Neck Masses in Children: Adenopathy and Malignant Disease

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Neck masses in children are a frequent occurrence and may tax the clinical acumen of even the most astute physician. The differential diagnosis is extensive, but generally includes congenital lesions, lymphadenopathy, and malignant masses. Although the fear of malignancy accompanies virtually every child with a neck mass, cancer of the head and neck comprises only about 15 per cent of such masses in children admitted to the hospital. A logical method of evaluation is needed to prevent becoming lost in a quagmire of possibilities. By reviewing anatomy and mode of presentation, and obtaining a detailed history and careful physical examination, the physician may often arrive at a proper diagnosis on clinical grounds and confirm it with appropriate laboratory examination. In the following section, congenital lesions of the neck, lymphadenopathy, and common malignant masses will be reviewed.

Surface anatomy of the neck is reviewed. The neck is bounded superiorly by the lower margin of the mandible, mastoids, and superior nuchal lines, and inferiorly by the clavicles and a line through the spinous process of the seventh cervical vertebra. Two cervical triangles are formed by the sternocleidomastoid muscle medially and the midline of the neck anteriorly and posteriorly. These triangles are important in the physical diagnosis of neck masses.

Since the differential diagnosis of a cervical mass is lengthy, review of certain historical and physical characteristics may lead the clinician in the appropriate direction. Lesions present at birth suggest congenital cysts or anomalies. Congenital cysts, however, may present later if they become infected and may be easily confused with regional lymphadenitis. Inflammation may be associated with congenital lesions as well as lymphadenopathy, and its presence does not allow one necessarily to predict the benignity of the lesion. Masses that enlarge slowly over several months generally are benign whereas rapidly enlarging masses, particularly nontender, matted nodes, suggest malignancy. Inflamed masses that are painful when eating suggest sialadenitis.

Physical characteristics point to possible diagnoses as well. Diffuse, soft, spongy masses may be vascular malformations, such as cystic hygromas or hemangiomas. Cystic hygromas may transilluminate, whereas a bluish hue over the mass suggests a hemangioma. A midline mass that retracts while swallowing classically describes a thyroglossal duct cyst. The neonate who presents with a head tilt may have a fibrous tumor in the sternocleidomastoid muscle, implying congenital muscular torticollis. Generalized adenopathy is a sign of systemic illness, and often other signs and symptoms will lead to the diagnosis. Chronic localized inflammation, however, may indicate mycobacterial adenitis.

In addition to physical characteristics, location of the cervivcal mass is an important detail. Excluding thyroid nodules, most masses anterior to the sternocleidomastoid muscle are benign. Thyroid nodules in children, however, should be suspected to be malignant until proven otherwise. Other malignancies are likely to be found as a single mass in the posterior triangle or as multiple masses extending across into both anterior and posterior triangles. It must be emphasized that while this is generally true, there are exceptions. Supraclavicular

adenopathy strongly suggests mediastinal disease, and granulomatous or lymphomatous disease should be sought assiduously. Masses along the anterior border of the sternocleidomastoid muscle, particularly if associated with a fistula, are most likely to be branchial cleft abnormalities.

Lymphadenopathy

Palpable cervical lymph nodes are a common finding in any pediatric practice, and are often a normal finding. It is estimated that there are greater than 500 lymph nodes in the body, ranging in size from less than 1 mm to 1 to 2 cm. The amount of lymphoid tissue is age dependent, with proliferation until puberty when lymphoid mass is twice adult values. Generally lymph nodes are easily palpable in children, with cervical, axillary, and inguinal nodes being particularly easy to palpate. In addition, the spleen may normally be palpated in 14 per cent of newborn infants and in 7 per cent of children less than 10 years of age. A thymic shadow, commonly seen in infancy, is generally not radiographically apparent, however, after three years of age. Regional drainage areas of cervical lymph nodes are demonstrated.

