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Co-existing ossifying fibroma and pleomorphic adenoma in the head and neck region – a case report and review of the literature

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Abstract
*Background***:** Presence of different cell lines in the head and neck region allows for the rare possibility of different neoplastic processes occurring simultaneously. The occurrence of these co-existing lesions could just be coincidental but occasionally may be due to a local or systemic cause. To the best of the authors' knowledge, there are no previous reports of co-existing ossifying fibroma and pleomorphic adenoma in the head and neck region in the English literature.
*Case presentation***:** A 39-year old female presented with a chief complaint of recurrent swelling on the right side of the neck of nine years' duration and left maxillary swelling of eight and a half years duration both of which were spontaneous in onset. The swellings had slowly increased in size to the dimension at presentation with no other significant findings in the medical and family history. Following other relevant history, examination and investigations a diagnosis of left maxillary ossifying fibroma and right recurrent parotid pleomorphic adenoma was made. Surgical excision of the two lesions were done with good outcome. We present a case of concurrent ossifying fibroma and pleomorphic adenoma occurring in the head and neck region. We also discussed the most important features, biologic behaviour and treatment of these two lesions and reviewed the literature.
Conclusion: Although the co-existence of these two lesions presented appear to be coincidental, however, the possibility of an underlying systemic link cannot be totally ruled out. Further reporting of similar cases may help to throw more light for better understanding of these multiple lesions.

Key words: *Co-existing, ossifying fibroma, pleomorphic adenoma, case report, maxillofacial.*

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Résumé
Contexte : La présence de différentes lignées cellulaires dans la région de la tête et du cou permet la possibilité rare que différents processus néoplasiques se produisent simultanément. L'apparition de ces lésions coexistantes pourrait être simplement fortuite, mais peut parfois être due à une cause locale ou systémique. À la connaissance des auteurs, il n'y a pas de rapports antérieurs de coexistence de fibrome ossifiant et d'adénome pléomorphe dans la région de la tête et du cou dans la littérature anglaise.
Présentation du cas : Une femme de 39 ans s'est plainte d'une tuméfaction récurrente du côté droit du cou depuis neuf ans et d'une tuméfaction maxillaire gauche depuis huit ans et demi, toutes deux spontanées. Les gonflements avaient lentement augmenté en taille jusqu'à la dimension à la présentation sans autres résultats significatifs dans les antécédents médicaux et familiaux. Après d'autres antécédents pertinents, un examen et une investigation, un diagnostic de fibrome ossifiant maxillaire gauche et d'adénome pléomorphe parotide récidivant droit a été posé. L'exérèse chirurgicale des deux lésions a été réalisée avec de bons résultats. Nous présentons un cas de fibrome ossifiant concomitant et d'adénome pléomorphe survenant dans la région de la tête et du cou. Nous avons également discuté des caractéristiques les plus importantes, du comportement biologique et du traitement de ces deux lésions et examiné la littérature.
Conclusion : Bien que la coexistence de ces deux lésions présentées semble être une coïncidence, cependant, la possibilité d'un lien systémique sous-jacent ne peut être totalement exclue. Davantage de rapports sur des cas similaires peuvent aider à jeter plus de lumière pour une meilleure compréhension de ces multiples lésions.

Mots clés : *Co-existant, fibrome ossifiant, adénome pléomorphe, rapport de cas, maxillo-facial.*

Introduction

Tumours in the head and neck region may arise from any of the cell lines present in this region. This allows for the rare possibility of multiple lesions arising from different cell lines. Several reports of such lesions

including hybrid, collision, concurrent and co-existing lesions are found in the literature [1-3].

While hybrid and collision lesions represent two or more distinct synchronous primary benign or malignant tumours appearing in the same anatomic region, the former are composed of different tumoural entities in a single neoplasm and the latter are lesions that originate in different sites but coalesce in a particular area. Co-existing lesions are two or more lesions occurring in the same or different anatomic regions of the body and present at the same time, a number of times these lesions are seen to originate from the same cell line. There are several reports of concurrent and co-existing fibro-osseous lesions in the mandible and maxillae, multiple salivary gland lesions within the parotids and Brown's tumour resulting from hyperparathyroidism [1-3].

However, it is still uncommon to find multiple lesions from different cell lines presenting in a patient at the same time. The presence of such lesions is sometimes an indication of a more pertinent systemic condition which must be taken care of to prevent flaring. Several concurrent and co-existing lesions have been previously documented in the head and neck region but to the best of our knowledge, ossifying fibroma (OF) co-occuring with pleomorphic adenoma (PA) has not been reported.

