UNUSUAL PRESENTATION OF ACINIC CELL CARCINOMA OF THE RIGHT PAROTID GLAND WITH LOCOREGIONAL LYMPH NODE METASTASIS IN A 18 YEARS OLD MALE: A CASE REPORT WITH REVIEW OF LITERATURE

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Abstract

Acinic cell carcinoma (ACC) is a slow growing and low grade epithelial neoplasm of the salivary glands, in which few tumor cells exhibiting acinar cell differentiation that is characterized by presence of cytoplasmic zymogen secretory granules in the tumor cell. Most frequently ACC occur in parotid gland with the initial presentation somewhat at younger age than other parotid gland neoplasms and preferentially more in female with female: male ratio is 3:2 and median age at time of presentation is 52 years. “Fine needle aspiration cytology (FNAC)” examination may also be useful tool for confirmation of the diagnosis. The treatment of tumor is essentially by surgical excision of the gland. In histo-pathological examination; the most common presentation of tumor is solid sheet and nesting pattern of the growth followed by microcystic, papillary-cystic and follicular pattern. The purpose of the present case is to present the clinical, cytological and histopathological features of of ACC of the parotid glands of 18 years old male child which initially present as a benign cystic lesion of parotid gland than finally diagnosed as ACC with metastasized to regional lymph nodes. To conclude, ACC is frequently arising in parotid gland and metastasis to the intra-salivary gland lymph nodes is a very rare finding in young male. Intra-operative frozen section might be helpful in the diagnosis of parotid gland ACC because of low specificity and sensitivity of CT scan and FNAC examination of ACC. The histo-morphological examination of paraffin embedded H/E stained section is the main tool to explain the microscopic findings of ACC and to classify ACC of parotid gland. Special stain like PAS, PAS-D and IHC examination might useful for diagnosis of ACC. Surgery with adjuvant post-operative radiation therapy is acceptable for final outcome of disease and the tumor should be managed uncompromisingly, despite of its slow growing and low malignant behaviour, due to its metastatic prospective which usually confirmed by distant metastasis and recurrence. Hence, these tumors require a long-term follow-up.

Key words: ACC: Acinic cell carcinoma

Introduction

Acinic cell carcinoma (ACC) is a slow growing and low grade epithelial neoplasm of the salivary glands, having low malignant potential, in which few of the tumor cells exhibiting acinar cell differentiation that is characterized by presence of cytoplasmic zymogen secretory granules in the tumor cell (1). ACC was firstly identified as pathological entity by Godwin et al in year 1954 (2). Most frequently ACC occur in parotid gland with the initial presentation somewhat at younger age than other parotid gland neoplasms and preferentially more in female. The most common
primary malignant tumor of salivary gland in adult population is mucoepidermoid carcinoma followed by adenoid cystic carcinoma and ACC. In the pediatric population, the mucoepidermoid carcinoma is the most common epithelial malignancy followed by ACC. Females are more commonly diagnosed with ACC with female: male ratio is 3:2 and median age at time of presentation is 52 years with slightly more than 16% of cases were under the age of 30 years (3). The loco-regional and distant metastasis, higher tumor grade and larger size of growth, were more commonly seen among patient’s age more than 30 years, are associated with tumor recurrence and poor prognosis (4). “Fine needle aspiration cytology (FNAC)” examination may also be useful tool for confirmation of the diagnosis. The treatment of tumor is essentially by surgical excision of the gland (5). In histo-pathological examination; the most common presentation of tumor is solid sheet and nesting pattern of the growth followed by microcystic, papillary-cystic and follicular pattern. Most of the time, there is single pattern of the growth with combination of two or three patterns may be present microscopically (6). The purpose of the present case is to present the clinical, cytological and histopathological features of of “acinic cell carcinoma of the parotid glands of 18 years” old male child which initially present as a benign cystic lesion of parotid gland than finally diagnosed as ACC with metastasized to regional lymph nodes.