Lymph nodes may enlarge through cellular proliferation intrinsic to the lymph node or by proliferation and invasion of cells normally extrinsic to the node. Stimulation of intrinsic lymphocytes may occur by various antigens, hyperthyroidism, and lymphomas. Histiocytes may proliferate in lipid storage diseases such as Gaucher's disease, or in histiocytosis X, or in the benign condition sinus histiocytosis. Nodal enlargement by cells extrinsic to lymph nodes occurs by invasion of polymorphonuclear leukocytes during bacterial and fungal adenitis, and by invasion of malignant cells into nodes in metastatic tumors or leukemia.

The evaluation of adenopathy properly employs knowledge of normal lymphoid development, a careful history, and detailed physical examination. The clinician should look specifically for location, shape, size, consistency, symmetry, mobility, signs of inflammation, suppuration, and overlying skin discoloration. Examination for more widespread or systemic disease should be completed. Overall, however, it may be helpful to divide the approach to cervical lymphadenopathy into regional or generalized lymphadenopathy.

Regional Adenopathy

Occipital nodes are commonly enlarged in afflictions of the scalp as in infections and seborrheic dermatitis. They may be enlarged in conditions that produce generalized adenopathy as well, or in specific viral illnesses such as rubella. They are normally palpable in about 5 per cent of children.

Preauricular nodes drain the temporal region and conjunctival sac and are commonly involved in "oculoglandular" syndromes, Parinaud's syndrome, or conjunctivitis and ipsilateral preauricular lymphadenopathy. Chlamydial conjunctivitis, adenovirus, cat scratch, and tularemia have been implicated as infectious etiologies, as have syphilis and tuberculosis. In addition, Hodgkin's disease may present with preauricular adenopathy. The clinician must rule out branchial cleft cysts and parotid inflammation as causes for swelling in this area.

Submaxillary and submental nodes enlarge with infections of the teeth, lips, and gums. Herpetic stomatitis, dental abscesses, and occasionally dry, chronically cracted lips may be associated with submaxillary or submental adenopathy. Salivary gland enlargement, particularly in cystic fibrosis, may be confused with enlarged lymph nodes. Over 90 per cent of children with cystic fibrosis over 2 years of age will have submandibular salivary gland enlargement.

By far, the most frequently involved groups of nodes include the superior and inferior deep cervical nodes, posterior cervical nodes, and superficial cervical nodes. These nodes enlarge with infections and enlargement may persist for long periods of time after the infection. One report demonstrated persistent adenopathy for 10 months afer a herpes infection. They may persist singly or multiply. The inferior deep cervicals drain a wide area including the entire head and neck, arm, thorax, lung, and mediastinum. Hence, these nodes may be affected by a large number of problems affecting a wide anatomic area.

Viral upper respiratory tract infection is the most common cause of enlargement, producing discrete, minimally tender, oval, soft nodes. Bacterial lymphadenitis usually produces systemic toxicity with unilateral or bilateral, swollen, acutely tender, sometimes fluctuant nodes with overlying warmth and erythema. *Streptococcus pyogenes* and *Staphylococcus aureus* have been isolated from lymph node aspirates. The staphylococcus is often penicillin resistant, and antibiotic therapy would require the use of a semisynthetic penicillin such as dicloxacillin. Rarely, *Hemophilus influenzae* and anaerobic bacteria have been isolated from lymph node aspirates as well. Mycobacterial adenitis will be discussed in detail in another article in this issue.

Cat-scratch disease may cause regional nonbacterial, tender lymphadenitis. A brief period of headache, malaiase, and fever usually follows a scratch from a cat, or rarely a dog or monkey bite. A primary pustule or papule forms and may persist for 2 to 7 weeks. Tender lymphadenopathy develops during the initial two weeks and may persist for 2 to 3 months. Suppuration occurs in 10 to 25 per cent of patients. Node pathology may range from reticulum cell hyperplasia to granuloma and abscess formation. Diagnosis is confirmed when three of the four following criteria are met: a primary lesion or history of animal contact or scratch; a sterile node aspirate with laboratory data excluding other possibilities; a lymph node biopsy consistent with cat-scratch disease; and a positive skin test to cat-scratch antigen. This antigen is not commercially available, however, and recently there has been some question as to its safety. In the majority of patients, no active intervention is necessary.