Ossifying fibroma is one of the types of benign fibro-osseous lesions of the jaw that are characterized by replacement of normal bone by fibrous tissue, containing varying amount of mineralized products [4]. Majority of OF in the head and neck region usually involve the mandibular or maxillary bone, however, OF arising in extragnathic sites including the temporal bone [5], nasopharynx [6], frontal bone [7], nasal cavity and paranasal sinuses [8], sphenoid [9] and ethmoid [10] have also been reported. The pathogenesis of OF remains controversial, while some authors have postulated the lesion to derive from multipotential mesenchymal cells of the periodontal ligament capable of forming cementum, bone and fibrous tissue [11,12], others have suggested residual embryonic nests to explain the gnathic and extragnathic site of occurrence [6,7]. Trauma, infection, as well as neoplastic and developmental process have been suggested to play a role in the pathogenesis [7,8].

Clinically OF usually presents as a well circumscribed round or ovoid expansile painless jaw bone mass that may displace the roots of adjacent teeth. If left untreated, it may reach considerable size as to cause severe disfigurement, compression effect on adjacent structures and functional impairment, however, root resorption or cortical erosion is rare and overlying epithelium is usually intact [2]. The commonest age of occurrence is the second and third decades of life while the gender and site predilection are the female and the mandible respectively. Radiologically, the appearance depends on the amount of calcified matrix produced by the neoplasm, ranging from complete radiolucency, mixed radiolucency/ opacity to opacity area with a well-defined and sometimes corticated margin [13]. Surgical excision is the preferred choice of management of OF, the tumour is usually well circumscribed and shells out well with enucleation, although large lesions may require resection. Prognosis is good, and recurrence is uncommon [14].

Pleomorphic adenoma (PA) is the most common parotid gland tumour accounting for 53 – 77 % of all parotid tumours [15], with majority (90%) being located in the superficial lobe of the gland. [15]. It is said to arise from myoepithelial cells with pleuripotential properties capable of differentiating to a variety of epithelial (ductal and non-ductal) and mesenchymal (fibrous, hyalinized, myxoid, chondroid and osseous) structures normally seen in the tumour albeit arranged in variable diverse and disordered structural pattern [16]. The exact aetiology remains unknown but genetic and environmental factors have been implicated [17,18]. About 70% of cases are associated with some form of chromosomal abnormality and three genes have been correlated with development of PA; pleomorphic adenoma gene1 (PLAG1), high mobility group AT-hook 2 gene (HMGA2), mucin 1 gene (MUC1) [17,19]. Suggested environmental risk factors include exposure to therapeutic irradiation [18], infection with the Simian virus [19] and use of mobile phones [20].

Clinically PA presents as a slowly progressive painless irregular, often lobulated mass located on the ramus in front or below the ear. It is usually mobile and firm in consistency although areas of cystic degeneration may be palpated in superficial lesions. If neglected, it can grow to grotesque proportion. PA can occur at any age but peak incidence is in the 4th to 6th decade with a slight female predilection [21]. Surgery is the treatment of choice for PA. With simple enucleation, recurrence rate varies from 20% to 45 % [22]. Incomplete capsules, satellite nodules, pseudopodia, positive surgical margin and tumour spillage have been suggested as possible explanation for the high recurrence [23]. However, with newer surgical approach of wide excision with adequate margin

involving superficial parotidectomy, total parotidectomy or extracapsular dissection, recurrence rate has dropped below 3% [24].

Case report

TVS is a 43-year-old female trader who presented in the Oral and Maxillofacial Surgery clinic of the University College Hospital Ibadan with a nine-year history of right neck swelling and eight-and-a-half-year history of left facial swelling both of which were spontaneous in onset. Patient noticed the neck swelling about 19 years earlier for which she had a surgical intervention at an outside facility. One year after the surgical intervention, patient observed a recurrence of the neck swelling for which nothing was done due to financial reasons until 9 years after when a second surgical intervention was done. The patient however presented with a nine-year history of another recurrent neck swelling and an eight-and-a-half-year history of right maxillary swelling at the University College Hospital, Ibadan There was no other significant finding in the medical and family history and there was no history of any previous remarkable event such as trauma.

