, matted nodes are more often lymphomas. Inflammatory masses are often of infectious origin.

A complete ENT examination of the oral cavity, pharynx, larynx, rhinopharynx and nasal cavities including a detailed endoscopy, is mandatory and additional information is sought (dental status, signs of Eustachian tube dysfunction, cranial nerves paralysis …). Palpation of the tonsils and base of tongue may reveal a suspect induration and lead to a high degree of suspicion.

Head and neck examination must include inspection of the scalp, skin, and ear canal. A surgical scar or radiodermatitis may orientate one towards a possible prior treatment for a skin neoplasm.

Making a diagnosis from the localization of a neck mass

Midline lesions are often developmental cysts and are commonly present from the first decades of life, even though they might present later.

The midline cervical masses include teratomas, dermoids and lesions derived from the thyroglossal duct. Thyroglossal cysts are most often situated in the mid-

Table 1
Lists differential diagnosis of cervical masses regardless of age of presentation or frequency.

Differential diagnosis of neck masses
Benign
Developmental
Inclusion cyst (sublingual and submandibular salivary cysts)
Thyroglossal duct cyst
Congenital vascular malformation
Branchial cleft cyst
Cystic hygroma
Laryngocele
Teratoma
Bronchogenic cyst
Lymph nodes, infective
Benign reactive hyperplasia
Bacterial lymphadenitis: *Staphylococcus aureus, Streptococcus pyogenes*, tuberculosis, cat-scratch fever, *Brucella*, atypical myco-bacteria tuberculosis, …
Viral lymphadenitis: Epstein-Barr virus, AIDS
Protozoa : *Toxoplasma, leishmaniasis*
Fungal : *Histoplasmosis, Blastomycosis, Coccidiomycosis*
Lymph nodes, granulomatous
Sarcoidosis
Foreign body reaction
Salivary gland (parotid or submandibular)
Infective : sialadenitis, sialolithiasis
Autoimmune : Sjögren's syndrome
Miscellaneous : AIDS related disease
Benign neoplasms
Haemangioma, lymphangioma
Thyroid nodule or goiter
Parathyroid adenoma
Lipoma
Fibroma
Neurofibroma
Sebaceous cyst
Aneurysm
Salivary gland tumour (parotid or submandibular)
Tumefactive fibroinflammatory lesion
Nodular fasciitis
Malignant neoplasms
Metastatic carcinoma, sarcoma, or melanoma in a lymph node
Lymphoma
Carotid body tumour
Glomus jugular tumour
Soft tissue, bone, or cartilage sarcoma
Primary major salivary gland tumour
Malignant melanoma
Adnexal carcinoma of the skin
Thyroid cancer
Parathyroid cancer
Direct extension of a head and neck neoplasm into the neck
Histiocytosis
Plasmocytoma
Carcinoid

line and move upward on swallowing. Dermoids are often associated with a dimple in the skin, from which project some hair.

The *lateral cervical malformations* include cysts and fistulas from the branchial apparatus, cystic hygromas, thyroid cysts, parotid cysts and the rare thymus remnants along the carotid sheath. Second branchial cysts occur superficially and lateral to the internal jugular vein and common carotid artery.

Lymphangiomas and cystic hygromas (two clinical entities, microcystic or macrocystic lymphatic malformations) may be found anywhere in the neck.

Conventionally, the neck is divided *into anatomical triangles.*[3] The lymph nodes in each triangle have defined drainage areas (Figure1) and metastatic spread for each primary first occurs to this area before progression to adjacent lymphatics. Skip metastasis are rare. Anatomical structures corresponding to drainage areas must be carefully scrutinised.[4,5]

When *multiple nodes* are present, the location of the largest mass gives the same clue as a solitary mass as to the probable location of a primary lesion.

Bilateral upper neck nodes (areas II and V) point to the nasopharynx, base of tongue, soft palate, supraglottic larynx or hypopharynx.