Infectious mononucleosis, or Epstein-Barr virus (EBV) infection, may produce localized cervical adenopathy or generalized adenopathy. Fever, malaise, tonsillopharyngitis, and hepatosplenomegaly may be associated with the illness in older children. Infants and young children often have atypical disease with silent or mild upper respiratory tract infections. Diagnosis is made by demonstrating a positive heterophil test. Young patients, however, may not have heterophil agglutinating antibodies. Twenty-seven to 91 per cent of 2 to 5 year old patients with EBV infection will be heterophil positive; 53 to 94 per cent of 6 to 10 year old children and 100 per cent of older children will be positive. Definitive diagnosis can be made by measuring specific EBV antibody titers. Definitive diagnosis can be made by measuring specific EBV antibody titers. Nearly half of children with

mononucleosis-like illnesses will be EBV negative. Cytomegalovirus infection, toxoplasmosis, and adenovirus infection have been identified in patients with clinically similar illnesses.

Sinus histiocytosis is a syndrome of massive, bilateral, painfless cervical adenopathy usually occurring in blacks. Occasionally other node groups are involved. Fever, leukocytosis with neutrophilia, elevated erythrocyte sedimentation rate, and hypergammaglobulinemia are other common features. This syndrome is benign and is characterized by persistent adenopathy for months to years and gradual resolution of the adenopathy. Occasional, extranodal sites such as the orbit may be involved. Histologically the lymph nodes show pericapsular fibrosis, dilated sinuses with intrasinusoidal histiocytes, and frequent plasma cells. The etiology is unknown, and the disease may recur.

Kawasaki's disease is characterized by acute nonpurulent swelling of cervical lymph nodes, fever lasting one to two weeks, conjunctivitis, dryness and fissuring of the lips, and rash of the trunk and extremities leading to membranous desquamation from the fingertips. Often there are elevations in the acute phase reactants, leukocytosis, thrombocytosis and urinary sediment abnormalities. Approximately 2 per cent of patients die of myocardial infarction owing to coronary artery aneurysms. The etiology is known and treatment with steroids and/or aspirin is controversial.

Generalized Adenopathy

Generalized lymphadenopathy occurs when nodes of two noncontiguous regions are involved in a pathologic process. Zuelzer and Kaplan provide an excellent review of generalized adenopathy. Systemic viral infections may cause generalized nodal enlargement, and illnesses that produce exanthems, such as rubella and scarlet fever, produce generalized lymphadenopathy as well. Bacterial infections including tuberculosis, syphilis, brucellosis, and typhoid fever also have been implicated. Other infections including histoplasmosis and toxoplasmosis may cause illness similar to EBV infection including adenopathy. In some immunodeficiency states, particularly chronic granulomatous disease and immune-mediated illness, generalized lymph node enlargement may be a prominent physical finding. In the acute stages of systemic lupus erythematosus and juvenile rheumatoid arthritis, two thirds of patients may have generalized adenopathy. Autoimmune hemolytic anemia occasionally has been associated with such adenopathy as to resemble lymphoma. The adenopathy of serum sickness generally resolves as the other major manifestations disappear. In lipid storage diseases such as Gaucher's syndrome, hepatosplenomegaly is present in addition to adenopathy. Sarcoidosis in children may be characterized by generalized adenopathy; the chest x-ray is usually abnormal, exhibiting hilar adenopathy, parenchymal fibrosis, or mottling. Chronic phenytoin administration has been linked with lymphoma-like syndromes with generalized enlargement of lymph nodes. Malignant conditions in children such as acute leukemia, histiocytosis, and metastatic neuroblastoma may have diffuse nodal enlargement. In general, however, all of these illnesses usually have other distinguishing signs or symptoms to aid in diagnosis.