(Figure 1A,). The intraoral component of the swelling consisted of a bucco-palatal well circumscribed mass extending from the region of upper left canine anteriorly to upper left 3rd molar posteriorly and to the midline palatally. Overlying mucosa appeared intact and there was full complement of firm teeth (Figure 1C). There was also a right multilobulated parotid-cervical soft tissue mass with intact overlying skin (Figure1B). Lesion was non-tender, non-discharging and not attached to underlying structure. There was no other abnormal finding on general physical examination apart from these two swellings. The provisional diagnosis was left maxillary ossifying fibroma and pleomorphic adenoma of the right parotid. Computerized tomography (CT) scan of the maxillary lesion showed a well circumscribed mass that appeared hyperdense with areas of hypodensity at the centre in the left maxillary region (Figure 2A). The CT scan also revealed a well circumscribed heterogeneously enhancing mixed density mass in the right parotid-cervical region (Figure 2B)

Fine needle aspiration cytology (FNAC) result showed the parotid-cervical mass to be a benign lesion while incisional biopsy of the maxillary

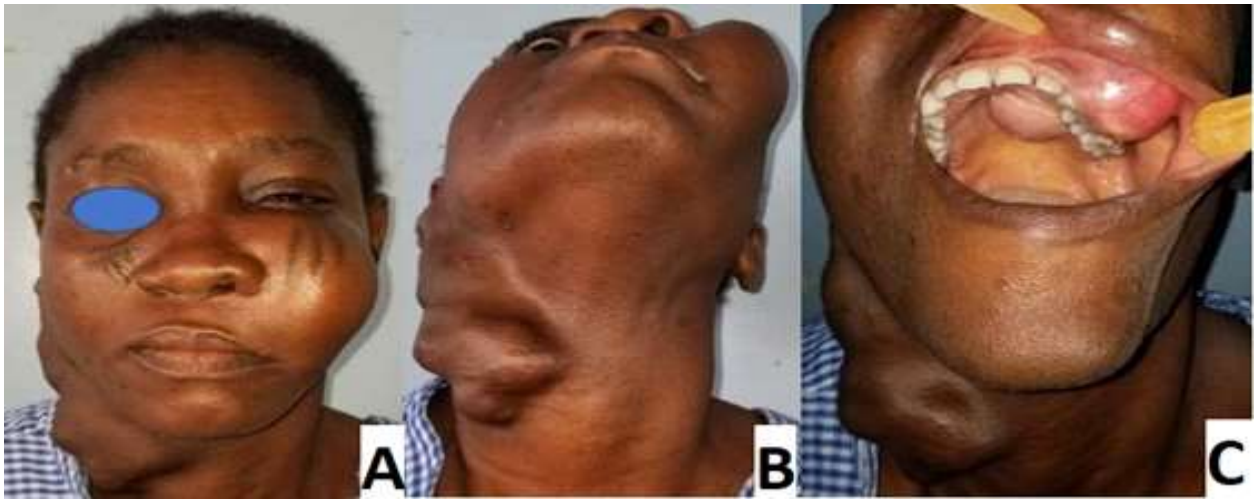

Fig. 1: Clinical picture of the patient showing the right parotid-cervical and left maxillary swellings (A) Frontal view of the patient (B) Worm eye projection of the patient, (C) Intra-oral view of the patient

Clinical examination revealed a middle-aged woman in no obvious distress, not pale, not jaundiced. Submandibular lymph nodes were bilaterally palpable and freely mobile. A right neck scar from a previous surgery was noted. There was facial asymmetry due to a well circumscribed left maxillary swelling extending supero-inferiorly from the infraorbital region to the upper lip and mesio-laterally from left alar of the nose to the zygomatic prominence measuring about 10cm by 9cm in widest diameter

lesion was histologically characterized by a non-encapsulated hypercellular fibroblast-rich stroma together with calcified bone trabeculae in keeping with fibro-osseous lesion. Blood chemistry and haematology were essentially normal.