Case Report:
A 18 years old male patient was apparently asymptomatic 5 months back when he developed swelling in front of the right ear which was gradual in onset, progressively increasing in size, not associated with pain and not associated with sour food. There were no aggravating or relieving factors. There was no history of fever, difficulty in swallowing or breathing, ear discharge, ear bleed, nasal discharge or decreased hearing. On local examination: approximately 4x3 cm palpable lump below right ear extending upto posterior mastoid tip. The lump was soft to cystic in consistency, non tender with overlying normal temperature. There was no clinically significant palpable cervical lymphadenopathy. Family history was non significant. Hematological investigation was within normal ranges and negative for viral markers. On radiological investigation, USG neck finding suggestive of multicystic areas with moving internal echoes within right parotid gland with a necrotic lymph node at the level I B and cervical lymphadenopathy likely infective etiology. USG suggested FNAC evaluation to rule out? tubercular pathology. Xray chest showed normal study and MRI face showed enlarged right parotid gland with multiple cystic lesions, right level IB and bilateral level II cervical lymphadenopathy. Initially on FNAC of right parotid swelling, 13 ml brown color fluid was collected and swelling regresses back to normal and cytological smears shows thick eosinophilic proteinaceous material with few inflammatory cells and finding suggestive of benign cystic lesion and advised to explore for any obstructed causes of parotid duct. After 1 days, swelling was filled again with cystic fluid and a repeat FNAC was advised. On repeat FNAC, 17ml fluid was collected and cytological smears show cells are arranged in clusters and forming papilliform structure . The tumor cells are large with round to mildly pleomorphic nucleus, few of them are eccentric, showing moderate anisonucleosis, coarse chromatin and small nucleoli in many. The cytoplasms of tumor cells are abundant, shows vacuolations and pink granularity in many cells. Few binucleate, multinucleate and few giant cells alongwith abundant pink amorphous to granular material and abundant macrophages are also seen. Finally FNA finding shows features of neoplastic with differential diagnosis of ACC, mucoepidermoid carcinoma and warthin’s tumor.

Patient underwent for right superficial parotidectomy under GA. On gross examination, right lobe of parotid measuring 5.5x4.0x0.5cm. Outer surface shows bosselated appearance and areas of hemorrhage. On cutting open, cut surface shows multiple cystic cavities, largest measuring 1.2x1.0x0.2 cm. On serial sectioning of attached fat, 4 lymph nodes are identified, largest measuring 0.8x0.4x0.3 cm. On microscopic examination, a multicentric poorly encapsulated carcinoma forming a microcystic pattern. Cells have round to pleomorphic nuclei with variable amount of clear cytoplasm and occasional prominent nucleoli. Many cells show intracytoplasmic clearing and mucin deposition. Lymphovascular emboli are present. Four out of total 10 lymph nodes shows metastatic deposits of carcinoma without perinodal extension. On special stain, PAS and PAS-D stain shows focal intraluminal and intracytoplasmic mucin positivity. Final impression on histopathological was ACC-microcystic type with regional lymph node metastasis. On follow up patient advised for adjuvant radiotherapy.
Figure 1: MGG stain on Cytological smears (100x)

Figure 2: MGG stain on Cytological smears (400x)

Figure 3: HE stain on Histological Section shows microcystic pattern of Acinic cell carcinoma (200x)

Figure 4: HE stain on Histological Section of lymph node shows metastatic deposits of Acinic cell carcinoma with perinodal extension (200x)

Figure 5: HE stain on Histological Section of lymph node shows metastatic deposits of Acinic cell carcinoma with perinodal extension (200x)

Discussion:

ACC of salivary gland was first described in the literature by Nasse in year 1892 as a benign tumor and was recognized as a clinic-pathological entity by Godwin et al in year 1954 (2). Most frequently, ACC occurs in the parotid gland with preferentially more in females. Other unusual primary sites in human body where ACC was reported in literature include ACC of oral cavity (7), ACC of lips (8), ACC of hard palate (9), ACC of larynx (10), ACC of mandibular bone (11), ACC of nasal cavity (12), ACC of paranasal sinuses (13), ACC of pancreas (14), ACC of stomach (15), ACC of lung (16), ACC of breast (17) and ACC of prostate (18). The possible hazardous factors that can causes ACC include radiation exposure (19), familial predilection (20), industrial workers include rubber and asbestos industries, plumbing industries, and automobile industries. The etio-pathogenesis of
salivary gland neoplasms shows strong relationship between Epstein Barr Virus (EBV) and lymphoepithelial carcinoma. Endogenous hormone receptors of androgen, estrogen and progesterone were reported in previous literature in a small number of cases of ACC suggesting that hormonal dependence of ACC like carcinoma breast (1). ACC of parotid gland typically presents as slow growing tumor in the parotid region with mild pain or tenderness or and facial nerve palsy in only some previous reported cases. Clinical presentation of ACC with metastatic lymph node or metastatic deposits is unusual finding, if present, usually by hematogenous route rather than lymphatic, with a more predisposition for cervical lymph nodes followed by lung and bone (4). Other metastatic sites reported in literature include the cavernous sinus, sternum, spine, liver, orbit, skin and intracranial extension of parotid gland ACC (21). The molecular pathogenesis of ACC of parotid gland showed the cytogenetic alterations of chromosomes 4p, 5q, 6p, and 17p, deletions of chromosome 6q, loss of Y and trisomy 21, suggesting the role of tumor suppressor genes with the oncogenesis of these tumors (22).