Malignant Tumors

Of seven children admitted with neck masses, one will have a malignant mass. The tumors usually are derived from mesenchyme. Lymphoid tumors tend to predominate, the cell

type with Hodgkin's disease and lymphosarcoma comprising 55 per cent of malignant head and neck tumors. Rhabdomyosarcoma is the most frequent solid tumor of the head and neck in children. Fibrosarcoma, neurofibrosarcoma, thyroid neoplasms, and neuroblastoma are less common.

Although lymphosarcoma occurs approximately twice as frequently as Hodgkin's disease in general, Hodgkin's disease presents twice as frequently (80 per cent) as lymphosarcoma (40 per cent) with a neck mass. Hence, Hodgkin's disease and lymphosarcoma occur with about equal frequency when presenting as a neck mass. Hodgkin's disease generally will present as a painless, slowly enlarging, unilateral (80 per cent), firm, nontender node located in the upper one-third of the neck. When lower neck masses are found, as in supraclavicular adenopathy, mediastinal involvement is frequent. Six per cent of Hodgkin's disease may present as preauricular adenopathy simulating parotid swelling. Hodgkin's disease generally affects children over 5 years of age and, in contrast to lymphosarcoma, fewer extranodal sites are involved. Lymphosarcoma, on the other had, is more frequent in the younger patient. Extranodal sites, such as the tonsils, are four times more frequent in lymphosarcoma than in Hodgkin's disease. The nodes are described as a rubbery, discrete, painless mass.

Rhabdomyosarcoma is the most frequent solid tumor of the head and neck, comprising approximately 10 per cent of malignant head and neck tumors. It presents as a painless mass virtually at any site, and its accompanying symptoms depend upon the organ of encroachment. The nasopharynx, middle ear, mastoid, and orbit are frequent sites of involvement.

Fibrosarcoma and neurofibrosarcomas may present as a painless mass arising from the cheek, jaw, nose, or sinuses. They make up about 5 per cent of malignant tumors in the head and neck. These tumors have a low tendency to metastasize.

Thyroid masses in children should be suspected of being malignant, particularly if there is a history of irradiation to the head or neck. Generally, midline or slightly lateral masses are in close proximity to the thyroid gland so that diagnosis is not very difficult. Most of these tumors are of the medullary or mixed papillary and follicular type.

Although neuroblastoma is the most common solid tumor in childhood overall, it ranked sixth in frequency in malignant tumors of the head and neck. Primary neuroblastoma of the neck occurred in nine of 178 cases and generally could be distinguished from metastatic neuroblastoma by the early onset of neurologic signs as Horner's syndrome. In contrast, metastatic neuroblastoma usually spread to lymph nodes, and neurologic signs depended on growth of the node to impinge on neural structures. This occurred relatively late.

Age is a factor in the type of tumor found, as alluded to above. Children under 6 years tend to have neuroblastoma, most frequently followed by lymphosarcoma, rhabdomyosarcoma, and Hodgkin's disease. Children from 7 to 13 years have Hodgkin's disease and lymphosarcoma with almost equal frequency, with thyroid cancer and rhabdomyosarcomas following. The primary tumor of the head and neck in adolescents is Hodgkin's disease.

Evaluation of the child with a malignant neck mass requires a careful general examinatin with special attention given to the reticuloendothelial system. In addition, since

one of every six malignant neck masses has an associated tumor of the nasopharynx, a thorough examination of the ear, nose, and throat is mandatory. Routine laboratory studies as well as vanillylmandelic acid (VMA) spot test and possibly bone marrow examination are also indicated. Lymph node biopsy may give a definitive histologic diagnosis. Should a lymph node be interpreted as nondiagnostic, however, patients should be followed until the adenopathy resolves or a diagnosis becomes apparent. Kissane and Gephardt reported on 37 patients with initial nonidagnostic lymph node biopsies. Six patients died within the five to 20 year follow-up. Four died of probable immune deficiency and thrombocytopenia and two died of malignant disease. Similarely, Lake and Oski found 17 per cent of 41 initial nondiagnostic node biopsies to have noticeable disease on subsequent node biopsy. Hence, follow-up of these patients is imperative.