Introduction

The head and neck region includes skin, bone, salivary glands, thyroid, soft tissue, and lymph nodes. All of which are subject to neoplastic and nonneoplastic changes [1]. Cytopathologists are requested by clinicians to sample a particular site or organ, but on some occasions the cytological findings are not compatible with the clinicians target organ. Has the cytopathologist or interventional radiologist missed the site requested by the clinician or...
Materials and Methods

The cytology archive database of multiple institutions in southern Iran and Australia covering the period (2001–2011) were searched using keywords: salivary gland, head, neck, FNAC, and cytology. The total number of 10,200 head and neck superficial FNAC were included in the study from which 48 cases showed discordance between the clinicians request and the actual site of pathology. All FNAC were done under the guidance of sonography by cytopathologists. All the extracted reports were reviewed. The reports which showed discordance between the clinician’s impression of the organ involved in FNAC request form, and the eventual cytological diagnosis were selected from total controversial reports. Metastatic tumor in a lymph node was considered discordant when the primary tumor site was outside the head and neck or in intracranial regions. Further investigations performed by the cytopathologist and physician to make the final diagnosis, were reviewed in available records. The cytological diagnosis was confirmed by surgical biopsy, cell block, and immunostaining, with assistance of imaging, clinical outcome, physical examination, molecular studies, or microbiological cultures.

Clinical data

The data base search revealed 48 cases showing discordance between the clinicians request and the actual site of the pathology demonstrated in FNAC.

Patients had an age range of 1–72 years. Clinical data, including the organ site on which the clinician requested the FNAC, along with the cytological and surgical pathology diagnoses and the procedure that assisted with the diagnosis such as the cell block, immunohistochemistry (IHC), molecular, microbiological culture, imaging, history, and physical examination, are presented in Table 1.

Requested organ

The clinicians requested fine needle aspiration biopsy (FNB) on the following target organs: salivary gland (20), lymph node (12), soft tissue (11), and skin (5). Besides histopathology, imaging, clinical history, physical examination, immunohistochemical studies, microbiologic culture, and molecular tests helped to finalize the target organ of pathology in 28, 6, 8, 10, 4, and 1 cases, respectively.

Labelled organ versus final organ pathology mismatch

Salivary gland

There were 20 FNAC requests for “salivary gland” FNA, including seven cases where an initial FNA diagnosis favored a salivary gland tumor, however, further excision, IHC and imaging study showed osteogenic sarcoma [2] (Cases 1 and 2) (Fig. 1), soft-tissue inflammation (Case 3) chondrofibromyxoma [3] (Case 4), ameloblastoma (Case 5) (Fig. 2), spindle cell rhabdomyosarcoma [4] (Case 6) (Fig. 3) and bone myxoma (Case 7). Two cases were diagnosed on FNA as epidermoid cyst and squamous cell carcinoma but these were actually an odontogenic keratocyst and epithelioma of Malherbe respectively (Cases 8 and 9). Four cases were diagnosed as secondary lymphoma and cellulitis (Cases 10, 11, 12, and 13) (confirmed by IHC and culture). Six cases came out as: lipoma (Case 14), odontogenic keratocyst (Case 15), Ewing’s sarcoma of mandible (Case 16), ganglioneuroblastoma [5] (Case 17), and two cases of brown tumor [6] (Cases 18 and 19) (confirmed by IHC, history, and imaging). In one of the 20 discrepant “salivary gland” cases, the cytological diagnosis was inconclusive but osteopetrosis was demonstrated by imaging and biopsy (Case 20).

Lymph node

There were 12 FNA request for “lymph node” FNA. The cytological diagnosis of five cases were carcinoma,
Table 1. Clinicopathologic data of 48 controversial FNACs with histologic diagnoses and complementary diagnostic modalities needed to confirm origin and diagnosis.

