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UNUSUAL BEHAVIOUR OF PAPILLARY THYROID CARCINOMA IN AN OTHERWISE FAVOURABLE VARIANT

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Abstract

Papillary thyroid carcinoma (PTC) is the most common thyroid malignancy in iodine replete area. There are twelve variants of PTC of which classic and follicular variant (FV) are the most common (>90%) and are associated with very good prognosis. Three cases of aggressive behaviour of PTC are discussed in this case report. Moreover, we searched the literature for possible explanation with emphasis on molecular study and the impact thereof on the American joint committee on cancer (AJCC) classification.

Introduction

Papillary thyroid carcinoma (PTC) is the most common thyroid malignancy in iodine replete area. There are twelve variants of PTC of which classic and follicular variant (FV) are the most common (>90%) and are associated with very good prognosis. Three cases of aggressive behaviour of PTC are discussed in this case report. Moreover, we searched the literature for possible explanation with emphasis on molecular study and the impact thereof on the American joint committee on cancer (AJCC) classification.

Case Reports

Case 1

A 46-year-old female patient presented with a 19-year history of a large goitre associated with progressive back pain and left parietal scalp mass of one year duration. She initially consulted the orthopaedic surgeons for bilateral lower limb paraparesis. CT (computed tomography) scan revealed lytic lesion on the left parietal bone and extensive lumbar and sacral metastasis. The fine needle aspiration cytology (FNAC) of the goitre diagnosed follicular variant of papillary thyroid carcinoma that was confirmed on histopathological report. Interestingly, her delayed presentation to a healthcare facility was attributed to a cultural barrier. The perception that thyroidectomy is an extremely dangerous operation is a deterrent to early surgery. After discussion in multidisciplinary team, there was no indication for neurosurgical intervention for the brain metastasis and palliative radiotherapy was suggested to alleviate bone pain. Radioactive iodine (RAI) was not an option considering the significant burden of the disease.

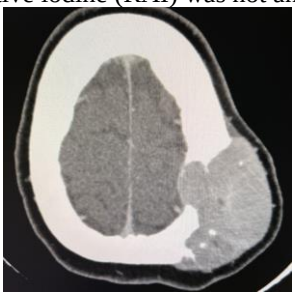

Fig. 1

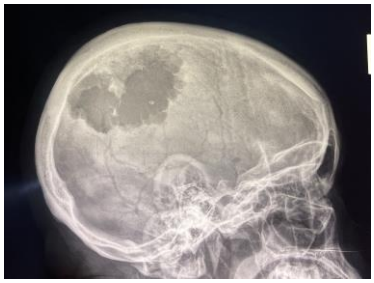

Fig. 2

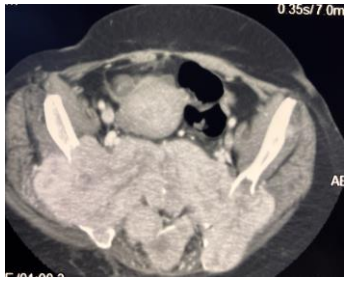

Fig.3

Fig. 1: CT brain (axial view): brain metastasis left parietal

Fig.2: Skull X-Ray: Lytic lesion left parietal bone.

Fig.3: CT pelvic: Extensive sacral and lumbar mass.

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Case 2

A 59-year-old female with a two-year history of a large benign goitre had total thyroidectomy for pressure symptoms. The histopathological report revealed follicular variant (FV) of papillary thyroid cancer (PTC). She subsequently developed complete paraplegia three weeks post thyroidectomy as a result of spinal metastasis at the level of the first lumbar vertebra confirmed on magnetic resonance imaging (MRI). She also developed pathological fracture of the left humerus treated with open reduction and internal fixation (ORIF). Spinal surgery is scheduled to stabilise the spine but unfortunately the neurological fall out is permanent.