On histopathological examination, usual presentation of ACC on gross examination as solitary lesion, usually well encapsulated with soft in consistency and cut surface shows greyish-white in appearance. If recurrence of growth occur, the growth often appears in bosselated manne with lobulated cut surface, the capsular surface may be present or absent with areas of hemorrhage and necrosis grossly. Microscopically, the commonest presentation of tumor is serous acinar cell differentiation with several other subtypes include intercalated ductal, acinar, clear, vacuolated, microcystic type as in present case, non specific glandular and solid lobular, follicular and papillary-cystic growth patterns (23).

The tumor cells in ACC are round or pleiomorphic with moderate to abundant lightly basophilic cytoplasm with presence of fine or coarse granules with few tumor cells have cytoplasmic vacuolation or clearing. The nuclei are eccentrically placed with inconspicuous nucleoli. On multiple sectioning of the salivary gland, the microscopic invasion of the overlying capsule can be detected and sometimes tumor nests may be detected outside of the capsule (2). On Microscopic examination, few microscopic features are frequently correlated with aggressive nature of tumor include frequent mitotic figures per high power field, presence of tumor necrosis, perineural or lymphovascular invasion, marked pleomorphism of the tumor cells, infiltration of tumor into surrounding structures, presence of stromal hyalination changes and those cases which shows dedifferentiation of the tumor from a lower grade to a higher grade of malignancy (1). Some differential diagnoses always kept in mind include oncocytomas, Warthin’s tumor, clear cell carcinomas, and mucoepidermoid carcinomas (2). FNAC examination had been well established diagnostic tool for diagnosis of salivary gland lesions as it provides useful information regarding the diagnosis and further treatment of these tumors. The FNAC findings of ACCs are usually characterized by abundant acinar differentiated tumor cells present within a clean background. Cells mainly arranged in clusters or with microacinar grouping. Tumor cells are mild to moderately pleiomorphic with abundant finely or fragile, vacuolated cytoplasm and nucleus showing mild to moderate anisokaryosis with bland chromatin. ACC of salivary gland is a commonest cause of false negative interpretation due to absence of morphological characteristic features of malignancy such as absence of markedly pleomorphic tumor cells, absence of tumor necrosis, and absence of high mitotic or proliferative activity. So, most of the time ACC of salivary gland is frequently misdiagnosed as benign salivary gland tumors for e.g. oncocytoma due to oncocytic nature of cytoplasm in ACC and even misdiagnosed as non neoplastic salivary gland parenchyma (24).

The utility of radiological examinations are for pre-surgical evaluation and management of the tumor which include ultrasonography (USG), CT, MRI, and nuclear scans. USG is useful for evaluation of tumor size, its location, and the nature of the growth. CT scan usually demonstrates contrast enhancement of the growth and useful tool for evaluation of size of growth, extension of the tumor, relationship of tumor to facial nerve and other structures, and presence of distant metastatic deposits. MRI scan show non specific signal intensity pattern in both ACC and by some benign salivary tumors. Electron microscopic examination show numerous cytoplasmic serous granules of varying electron density in ACC(23).

The management plan of ACC consists of complete surgical removal of the growth, by total or subtotal parotidectomy, and postoperative radiation therapy which might be useful for recurrent lesion and undifferentiated or dedifferentiated cases of ACC,
positive surgical margins, and advanced tumor stage with cervical lymph node or metastatic spread of the growth (4). A total parotidectomy with surgical removal of the facial nerve and neck dissection might be necessary for the tumor stage T3 and T4 cases. ACC usually considered as chemoresistant tumor, which is probably due to its slow rate of metabolism (3). Few previous studies suggested that postoperative radiation therapy was useful for those cases of ACC which shows following characteristics: (1) recurrence nature of tumors, (2) positive surgical margins of tumor after initial surgical removal, (3) growth lying adjacent to or involving the facial nerve, (4) deeper lobe of gland involvement, (5) presence of loco-regional or distant lymph node metastatic deposits, (6) extraglandular extensions of the growth, and (7) larger tumor size (>4 cm) (25). Few prognostic factors of ACC are studied in literature include age of the patient, association of pain or tenderness, sex, race, previously inadequate surgical removal or positive surgical margins, advanced TNM stage, and invasion of the growth to the base of skull (26).

Conclusion:

To conclude, ACC is rare malignant tumor, frequently arising in parotid gland and metastasis to the intra-salivary gland lymph nodes is a very rare finding in young male. Intra-operative frozen section might be helpful in the diagnosis of parotid gland ACC because of low specificity and sensitivity of CT scan and FNAC examination of ACC. The histo-morphological examination of paraffin embedded H/E stained section is the main tool to explain the microscopic findings of ACC and to classify ACC of parotid gland. Special stain like PAS and PAS-D and IHC examination might be useful for diagnosis of ACC. Surgery with adjuvant post-operative radiation therapy is acceptable for final outcome of disease and the tumor should be managed uncompromisingly, despite of its slow growing and low malignant behaviour, due to its metastatic prospective which usually confirmed by distant metastasis and recurrence. Hence, these tumors require a long-term follow-up.

References:


