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TURNER SYNDROME: DIAGNOSIS AND TREATMENT CHALLENGE IN A DEVELOPING COUNTRY.

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ABSTRACT

Turner syndrome is one of the rare genetic diseases when there is a partial or complete missing of the X chromosome in females. Short stature and late puberty are the most common manifestations and the main target of treatment. However, not all Turner syndrome patients can get both treatments. We herein report the challenges in treating Turner syndrome patients in a developing country with a chief complaint of short stature and whose breasts had not grown. The patient was diagnosed late because the parents thought her short stature was normal. The patient denied growth hormone therapy because the treatment was expensive and the government's insurance program did not cover it. Therefore, we optimized her treatment in another aspect, which was inducing her puberty with low-dose estrogen. In developing countries, late diagnosis, expensive treatment, and no insurance coverage are challenges in treating patients with rare diseases such as Turner syndrome.

Keyword: Chromosomes, Diagnosis, Developing countries, Treatment, Turner syndrome.

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UNICENTRIC CASTLEMAN'S DISEASE PRESENTING AS A BREAST LUMP.

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ABSTRACT

Castleman's disease is a rare and complex lymphoproliferative disease with unknown etiology. It can be classified clinically into unicentric or multicentric and histologically into hyaline vascular or plasmacytic variants. Unicentric Castleman's disease in breast is rarely reported worldwide. We report a case of a young lady presenting with complaint of solitary right breast lump, for which she underwent excision biopsy and was diagnosed of having unicentric Castleman's disease of breast, hyaline vascular variant.

Keywords: Breast, Castleman Disease, Lymphoproliferative disorders, Neoplasm, Unicentric.

INTRODUCTION

Castleman's disease (CD), also known as giant angiofollicular lymphoid hyperplasia, is a rare complex lymphoproliferative disease first described by Benjamin Castleman in a cohort study of patients with hyperplastic mediastinal lymph nodes.[1,2] It is a rare disease of unknown etiology, categorized into two clinical entities; unicentric (localised) and multicentric (systemic). Histologically classified into hyaline vascular or plasma cell variant.[3,4] Unicentric Castleman disease (UCD) accounts for nearly 90% of CD.[5] Most of the patients have no specific imaging features and diagnosis of CD is made with histological findings post-surgical resection.[1] Study showed most unicentric cases involved lymph nodes in thorax, neck and abdomen.[5] There was no data worldwide regarding the prevalence of breast CD and consensus on management for breast CD. Breast CD presentation may mimic other benign or malignant breast condition,[5] thus it is of paramount that prompt diagnosis need to be made for subsequent management. There are only six previously reported cases of breast CD, thus more publication are needed to improve knowledge about the disease. We report a case of a young lady presenting with complaint of solitary right breast lump, for which she underwent excision biopsy and was diagnosed of having unicentric Castleman's disease of breast, hyaline vascular variant.

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CASE REPORT

A 30 years old Malay lady, with no comorbidi-

comorbidity, presented with complaint of right breast lump for 1 month period, otherwise no nipple discharge, no overlying skin changes, with no increase in size of the lump. She also denied family history of breast malignancy, or taking any hormonal therapy. Clinical examination reviewed a mobile, firm lump measuring about 3x3cm in size, located in the right inner lower quadrant of breast about 5cm from nipple areolar complex. Otherwise, no palpable lymph nodes were found in the bilateral axillae or neck.

Ultrasound of breast (Figure 1) was done, which showed well defined lobulated hypoechoic lesion seen in 5 o'clock position 5cm from nipple, measuring about 3.2 x 1.9 x 2.5cm. Core needle biopsy of the lump was performed which showed features suggestive of lymphoid stroma corresponding to primary follicle of lymph node. Thus, surgery of excision biopsy was offered to patient.

Surgery was scheduled as daycare elective case. Excision biopsy of right breast lump was performed. Intraoperatively the lump was deep to breast tissue lying just above pectoralis muscle layer. Lump was excised wholly with rough measurement about 4x4cm in size.