| Case number | Age/sex | Requested organ | Cytology organ diagnosis | Histology | Complementary diagnostic modality |
|-------------|---------|-----------------|--------------------------|-----------|-----------------------------------|
| 1 [2]       | 70/F    | Salivary gland  | Salivary gland tumor     | Osteosarcoma | Imaging1 |
| 2           | 22/F    | Salivary gland  | Salivary gland tumor     | Mandibular osteosarcoma | Imaging |
| 3           | 44/F    | Salivary gland  | Salivary gland tumor     | Soft-tissue inflammation | |
| 4 [3]       | 60/F    | Salivary gland  | Salivary gland tumor     | Chondrofibromyxoma | Imaging |
| 5           | 45/M    | Salivary gland  | Salivary gland tumor     | Ameloblastoma | Imaging |
| 6 [4]       | 14/F    | Salivary gland  | Salivary gland tumor     | Spindle cell rhabdomyosarcoma | IHC |
| 7           | 17/F    | Salivary gland  | Salivary gland tumor     | Bone myxoma | Imaging |
| 8           | 23/M    | Salivary gland  | Epidermoid cyst          | OKC       | |
| 9           | 17/M    | Salivary gland  | Squamous cell carcinoma  | Epithelioma of Malherbe | |
| 10          | 12/F    | Salivary gland  | Lymph node               | Lymphoma  | IHC |
| 11          | 22/F    | Salivary gland  | Lymph node               | T cell Lymphoma | History and IHC2 |
| 12          | 46/F    | Salivary gland  | Lymph node               | Systemic lymphoma3 | IHC, imaging and P/E |
| 13          | 12/M    | Salivary gland  | Lymph node               | Cellulitis | Culture and P/E |
| 14          | 55/M    | Salivary gland  | Salivary gland tumor     | Not sufficient for diagnosis | Lipoma |
| 15          | 48/F    | Salivary gland  | Salivary gland tumor     | OKC       | Imaging |
| 16          | 1/M     | Salivary gland  | Ewing mandible           | Ewing mandible | IHC and imaging |
| 17 [5]      | 15/M    | Salivary gland  | Ganglioneuroma           | Ganglioneuroma | IHC, history and Imaging |
| 18          | 47/F    | Salivary gland  | Brown tumor              | Brown tumor | History and Imaging |
| 19 [6]      | 30/M    | Salivary gland  | Brown tumor              | Brown tumor | History and Imaging |
| 20          | 11/F    | Salivary gland  | NC                       | Osteopetrosis | Imaging |
| 21 [7]      | 46/M    | Lymph node      | Cancer                   | Metastatic meningioma | Imaging |
| 22          | 51/F    | Lymph node      | Granuloma                | Spindle squamous cell carcinoma | IHC and history |
| 23          | 2/F     | Lymph node      | Small round cell tumor   | Mandibular neuroblastoma | IHC |
| 24          | 46/F    | Lymph node      | Epidermoid cyst          | Metastatic squamous cell carcinoma | P/E |
| 25          | 42/M    | Lymph node      | Mixed tumor              | Skin adnexal tumor | |
| 26          | 32/F    | Lymph node      | Carotid body tumor       | Carotid body tumor | Doppler sono + IHC |
| 27          | 34/F    | Lymph node      | Neurofibroma             | Neurofibroma | History and P/E |
| 28          | 2/F     | Lymph node      | Neurofibroma             | Neurofibroma | IHC and imaging |
| 29          | 55/F    | Lymph node      | Salivary lymphoepithelial lesion | ND4 | Imaging |
| 30 [8]      | 50/F    | Lymph node      | Calcified material       | Calcified Goitre | Imaging |
| 31          | 15/M    | Lymph node      | NC                       | ND         | Imaging (salivary stone seen in sialography) |
| 32          | 66/F    | Lymph node      | Epidermal inclusion cyst | Epidermal inclusion cyst | P/E |
| 33          | 66/M    | Soft tissue     | Skin                     | Basal Cell Carcinoma | History |
| 34 [15]     | 35/M    | Soft tissue     | Cyst                     | Hydatid cyst | Imaging |
| 35          | 64/F    | Soft tissue     | Salivary gland tumor     | Mixed tumor | |
| 36          | 55/F    | Soft tissue     | Chondroid tumor          | Chondrosarcoma | Imaging |
| 37          | 62/M    | Soft tissue     | Squamous cell carcinoma  | Squamous cell carcinoma5 | History5 |
| 38          | 6/F     | Soft tissue     | Histiocytosis            | Histiocytosis of bone | Imaging and P/E |
| 39          | 4/M     | Temporal soft tissue | Histiocytosis | Histiocytosis of bone | Imaging |
| 40          | 34/M    | Soft tissue     | NC                       | Fibrous dysplasia | Imaging |
| 41          | 55/M    | Soft tissue     | NC                       | Fibrous dysplasia | Imaging |
| 42          | 40/F    | Soft tissue     | Actinomycetoma           | ND4 | Imaging and Culture |
| 43 [9]      | 71/F    | Soft tissue     | Multiple myeloma         | ND4 | Imaging and IHC |
| 44          | 56/M    | Skin            | Salivary gland tumor     | Adenoid cystic carcinoma | P/E, imaging |
| 45          | 47/F    | Skin            | Soft-tissue inflammation | Soft-tissue fungal infection | Culture |
| 46          | 27/F    | Skin            | Inflammatory process     | Osteomyelitis | Imaging and culture |
| 47 [16]     | 22/M    | Skin            | Lymph node               | LLL       | P/E |
| 48 [16]     | 57/M    | Skin            | Lymph node               | LLL       | P/E, molecular (PCR) |

