

Research Article

Branchial Cyst: A diagnosis of exclusion

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Abstract

The incidence of cancer in lateral neck cysts which were clinically diagnosed as branchial cysts was assessed retrospectively in two different periods in two different geographical locations over a period of 12 and 10 years. The incidence of cancers in these clinically benign cysts was nearly 14%. Although clinically these are labelled as branchial cysts, they ought to be investigated as cystic metastases from a nearby primary cancer, usually the tonsil, and a concerted search for a primary site ought to be made at the same time as excising them for histology.

Key words: Branchial cyst, lateral neck cyst, squamous cancer, Human Papilloma Virus, cystic metastasis.

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Introduction

Branchial cysts are considered developmental and related to the branchial apparatus. However, they generally present later in life. A significant number of these are malignant, i.e. they are cystic metastases from the tonsil or base of tongue. Human Papilloma Virus (HPV) related tonsillar cancers are on the rise lately in younger people where smoking and drinking may not be a factor but risky sexual behaviour might. A reasonable proportion of these HPV related tonsillar tumours present with neck metastases which are cystic in nature and thus they often mimic branchial cysts. All lateral neck cysts should therefore be managed with caution and investigated aggressively for possible cancer. Branchial cyst carcinomas themselves are rare enough for a case to be made to doubt their existence. Here too a nearby primary malignancy is a strong possibility for which a search ought to be made. Every lateral neck cyst therefore must be viewed with suspicion and is best considered cancerous and investigated and managed as such.

Material and Methods

This was a retrospective analysis of notes at two different hospitals in two different periods. The notes of all patients in the two periods who were coded as branchial cyst in the hospital coding system were selected. The coding system is applicable for in-patients only, therefore any patients who did not have an operation for whatever reason would not have been selected. This study was for the period of 1995 – 2007 at Kettering General Hospital and for the period of 2008 – 2018 in Teaching Hospital Kegalle, Sri Lanka. Those patients who had an apparent malignancy, where the Fine Needle Aspiration (FNA) showed cancer on cytology, those with any other head and neck malignancy or those who had a history of head and neck irradiation were excluded. The patients in this study therefore were those who would normally clinically be diagnosed as a branchial cyst.

Results

A total of 79 patients in total presented with a clinical diagnosis of branchial cyst or more specifically a lateral neck cyst. None of these patients had any clinical or cytological sign of cancer in the neck cyst or in the Waldeyer's ring. 44 patients in the earlier 13-year period of 1994 to 2007 were from Northamptonshire, England and 35 patients in the latter 10-year period (2008 to 2018) were from Kegalle, Sri Lanka. 11 of the cysts in these 79 patients were cancerous and the primary cancer was found in ten. These cysts therefore were actually cystic metastasis from these cancers. The overall incidence of cancer in such clinically benign cysts was 13.92%. The primary cancer site was in the nasopharynx in 3 patients, the tonsil in 3 patients, in the thyroid in four and in one patient a primary cancer site was not found during the five years of his follow up included in the study. This patient was given radiotherapy to the Waldeyer's ring and nasopharynx after a neck dissection as treatment of his malignant cyst which could have successfully treated a primary cancer there.

The age of those who had a primary cancer nearby ranged between 21 and 61 years with an average of 41.7 years. Patients with tonsillar cancers were between 49 and 61 years and those with nasopharyngeal cancer were between 25 and 59 years. Patients with thyroid cancers were younger, between 21 and 31 years with an average age of 28.5. Six patients with cancer were women and five were men. The patients who had cancer presented between two and six months after noticing the neck mass, the average time being 3.18 months. All these patients with cancer had definitive surgery within two months (average 1.59 months). All patients except one had a modified radical neck dissection. The seven patients with squamous cancer had their neck cancer treated with modified radical neck dissection with or without radiotherapy. Four patients had thyroid cancer. Three of these had neck dissections and all of these three had radio-iodine as well. The fourth had a total thyroidectomy and was disease free for six years of follow-up during the study. The three who had radioiodine as well had a follow-up of between three and 5.5 years during which they did not have a recurrence. Two patients did not have a FNA. Both of these had a nasopharyngeal carcinoma. The FNA in the rest of the nine patients did not show any sign of malignancy. This study included only those with a non-malignant FNA.

Discussion

Our incidence of 14% cancer in lateral neck cysts is in keeping with other such reports (6.9% - 22%)^[1,2,3]. This study was initiated in 2003-4 after two 'near misses' in such lateral cysts in whom the cancer was picked up by the senior author who had not long since joined the team in Northamptonshire. It was emphasised that all such lateral cysts ought to henceforth be treated as potential cancers and that all such cysts must not just be excised for detailed histology but that these patients should also have biopsies of their Waldeyer's ring in the way of an ipsilateral tonsillectomy, biopsies of the base of the tongue and biopsy of the post nasal space as a routine.