Inflammatory masses

Many viral agents like *Cytomegalovirus* (CMV), *Epstein-Barr virus* (EBV), measles, *Adenovirus*, *Echovirus*, *Rhinovirus* and *Respiratory Syncitial Virus* (RSV) produce cervical lymphadenitis. In most cases many lymph nodes
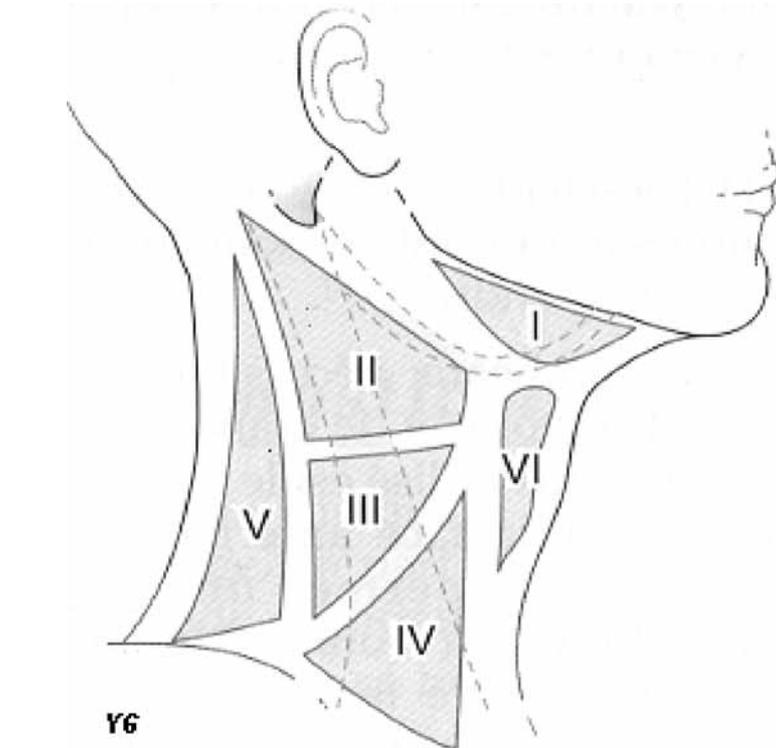

Figure 1

Location of cervical lymph nodes most frequently affected by metastasis from named primary sites in the head and neck.

Area I: cancer of the anterior floor of the mouth, lip, anterior two thirds of the tongue, gums, mucosa of the cheek and larynx; **Area II**: nasopharynx, oral cavity, pharynx or larynx; **Area III**: nasopharynx, oral cavity, oropharynx, hypopharynx or larynx, thyroid; **Area IV**: thyroid, pyriform sinus, upper oesophagus, primary below clavicle; **Area V**: nasopharynx, oral cavity, pharynx, thyroid, skin of the posterior scalp; Area VI: thyroid, hypopharynx, larynx.

are involved bilaterally and the reactive hyperplasia may persist for weeks.

An EBV infection is usually found in young adults. IgM antibodies are elevated and the MNI test is positive. Ig against EBV-VCA can be elevated in undifferentiated carcinoma of the nasopharynx (UCNT), frequently diagnosed by cervical lymphadenopathy.

Bilateral cervical lymphadenopathy lasting for more than 3 months is encountered in HIV infection. Elisa testing is positive.

Bacterial agents responsible for upper airway infections tend to produce acute cervical lymphadenitis limited to one group of

lymph nodes. *Staphylococcus aureus* and *Streptococcus pyogenes* account for 80% of cases. The source should be sought: a pharyngitis, dental infection or skin infection account for two thirds of cases but the aetiology may remain unapparent. Anaerobes are usually of dental origin.

Granulomatous infections involving the cervical lymph nodes include cat-scratch disease, tuberculosis, atypical tuberculosis and rarely, actinomycosis. Positive IgM antibodies for *Bartonella henselae* support the diagnosis of cat-scratch disease.