FNAC, fine needle aspiration cytology; OKC, odontogenic keratocyst; IHC, immunohistochemistry; LLL, localized leishmania lymphadenitis; ND, not done; NC, noncontributory; P/E, physical examination; M, male; F, female.

1Any radiology work up.
2Previous lymphoma of breast.
3Lymphoma with secondary involvement of Salivary gland lymph node.
4Cell block only.
5Previous squamous cell carcinoma (SCC) of esophagus.
granuloma, small round cell tumor, epidermoid cyst, and pleomorphic adenoma and these cases were shown to be metastatic meningioma [7] (Case 21), spindle cell squamous cell carcinoma (Case 22), mandibular neuroblastoma (Case 23) (Fig. 4), squamous cell carcinoma (Case 24), and skin adnexal mixed tumor (Case 25), respectively (confirmed by history, IHC, histology, imaging, and physical examination).

One case on cytology and histology was a carotid body tumor (Case 26) and two cases were mandibular neurofibromas (Cases 27 and 28) (physical examination, imaging and IHC helped confirm the diagnosis). The diagnoses on FNA in three cases were salivary lymphoepithelial lesion (Case 29), calcified material [8] (Case 30 and 31), and epidermal inclusion cyst (Case 32), interestingly all these four case histology was noncontributory, and diagnosis were confirmed on imaging and clinical examination.

**Soft tissue**

There were 11 requests for FNA on “soft tissue”. In two cases the lesions were skin basal cell carcinoma (Case 33) and hydatid cyst (Case 34) based on cytology, surgical biopsy, and imaging. In another five cases the diagnoses

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**Figure 1.** Imaging of this salivary-like mass confirmed bony origin (mandibular mass) (A, arrow), cytology showed spindle cells and multinucleated giant cells (B and C Wright, 200x), which by cell block showing malignant osteoid, osteosarcoma was proved (D) (hematoxylin eosin, 200x).

**Figure 2.** Imaging of this salivary-like mass confirmed bony origin (mandibular mass) (A, arrow), cytology showed spindle cells and diagnosed as mixed tumor (B, arrow Wright, 200x), which histology proved ameloblastoma (C) (hematoxylin eosin, 200x).

**Figure 3.** Clinical and imaging of this salivary-like soft-tissue mass (A, arrow) (B, arrow), which cytology showed spindle cells and diagnosed as mixed tumor (C Wright, 200x), histology, and immunohistochemistry proved showed Spindle cell rhabdomyosarcoma.
were salivary gland pleomorphic adenoma (Case 35), bone chondrosarcoma (Case 36), metastatic squamous cell carcinoma (Case 37), and histiocytosis (Cases 38 and 39) based on FNA biopsy, imaging, IHC, history, and physical examination. In two cases, the FNA was noncontributory but the surgical diagnosis was fibrous dysplasia (Cases 40 and 41) supported by imaging. In two cases, the cytology diagnosis was actinomycetesoma (Case 42) and multiple myeloma [9] supported by microbiological culture, IHC, and imaging (Case 43).

**Skin**

There were five requests for FNA of “skin” and the final target diagnoses of three cases were adenoid cystic carcinoma (Case 44), soft-tissue fungal infection (Case 45) and osteomyelitis (Case 46) confirmed by physical examination, microbiological culture, imaging, and histology. The final two diagnoses were leishmania lymphadenitis supported by physical examination and molecular studies (Cases 47 and 48).

**Discussion**

Head and neck lesions can be easily seen and palpated due to their superficial locations and are highly suitable targets for FNA as the initial diagnostic test because of its high sensitivity and specificity for both neoplastic and nonneoplastic lesions [10–13]. Ultra sonographic-guided FNA of superficial organs is increasingly performed by with high accuracy to a variable extent depending on the site. However, understanding the complex anatomy, disease processes, and patterns of nodal spread in the head and neck make this technique ideal when applied with adequate clinical informations.