Histopathological examination (Fig. 2) showed well-encapsulated lymphoid tissue with follicular hyperplasia. Lymphoid follicle showed broad mantle zone with small lymphocytes arranged in layers giving an onion skin appearance. Some of the hyaline follicles showed penetration of the mantle zone by vessels (lollipop appearance) The interfollicular areas showed increased vascular network with hyalinization.

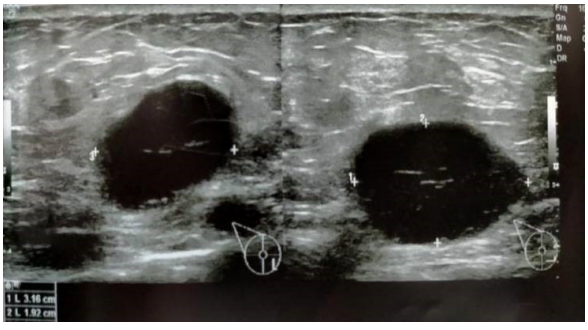

Figure 1: Ultrasonography images of right breast lump, which displayed well defined hypoechoic lesion.

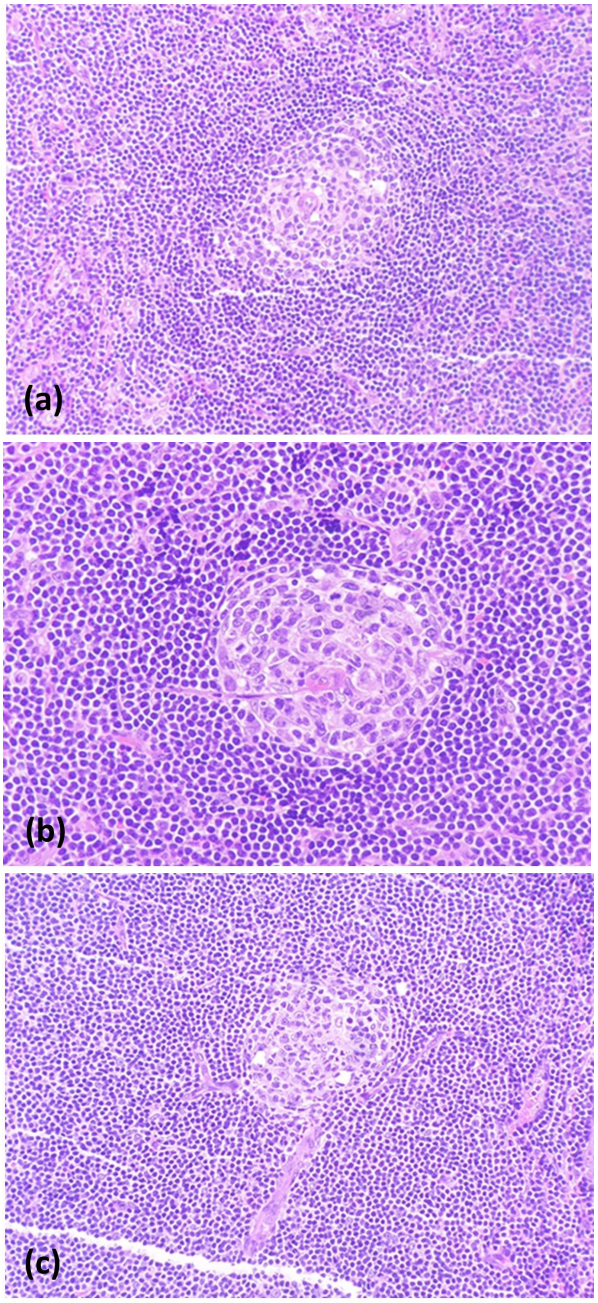

Figure 2: (a) Lymphoid follicle shows broad mantle zone consists of small lymphocytes arranged in layers giving an onion skin appearance at x200 magnification (H&E x200), (b) at x400 magnification and (c) Penetration of the mantle zone by vessels ensheathed with collagen, giving a lollipop appearance. (H&E x200). (Click to enlarge image)