A positive family history and skin test for mycobacteria support this diagnosis, and may not be

associated with radiographically demonstrable pulmonary tuberculosis. *Mycobacterium tuberculosis* and atypical mycobacteria (mostly *Mycobacterium kansasii and Mycobacterium scrofulaceum*) may present with enlarged cervical nodes, but the diagnosis must be based on culture and histopathology isolated from a fine-needle aspiration or excisional biopsy (PCR identification of mycobacterium genomes is the most sensitive diagnostic technique available).

Other bacterial infections such as actinomycosis, tularemia (*Francisella tularensis*), infection due to *Pasteurella multocida,* syphilis *(Treponema pallidum),* brucellosis *(Brucella),* and rat - bite fever *(Spirillum minus)* are rare in our region but should be kept in mind in travellers or in the newly immigrated population.

Toxoplasmosis is usually asymptomatic and most adults are immunized but long lasting bilateral, non-suppurative cervical lymphadenitis is present when late seroconversion occurs.[1,2,6]

Imaging of a neck mass

Modern imaging plays an essential role in the work-up of a patient presenting with a neck mass.

Ultrasonography can accurately differentiate between cystic lesions, salivary gland tumours, reactive and metastatic nodes by using nodal size, vascularity pattern, and Doppler analysis.[7,8]

Ultrasonography has a definitive place in the initial assessment of a neck mass in the younger patient, in thyroid and salivary gland lesions and in suspicious lymph nodes.

However, ultrasound studies do not permit an evaluation of the upper aerodigestive tract and a possible primary lesion. Ultrasound imaging is highly operator dependant and does not allow an easy review of the studies by other physicians. Thus it is not recommended as first imaging studies in evaluating patients with a neck mass when the suspicion of malignancy is high (age > 40years, clinical presentation, history of smoking).

The fact that ultrasound imaging can be used to direct fine-needle aspiration when the mass is deeply located or non-palpable is an advantage although rarely an issue in patients presenting with an obvious neck mass.

Computed tomography (CT) scanning and magnetic resonance imaging (MRI) are the principal imaging modalities used in evaluating a neck mass.

Two major imaging criteria are used to detect pathological nodes: morphological abnormalities (central necrosis, peripheral stranding, abnormal internal architecture) size[9,10]

Much has been written on the superiority of CT over MRI imaging in the assessment of neck masses and nodal metastases[11] but both modalities are adequate in routine clinical practice.

In the evaluation of masses situated in the area of the major salivary glands, CT scanning and MRI have mostly replaced sialography due to their high sensitivity. Although there is relatively little evidence suggesting the superiority of MRI over CT scanning, MRI seems to perform better in the differential diagnosis of salivary gland tumours (identifying the tumour, perineural spread, …).[12,13]

CT scan studies in cystic lesions can help differentiate between benign and malignant cysts by recording the thickness of the outer wall, internal nodularity and the presence of septations but have not been universally discriminatory.

Positron emission tomography for imaging neck masses[10,14,15] allows one to identify an abnormally increased metabolism. PET is promising in the evaluation of cancer staging, diagnosis of local recurrence especially after radiation therapy, and possible detection of occult primary tumours. Because PET is expensive, provides poor anatomical detail, unless the modern fusion technique with a CT scan is used, and will demonstrate abnormal fixation not only in neoplastic lesions but also in inflammatory lesions, it is not routinely recommended for evaluation of cervical masses.

Fine needle aspiration cytology

Solid neck masses without obvious aetiology should be investigated using fine needle aspiration cytology.

This rapid technique does not cause seeding of tumour cells and/ or increase the risk of local recurrence for salivary gland tumours or metastatic squamous cell carcinoma.

The diagnostic reliability of 350 aspiration biopsies of lymph nodes indicated a sensitivity[16,17] of 85% and a specificity of 99%. Fine needle aspiration may however not provide adequate material for a detailed pathology analysis of lymphomas.