In our experience, physicians often request FNAC for any abnormal growth before they take thorough history, perform an adequate physical examination, diagnostic ultrasound or other imaging studies [14]. Inadequate clinical evaluation may lead to requests for FNAC on the wrong organ. Clinicians may make a mistake in detecting accurate location of head and neck lesions due to variations in the presentation of the lesions, for example, the sites and range of pathology in major and minor salivary gland areas and their mimics in soft tissue and bone of these sites [12]. All these errors may have adverse outcome for the patient including cost burden and surgical complications.

The clinical features of palpable mass lesions in the head and neck region overlap for skin, soft tissue, salivary gland, and bone or even with the frequency of different organ pathology (infectious and neoplastic processes). This very overlapping of clinical presentation makes the FNAC such an excellent minimally invasive first diagnostic test for head and neck lesions. Clinician’s presenting history, physical examination, and imaging of head and neck growth need to be best correlated with the FNAC findings.

Providing a previous history of malignancy by the referring clinician will assist the pathologist in assessing lymph nodes and other palpable lesions according to patterns of nodal spread in head and neck. Proper history was complementary in lymphoma involvement (Case 11), metastatic meningioma [7] and ganglioneuroblastoma [5] (Cases 21 and 17), uterine cervical squamous cell carcinoma metastasizing in neck as a “spindle cell SCC” incorrectly diagnosed as “granuloma” in FNA (Case 22) and skin tumor presenting as a recurrence (Case 33).

Thorough physical examination of skin lesions of histiocytosis or neurofibromatosis (cafe au lait spots) by cytopathologist can be clues to correctly diagnose a bone or neural lesions which were missed/not mentioned by referring clinician (cases 27 and 38).

Multifocal lesions on the face suggest a primary skin lesion rather than a pleomorphic adenoma (Case 32), although recurrent pleomorphic adenoma can be multifocal, or the previously undetected submandibular tumor in a patient with requested skin FNAC (Case 44), or in...
endemic areas for leishmaniasis the recognition of skin lesions that direct a FNAC of the localized leishmanial lymphadenitis and its diagnosis (Cases 47–48).

Recently, cytopathologists have learned to use ultrasound machines to assist them in performing FNA procedures. Imaging particularly the more readily available and clinically flexible ultrasonography should be used as an ancillary tool for both clinicians and pathologists to significantly improve FNAs in smaller, nonpalpable lesions and target complex lesions to confirm both organs of origin as well as the diagnosis with confidence and accuracy, and achieving a better outcome. For example, mandibular tumors can be cytologically and histologically mistaken for salivary tumor [2, 3] (Cases 1, 2). Odontogenic tumors with soft-tissue extension can be distinguished from skin or salivary lesions (Cases 5, 8).

FNA biopsy of bone lesions is a reliable diagnostic test for metastatic and primary bone tumors. Areas of difficulty were due to inadequate sampling or misclassification with regard to the exact site of malignancy (Cases 1, 2, 4, 7, 16, 18, 19, 20, 36, 38, 39, 40, 41, 43, 46). A bony mandibular lesion with an overlying suppurative sinus is suggestive of actinomycetes or osteomyelitis (Cases 42, 46).

Imaging also helps confirming a calcified goiter or salivary duct stones (Cases 30, 31). Color Doppler and immunostains on cell block helps in diagnosis of a hypocalcemic carotid body tumor (Case 26). Demonstration of bilaterality of salivary lesions and the absence of a true mass in imaging, helps to diagnosis lymphoepithelial disease rather than lymphadenitis (Case 29).

Cell blocks where available can be corroborated with immunophenotyping and immunocytochemistry as a method complementary to cytology in “tumor of origin/diagnostics” of lymphoma, round cell tumors, and spindle cell carcinomas [15, 16] (Cases 6, 10, 11, 12, 22, 23, 26). And in the same way, molecular testing can be useful, for example, polymerase chain reaction (PCR) to confirm mycobacterial or, among our cases, leishmaniasis (Case 48).