The first part of the study was initiated to emphasize the local rates of squamous cancer in lateral neck cysts, which was found to be 6.8% (3 cancers in 44 such cysts). These figures were discussed in our local educational meetings when the high incidence of cancers in such apparently benign cysts was effectively demonstrated, not least because these were our own local figures from the same hospital.

By the end of the first period the increasing incidence of HPV related cancers in the tonsils^[4,5] was becoming very apparent. The second part of the study was therefore continued hoping to document this increase even though it was done in a different part of the world, where the main author has now taken up his teaching post and practice. The incidence of squamous cancers in such lateral cysts here in Sri Lanka was 8.57% (3 in 33 patients). The incidence of all cancers in these lateral neck cysts however was much higher. Seven of these 35 cysts had cancer (20%). Four of these were from thyroid cancers. This large number of thyroid related cystic metastases is likely due to the higher proportion of thyroid related disease treated by the second author in his practice.

Role of FNAC

Efficacy of FNAC of these lateral neck cysts is limited in differentiating between benign cysts and cancers because branchial cysts are lined with stratified squamous epithelium (90%), respiratory epithelium (8%) or a combination of both and are typically surrounded by a variable amount of lymphoid stroma. This makes it difficult to reliably differentiate them from squamous cancers in the absence of clear malignant features. Differentiation between the two rests on higher number of inflammatory cells, fewer squamous cells with bland features and the presence of a lot of crystals in benign cysts as opposed to a large number of squamous elements with hyperchromasia, increased nuclear cytoplasmic ratio and possible nuclear membrane irregularity in the malignant cysts. Cells from squamous cancers can be deceptively bland making them appear benign. Similarly, a hypocellular metastasis from a thyroid papillary cancer too can look benign.

A case can be made for emptying the cyst and then repeating the FNA under ultrasound control, but such a high level of pathology and radiology support is unlikely to be available in most clinics. For these reasons a FNA report showing the absence of any definite malignant features is best ignored and further investigations towards searching for a primary site are best continued.

Radiology

An ultrasound can help confirm the cystic nature of the lump, although this is rarely a clinical difficulty. It is most valuable in picking up unsuspected thyroid nodules which may need a biopsy in less than straightforward cases.

An enhanced Computerised Tomogram scan is valuable in confirming the presence of vascularised solid areas in the cyst as well as increased blood flow, although benign cysts are often inflamed, thus causing confusion. Primary sites can often be picked up, or at least areas which are suspicious enough to warrant a biopsy.

Magnetic resonance scan with gadolinium is helpful by assessing the fluid nature and the internal architecture in the T1 and T2 settings and any enhanced signal from nearby areas in the tonsil and base of tongue are invaluable

in ascertaining possible primary sites. It is helpful to get an idea of surrounding nodes. MRI seems to be used more often for all of these reasons.

Positron Emission Tomograms are not easily accessible in many units. These are most useful in searching for the primary site after the cyst is found to be cancerous on FNA or on a needle biopsy and the MRI has not shown any obviously suspicious areas.

Branchial Cyst Cancers

Branchial cleft cysts are often from the second cleft and the many theories proposed about their origin range from incomplete involution of the branchial cleft mucosa, incomplete obliteration of the cervical sinus, incomplete obliteration of the thymopharyngeal duct to cystic transformation of lymph nodes caused by trapped epithelium.

Cancers in these branchial cysts, i.e. true branchiogenic cancer, is rare enough that many have wondered about its existence. Branchiogenic carcinoma was first proposed by Dr von Volkman in 1882^[6]. Since then there have been numerous reports of these but most reports were without a detailed search for a primary tumour. Large studies by Martin et al ^[7] Neel and Pemberton ^[8], Gourin and Johnson ^[9] showed that these apparent branchiogenic carcinomas were mostly cystic metastases. Martin et al ^[7] proposed their criteria for diagnosis of branchiogenic carcinoma, which required that they be at the site of a possible branchial cyst, i.e. on a line between the tragus to the clavicle, be histologically consistent with tissue originating from branchial cleft cyst, show a transition between normal epithelial tissue and carcinoma and have had at least a five-year period of follow up during which no primary tumour appeared. The first three criteria are fulfilled by most such cystic tumours. The last is the most contentious and a thorough and prolonged search has often shown a primary site, which can be very small and is often in the tonsil. There have been reports of tonsillar cancers appearing between 5 and 11 years later ^[10,11], which makes a very strong case for managing these cysts as cystic metastases from a nearby primary cancer and conducting a thorough search for a primary site.