Ultrasound guidance FNA can be used in patients with poorly defined lesions but may not provide adequate material for the detailed pathology analysis of lymphomas.

In cases where the validity of a FNA is questionable, the use of an intra-operative frozen section evaluation may be the only way to determine the diagnosis.

Cervical cystic lesions represents a different challenge as in malignant cystic lesions of the neck, the false-negative rate associated with FNA cytology is in excess of 50%, presumably because the metastatic epithelium desquamates only at a late stage.[18,19] Thus a surgical excision with a frozen section is recommended in cystic masses (see below).

Initial management according to pathology

In a French series of 8500 patients with head and neck neoplasms, 475 presented with isolated lateral neck masses[4]: 190 (40%) in this subset had metastatic squamous cell carcinoma from unknown primary sites (CUP syndrome– carcinoma of unknown primary), 188 (39.5%) had lymphoma, and the remainder had either benign disease (78 patients, 16.5%), sarcoma (10, 2%), or chemodectomas (9.2 %).

The origin of metastatic *squamous cell carcinoma's* in patients with a cervical metastasis was investigated.[4,5,17] In one series of 267 patients, 74 % of neck metastasis developed from head and neck primaries, and only 11% origonated from primaries outside that region.

In a recent publication an estimated 5% of patients with cervical metastatic squamous cell carcinoma did not have a demonstrable primary (CUP).[20]

An *adenocarcinoma* in a metastatic lymph node almost always originates from a primary below the clavicles, but if it occurs in the upper neck, a search for a major or minor salivary gland tumour, thyroid cancer, or a rare parathyroid cancer is required.

Management of cystic swelling

The cystic nature is usually suspected on physical examination and is proved by ultrasound imaging or CT scanning examination. The differential diagnosis includes branchial cleft cysts, thyroglossal cysts, thymic and thyroid cysts, dermoid cysts, lymphangiomas and cystic lymph node metastases from squamous cell (tonsillar fossa) or papillary thyroid carcinoma.[21]

Lateral cystic swellings of the neck in adults are most often branchial cysts. However there is an increased proportion in the over 40 age group subsequently diagnosed as being squamous cell carcinoma cystic lymph node metastases arising from an occult primary located in Waldeyer's ring.[18,21] The prevalence of carcinoma in lateral cystic masses ranges[18,19,22] from 10% to 50 %.

Should the primary be located in the tonsil, it is not usually clinically obvious and these tumours seem to behave differently than other squamous cell carcinoma's.[23] Cystic squamous cell carcinoma metastases from an occult primary are generally not associated with the usual risk factors of smoking and drinking habits. The primary tumours located in the tonsil that present with a cystic neck metastasis seem to grow at a slower rate than expected when compared to solid squamous cell carcinoma metastases. The primary in the tonsil may remain occult for years.

The overall 5-year survival rate for solid metastases[24] is reportedly 45%, whereas the 10-year survival rate for cystic metastatic lesions is 50 %.

A controversy persists between cystic squamous cell carcinoma and the possible branchiogenic carcinoma, because the upper jugular lymphatics and many branchial cysts are found in similar locations. However, the existence of branchiogenic carcinoma is questionable.[24,25]

Even though a FNA has been recommended for the initial management in a lateral cystic swelling of the neck in the over 40 age group of patients, the false negative rate is significant and only surgical resection will provide a definitive diagnosis.

Surgery for a lateral cystic swelling in adults should be carried with a high suspicion of malignancy.[22] In case of positivity for carcinoma on a frozen section, a full neck dissection with panendoscopy, ipsilateral tonsillectomy and random biopsies of Waldeyer's ring should be carried out.