In conclusion mislabeling of the target organ for a FNA requested by a clinician may be due to the overlapping clinical and imaging findings of head neck lesions but is exacerbated by an inadequate history taking or incomplete or poor physical examination by the clinician. The clinicians should provide us with all possible clinical and radiological information, it is also good practice to look for this information if the morphological findings do not fit the clinical suspicion, especially in the current era of electronic medical records or a phone call should suffice. Cytopathologists should be ready to seek clinical clues by directly questioning the patient and examining the patient as required, prior to performing the FNAC, or returning to ask questions of the patient after rapid on site assessment of the FNAC material. Imaging prior to the FNAC or at the time of the FNAC plays a crucial role in defining the site and organ involvement of the lesion. Microbiological cultures, immunocytochemical study of FNA, and cell block biopsy material and molecular methods are essential ancillary tests to confirm the diagnosis, when available.

FNAs of the Head and neck can be easily confused, not only because of the clinical similarity between lesions but also because of the overlap in cytomorphologic features of the aspirated cells. Although no one single cytomorphologic feature is diagnostic, a combination of clinical parameters noted earlier should raise the possibility of diagnosis.

Proper technique and recognition of these pitfalls, as well as simultaneous cytopathologist and clinician work ups are needed to achieve a successful FNA diagnosis and avoid discrepancy of target sites between clinician and cytopathological reports.

Conflict of Interest

None declared.

References

1. Sternberg, S. S. 1997. Histology for pathologists. 5th ed. Lippincott-Raven, New York, NY.
2. Daneshbod, Y., and B. Khademi. 2009. Mandibular osteosarcoma: a diagnostic pitfall on aspiration cytology of the salivary glands. Cytopathology 20:136–139.
3. Daneshbod, Y., and B. Khademi. 2008. Chondromyxoid fibroma of the mandible: a diagnostic pitfall on aspiration cytology of parotid. Acta Cytol. 52:636–638.
4. Daneshbod, Y., and B. Khademi. 2005. Exfoliative cytologic findings of maxillary sinus spindle cell rhabdomyosarcoma. Acta Cytol. 54:358–361.
5. Daneshbod, Y., H. N. Khojasteh, B. Zamiri, and K. Daneshbod. 2007. Metastatic ganglioneuroblastoma in head and neck diagnosed by fine needle aspiration: a case report. Acta Cytol. 51:429–433.
6. Daneshbod, Y. 2008. Images in clinical medicine. Renal osteodystrophy of the palate. N. Engl. J. Med. 359:74.
7. Omidvari, S., H. Nasrolahi, Y. Daneshbod, N. Bagheri, S. Negahban, M. Mohammadianpanah, et al. 2010. Cervical lymph node metastases from meningioma: report of two cases and treatment outcome. Middle East J. Cancer 1:51–56.
8. Mirfazaelian, A., B. Khademi, and Y. Daneshbod. 2013. A hard place: calcified neck mass. Am. J. Med. 126:871–872.
9. Daneshbod, Y., M. A. Arabi, M. Ramzi, and K. Daneshbod. 2008. Jaw lesion as the first presentation of
multiple myeloma diagnosed by fine needle aspiration. Acta Cytol. 52:268–270.
10. El Hag, I. A., L. C. Chiedozi, F. A. al Reyees, and S. M. Kollur. 2003. Fine needle aspiration cytology of head and neck masses. Seven years’ experience in a secondary care hospital. Acta Cytol. 47:387–392.
11. Liu, E. S., J. M. Bernstein, N. Sculerati, and H. C. Wu. 2001. Fine needle aspiration biopsy of pediatric head and neck masses. Int. J. Pediatr. Otorhinolaryngol. 60:135–140.
12. Daneshbod, Y., K. Daneshbod, and B. Khademi. 2009. Diagnostic difficulties in the interpretation of fine needle aspirate samples in salivary lesions: diagnostic pitfalls revisited. Acta Cytol. 53:53–70.
13. Boccato, P., G. Altavilla, and S. Blandamura. 1998. Fine needle aspiration biopsy of salivary gland lesions. A reappraisal of pitfalls and problems. Acta Cytol. 42:888–898.
14. Wong, K. T., Y. Y. P. Lee, A. D. King, and A. T. Ahuja. 2008. Imaging of cystic or cyst-like neck masses. Clin. Radiol. 63:613–622.
15. Daneshbod, Y., and B. Khademi. 2009. Hydatid disease of the submandibular gland diagnosed by fine needle aspiration: a case report. Acta Cytol. 53:454–456.
16. Daneshbod, Y., K. Daneshbod, B. Khademi, S. Negahban, and G. R. Bedayat. 2007. New cytologic clues in localized Leishmania lymphadenitis. Acta Cytol. 51:699–710.