HPV related Tumours

HPV is a known cause of oropharyngeal squamous cancers, associated with high risk sexual behaviours. Its incidence is increasing. Two thirds of oropharyngeal cancers are caused by HPV infection ^[12,13]. HPV type 16 accounts for most of these cancers. This usually effects the tonsil (or nearby base of tongue) and often presents with cystic metastases mimicking branchial cysts.

These HPV related cancers are clinically and pathologically different to the conventional smoking related oropharyngeal squamous cancers. These occur in younger patients who may not have smoked or regularly had alcohol. They are poorly differentiated non-keratinising squamous cancers, often with basaloid features. They are often small themselves and present as neck metastases which are cystic. These tumours respond better to radiotherapy and chemotherapy and are best treated with these organ sparing treatment modalities. Their prognosis is much better than the smoking related squamous cancers.

Management of Lateral Neck Cysts

Patients with lateral neck cysts must always undergo a thorough search for a nearby primary tumour. FNAC is usually not very helpful because the fluid from benign cysts will also contain squamous elements. Most of these patients will have a primary site in the Waldeyer's ring and imaging in the way of an enhanced CT or a MRI scan could show the primary site itself or at least will be useful in pointing out the suspicious area to biopsy. Tonsillectomy may avoid the need for excision of the neck cyst thus leaving the neck undisturbed for definitive surgery in smoking related squamous cancers, or leaving the neck undisturbed for early initiation of radiotherapy in HPV related poorly differentiated basaloid cancers in younger non-smokers. A definite diagnosis of a tonsillar

or base of tongue carcinoma will also allow the nasopharynx to be spared from radiotherapy, thus reducing the risk of damage to the pituitary.

A diagnosis of a benign brachial cyst in anyone older than a young adult ought to be made with great caution in the absence of a branchial fistula or a definite tract leading to the tonsil or the ear canal. All such cysts must always be considered malignant and investigated accordingly. If no primary is found they ought to be followed up carefully, as the primary may show itself a few years later.

Key Message

Lateral neck cysts have a high chance of being a cystic metastasis from a tonsillar or thyroid cancer. These must be investigated and treated as potentially malignant cysts.

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TABLES

Patient Number	Age	Sex	Size (cm)	Symptom	FNAC	Histology	Primary Site
1	51	F	5x4	6	not done	SCC	Nasopharynx
2	61	M	1.5x2	2	no ca	SCC	Tonsil
3	41	M	7x5	2	no ca	SCC	Unknown
4	25	F	3x3	3	Not done	SCC	Nasopharynx
5	58	M	4x2	3	no ca	SCC	Tonsil
6	31	M	5x2	2	no ca	Papillary Ca	Thyroid
7	34	F	5x4	3	no ca	Papillary Ca	Thyroid
8	28	F	3x3	3	no ca	Papillary Ca	Thyroid
9	21	F	2x2	4	no ca	Papillary Ca	Thyroid
10	59	M	2.5x3	3	no ca	Papillary Ca	Nasopharynx
11	49	F	3.5x4	4	no ca	SCC	Tonsil

Table 1a

Ca - cancer

SCC- Squamous Cell Carcinoma

Patient No: 1-4 are from first (Northamptonshire) series of 44 patients

Patient No: 5-11 are from the second (Sri Lanka) series of 35 patients

Patient Number	Treatment of primary	Treatment of neck	Interval between cyst excision and surgical treatment of neck (months)	Follow-up (months)
1	XRT	Mod RND	1	4
2	Tonsillectomy, XRT	Mod RND	2	24
3	XRT	Mod RND +XRT	2	60
4	XRT	Mod RND, XRT	2	12
5	Tonsillectomy, XRT	Mod RND	1.5	32
6	Total thyroidectomy	Mod RND +I ¹³¹	2	36
7	Total thyroidectomy	Mod RND +I ¹³¹	1	24
8	Total thyroidectomy	Mod RND +I ¹³¹	2	66
9	Total Thyroidectomy	-	2	72
10	XRT	Mod RND +XRT	1	18
11	Tonsillectomy, XRT	Mod RND		

Table 1b

Mod RND – Modified Radical Neck Dissection

XRT – Radiotherapy

Patient No: 1-4 are from first (Northamptonshire) series of 44 patients

Patient No: 5-11 are from the second (Sri Lanka) series of 35 patients