Panendoscopy

Endoscope examination of the upper aerodigestive tract should be performed under general anaesthesia if no cause for the mass is found or if metastatic squamous cell carcinoma is suggested.[4,6] A biopsy should be taken of any suspicious area. Random samples from the nasopharynx and the base of tongue are recommended. Ipsilateral tonsillectomy is recommended in the absence of an overt primary at the end of procedure.

Excisional biopsy

The incision should be planned to facilitate subsequent comprehensive neck dissection, if indicated. In case of surgical exploration of the neck, an excision biopsy with

frozen section analysis is required. Because wedge excision of a metastatic lymph node generates an extracapsular spread into the neck, it should be avoided.

When undertaking surgery for a neck mass of unproven origin, the surgeon must be prepared for the various pathologic findings and their surgical consequence. Depending on the frozen section results, an immediate comprehensive neck dissection may be recommended.

The prognosis of head and neck cancer is directly dependant upon the extent of nodal disease in the neck. Thus, the possible adverse effect of an incision biopsy remains debated as it creates a potential for seeding of tumour cells in the neck.[26,27] Violation of the neck by an open biopsy has an adverse effect on local recurrences (increased local failures 2-3 times) and survival.[28,29] Other studies have not shown a detrimental effect on neck control or survival in patients who have had a preliminary open biopsy.[30] The evidence is still controversial. Caution and common sense are however required as less invasive techniques such as fine needle aspiration may provide risk free cytologic samples.

Open biopsy may be detrimental to clinical management as it encourages fungation, potentially increases the risk of subsequent recurrence in the neck and complicates subsequent surgery of the neck required for definitive treatment, with subsequent increased morbidity.

Patients who have had previous open biopsy of a metastatic lymph node should undergo a comprehensive radical or modified radical neck dissection along with re-excision of the biopsy scar and

frequently additional radiotherapy.

Patients with open biopsy for pleomorphic adenoma should be treated by formal parotidectomy and scar excision if the tumour was not microscopically totally resected.[31]

Summary of investigations and algorithm (Table 2.)

Patients presenting with a cervical mass should be investigated by:

In-depth ENT examination

Laboratory investigation and testing (modified according to presentation)

Leukocyte count, full blood count, sedimentation rate, C-reactive protein, anti-streptomycin O titers, monospot, HIV 1-2 testing, IgM and IgG antibodies for EBV, *Toxoplasma gondii*, *Bartonella henselae,* syphilis, CMV

Tumour markers: CEA, ferritin, thyrocalcitonin, a-foetoprotein levels.
Skin test for *Mycobacterium tuberculosis* and *Mycobacterium kansasii and scrofulaceum* (when extracts are available)

Imaging

Ultrasonography
CT scanning of the head and neck and/or MRI.
CT is recommended when there is a high suspicion of a metastatic lymph node.
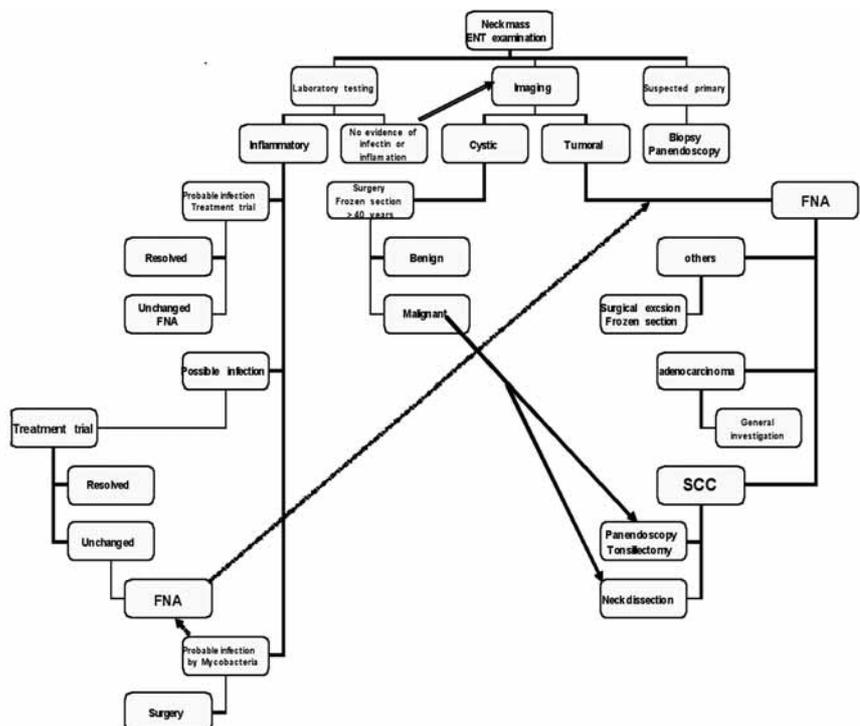MRI may be preferred in suspected salivary gland lesions.
Chest X-ray.