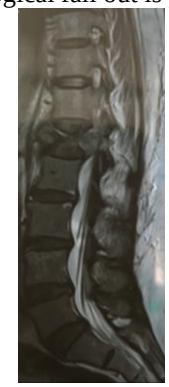

Fig. 4.

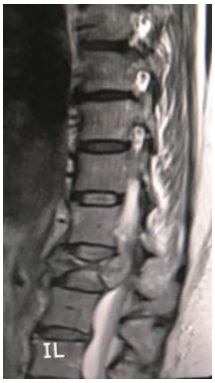

Fig.5

Fig. 4 &5: MRI shows metastasis at the level of the first lumbar vertebrae with spinal cord compression.

Case 3

A 69-year-old female presented with a goitre of three-year duration followed by hoarse voice over the past few months. She also had pressure symptoms from a large left retrosternal thyroid nodule associated with cervical lymphadenopathy, right tracheal deviation and multiple lung and liver metastasis. The magnitude of liver and lung metastasis precluded radioactive iodine adjuvant treatment post total thyroidectomy and modified neck dissection. The histopathology confirms follicular variant of papillary thyroid carcinoma.

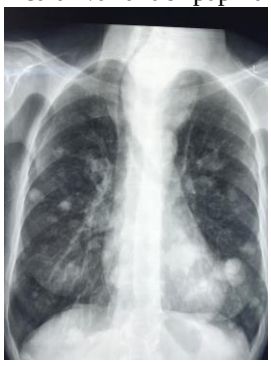

Fig. 6

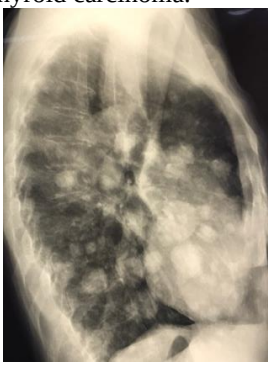

Fig. 7

Fig 6 & 7: Chest X-Ray: Extensive lung metastasis.

DISCUSSION

PTC is the most common well-differentiated malignancy of follicular origin in iodine replete area[1]. There are multiple variants of the PTC of which the FV and the classical variant are the most common (> 90%) and have very good prognosis with a 5 years survival of 97.5% and a 10-year disease-specific survival of 98%[2,3]. The variants that usually have the worse prognosis are usually tall cell, insular and hobnail[4,5]. Recognized features of aggressive behaviour are angiolymphatic invasion, extrathyroidal extension, or non-encapsulation[6]. However, our 3 cases of FV of PTC behaved aggressively. The basis of this aggressive behaviour is believed to be genetic. According to the recent research, there is a correlation between aggressive behaviour and genetic subtypes, particularly the B-type Raf kinase (BRAF) and Telomerase reverse transcriptase (TERT) genes[7,8].

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The poor prognosis of BRAF mutation has been widely investigated and most studies revealed an association with aggressive characteristics and a high tumor recurrence. and studies have even considered using identification of BRAF mutations on fine needle aspiration (FNA) as a useful tool for preoperative risk stratification for PTC[9]. Moreover, BRAF mutation analysis on FNA has also shown to reduce the instances of false negative PTC[10]. Moreover, recent studies have used integrated microarray analysis and found differentially expressed genes in PTC and have recommended that more research be done on the specific pathways[11]

However, in contrast to the above-mentioned studies, a recent large Japanese cohort study demonstrated that the BRAFV600E mutation was not associated with either tumor recurrence or aggressive clinicopathological characteristics[12]. A number of studies from a variety of ethnic groups and locations also reported no association between BRAF V600E and aggressive clinical features[13,14]. The American Joint Committee on Cancer (AJCC) has adopted the eighth tumour, node, metastasis (TNM) classification system[15]. The molecular subtype has not been added to the classification as yet.

It is unfortunate that the above listed case reports could not be worked up in terms of their molecular basis, since this is not yet routine practice. The future work up should include genetic screening to profile the thyroid malignancy in order to prognosticate accurately and to play a preventative role.

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