Patient was scheduled for surgery and had surgical excision of both lesions. The maxillary lesion was approached using an intraoral vestibular incision and a limited maxillectomy involving teeth 21 to 27 was done. A lazy S incision was made in the lateral

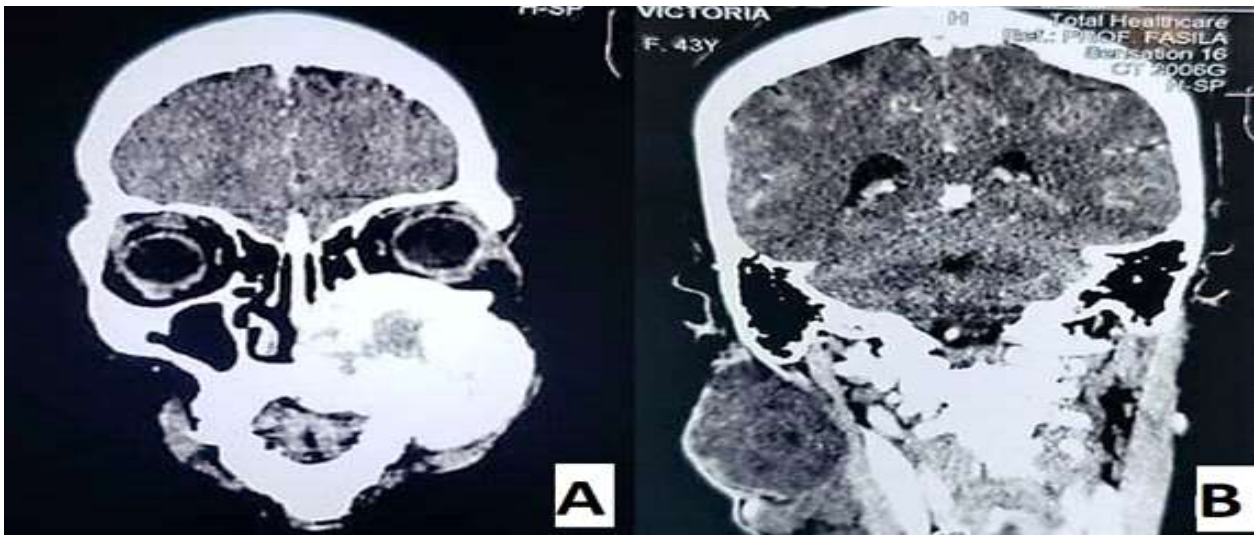

Fig. 2: Craniofacial coronal computed tomography scan of the patient showing (A) a well circumscribed hyperdense mass with areas of hypodensity at the centre in the left maxillary region, (B) a circumscribed heterogeneously enhancing mixed density mass at the right lateral aspect of the jaw

neck and the neck lesion was delivered en bloc with 1 cm margin of safety. Post-operative period was uneventful, and patient was subsequently discharged home. Histological examination of the tissue resected in the left maxillary mass revealed a single and bilayered ductal structures with the outer layer appearing to shed off into the abundant chrondromyxoid areas giving an overall appearance suggestive of pleomorphic adenoma (Figure 3a). Histological examination of the right parotid-cervical mass revealed irregular islands of immature bone with minimal osteoblastic rimming with dense fibrous connective tissue stroma and marked peritrabeculae clefting with overall features suggestive of ossifying fibroma (Figure 3b).

Discussion

Reports have previously documented various combinations of concurrent lesions in different regions of the body [25,26], however the occurrence of concurrent OF and pleomorphic adenoma is rare and to the best of our knowledge this is the first report of such combination in the head and neck region.

Presence of multiple maxillofacial lesions is a pointer to the possibility of a systemic basis for a disease [3]. The literature is replete with reports of multiple fibro-osseous mandibular and maxillary lesions secondary to systemic disease [1,3,27]. Haven et al. reported 1q25-q31 as the chromosome causing hyperthyroidism jaw tumour seen in 11 members of a Portuguese family [28].