Fine needle aspiration cytology

Panendoscopy

A panendoscopy should be carried out if there is a high degree of suspicion of metastatic lesion in the neck. A biopsy should be taken of any suspi-

Table 2
Decision algorithm for a neck mass in adults.

cious area. Random samples from the nasopharynx and directed biopsies of the base of tongue are recommended.

Excision of the mass / frozen section

The incision should be planned to facilitate neck dissection. A high degree of suspicion should remain during surgery and a frozen section analysis of the excised mass or cyst should be performed. If the sample proves malignant, the surgery should be extended to a neck dissection. Further treatment depends on whether a primary lesion is found.

Tonsillectomy

This is indicated at the end of the panendoscopy when no primary can be found for a metatastic carcinoma of the head and neck.

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CME questions

1. Lateral neck masses in patients over 40 years are caused by malignant tumours in:

   A - 10%
   B - 40%
   C - 75%
   D - 90%
   of these patients

2. In the absence of overt signs of infection, a lateral neck mass in an adult patient is a:

   A - metastatic squamous cell carcinoma
   B - branchial cyst
   C - cervical adenitis
   D - tuberculosis
   unless proved otherwise

3. The primary tumour can be detected in up to:

   A - 75%
   B - 50%
   C - 25%
   D - 10%
   of patients by careful clinical examination alone and in a further 10-15% by panendoscopy of the upper aerodigestive tract

4. The technique of choice for assessing histology in a lateral neck mass after initial clinical examination is:

   A - MRI examination
   B - fine needle aspiration biopsy
   C - positron emission tomography
   D - surgical excision

5. An incision biopsy of cervical metastases is:

   A - the technique of choice for obtaining histological material
   B - risk-free
   C - probably result in an increased incidence of regional treatment failures
   D - not necessary when imaging is conclusive

6. An excision biopsy of parotid tumours:

   A - risks damage to the facial nerve
   B - may create seeding in the wound
   C - increases the risk of recurrence
   D - all of above

7. Lateral cystic lesions in adults over 40 years are often:

    A - cystic metastasis of squamous cell carcinoma
    B - cystic metastasis of thyroid carcinoma
    C - branchioma
    D - A and C and the surgery should be carried with this in mind and frozen section analysis

8. Nasopharyngeal carcinoma most frequently affects lymph nodes in:

    A - Area I and VI
    B - Area II, III and V
    C - Area I, II, III
    D - Area V

9. The triad of nasal obstruction, nasopharyngeal mass and recurrent epistaxis in a young male may likely represent a:

    A - chronic adenoiditis
    B - juvenile angiofibroma
    C - nasopharyngeal carcinoma
    D - B and C

10. The most common oral minor salivary gland cancer is:

    A - adenoid cystic carcinoma
    B - adenocarcinoma
    C - calcifying adenoma
    D - mucoepidermoid carcinoma

Answers: 1.C; 2A; 3A; 4B; 5C; 6D;7D; 8B; 9D; 10A