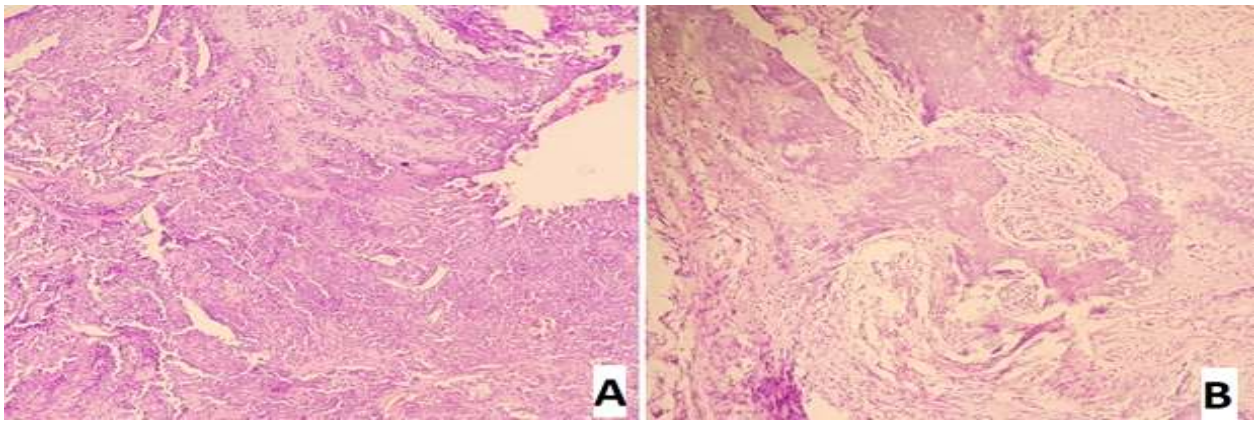

Fig. 3: (A) Photomicrograph of the right parotid-cervical lesion showing a benign salivary gland neoplasm composed of single and bilayered ductal structures with the outer layer appearing to shed off into the abundant chrondromyxoid areas. Overall appearance suggestive of pleomorphic adenoma, (B) Photomicrograph of the left maxillary lesion showing, irregular islands of immatured bone with minimal osteoblastic rimming with dense fibrous connective tissue stroma and marked peritrabeculae clefting. Overall features suggestive of ossifying fibroma.

Yamashita *et al.* also noted loss of heterozygosity at 1q24-q32 with allelic loss in some but not all parathyroid tumours associated with hyperthyroidism jaw tumour [29]. Kaya *et al.* reported a case of Simpson-Golabi-Behmel Syndrome (SGBS) an X-linked overgrowth syndrome characterized by pre and post-natal overgrowth, typical facial appearance and multiple visceral, skeletal, and neurological anomalies where the patient presented with pathologically distinct lesions including odontogenic keratocyst, ameloblastoma, lateral periodontal cyst, dentigerous cyst and mucous retention cyst in both mandible and maxilla [3].

OF and PA are two different entities with distinct and varying aetiopathogenesis, clinical courses, treatment options and prognosis. Different theories have been proposed for the occurrence of multiple lesions in different regions of the body [25,26]. These include certain unidentified carcinogens, common gene and residual embryonic structures. These three factors have been implicated in the development and progression of concurrent tumours [27]. Other theories include those of collision tumours and the presence of a lesion displacing a tooth and preventing its eruption to initiate concurrent dentigerous cyst and Adenomatoid Odontogenic tumour [26].

Ossifying fibroma of the jaws commonly occur in the 2nd and 3rd decades of life as a well circumscribed swelling; in the present case, the patient was 34 years old when she first noticed the circumscribed maxillary lesion. Synchronous ossifying fibroma of the jaws is also well reported in the literature often involving multiple cranial bone [2,11]. The first synchronous occurrence of this lesion was reported by Bradley and Leake in a 6-year-old girl with maxillary and mandibular lesions of 4 years duration [30]. Yih *et al.* reported multiple familial ossifying fibromas as a heritage disorder [31]. However, Wang et al. reported 2 cases of sporadic multiple ossifying fibroma with no associated genetic mutation [32]. Several synchronous multifocal Central Giant Cell Granulomas of the maxillofacial region have also been reported both in the syndromic state and the non-syndromic state with the syndromic variant being more common [27,33]. In addition, multiple lesions within the salivary glands was also previously reported unilaterally by Horisk and bilaterally by Filippo and Sahoo who reported a case of two concurrent large epidermoid cysts in sublingual and submental region resembling plunging ranula [34,35].

Despite these reports presenting simultaneous odontogenic lesions or simultaneous odontogenic and nonodontogenic lesions that are described as combined/hybrid lesions [36], co-occurrence of entirely independent and distinct lesions is extremely rare [37]. From our literature search, this is the first report of a simultaneous occurrence of recurrent pleomorphic adenoma of the parotid gland and a maxillary ossifying fibroma.

Although the simultaneous occurrence of these two distinct lesions in the present case appears to be more of a coincidence, the possibility of an underlying systemic link however cannot be totally ruled out. Being the first and a single case report, it is difficult to make strong assertions, further reporting of similar cases may help to stimulate further research for more understanding of these multiple lesions.

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