Immunohistochemical studies demonstrated that CD3, CD5, CD20 displayed mixed population of T and B cells and BCL2 showed a reactive pattern. Ki67, CD10 and BCL6 highlighted germinal centres, while Cyclin D1 stained negative. With the given result ,conclusion was consistent with Castleman disease, hyaline vascular variant. Patient was followed up in our clinic about 1 year from surgery. She remains clinically well, and clinical examination revealed no other lympadenopathy.

Patient was well and reviewed 1 month post-surgery, with excision scar site completely healed. Clinical examination did not reveal any other palpable nodes or breast lump.

DISCUSSION

Castleman's disease (CD) is a rare lymphoproliferative disease for which the primary etiology and pathogenesis still remain largely unknown.[5] Unicentric disease constituted most of the CD cases, usually has a benign course and can be treated by surgical excision alone; while multicentric disease has worse prognosis and necessitates adjuvant treatment.[5] Studies by Blankenship ME et al, stated that localised disease has low risk of malignancy with 100% 5 year survival rate and cured after surgical excision of lesion.[7]

Clinically, UCD symptoms are closely linked to its pathological type. Most patients are asymptomatic and follow a benign course.[1] UCD in breast is rare and may present as painless breast lump or axillary lympadenopathy which can mimic breast cancer.[8] UCD affects both gender equally, with most patients present at 3rd to 5th decades of life. However, there are cases reported in paediatric age group as young as 2 months.[2] Prior reported cases revealed patient's age ranging 15 - 80 years, with most presented with solitary breast lump except one case reports that patient presented with both breast and axillary nodule (Table I). In this case, patient is young lady about 30 years of age and presented with non-progressive breast lump for 2 years. Clinically demonstrate well defined lump mimicking benign breast lump.

In UCD, imaging with ultrasonography showed uniform hypoechoic lesion and Doppler ultrasonography showed peripheral hypervascularity. Megumi Fukuoka et al reported a case of breast CD where ultrasonography showed hypoechoic mass with Doppler signal detected vascularities in the mass. Magnetic resonance imaging (MRI) was done and demonstrated hyperintense lesion on T2-weighted imaging, with fast washout enhancement picture at the peripheries.[8] Computed tomography (CT) scan showed homogenous enhancing mass with early rapid enhancement during arterial phase but decrease in portal venous phase.[2] In our case report, the patient underwent ultrasound of breast with well-defined lobulated hypoechoic lesion. CT scan of thorax, abdomen was performed after surgery which showed absence of other lymphadenopathy.

There are two main pathological subtypes, namely hyaline vascular variant (HVV) and plasma cell variant (PCV). Generally, unicentric diseases are associated with HVV while systemic diseases are associated with PCV.[2] Histological and immunohistochemical studies after surgical resection are needed for definite diagnosis of UCD.[1] Histology examination of HVV showed abundant hyalinized vessels, surrounding small lymphocytes in peripheral wide zone and characteristic 'onion -peel' appearance in germinal center due to concentrically arranged mantle zone.[1,4]

Immunohistochemical studies showed Ki67, BCL-6 and CD10 stained positive in germinal centre, CD20 stained positive in B lymphocyte and CD3 and CD5 stained positive in T lymphocytes. Cyclin D1, BCL-2, CD56 and

TDT stained negative.[9] Prior case reports showed all patients presented with breast CD are of hyaline vascular variant (table I). In this reported case, histological examination and immunohistochemistry demonstrated similar findings with previously reported cases, thus diagnosis of Castleman disease with hyaline vascular variant was made.

The mainstay of treatment for hyaline vascular type UCD is still complete surgical resection, with good outcome and 100% 5 year survival rate reported.[7] In study by Talat N et al, mortality after 10 years following lymph node excision in axilla, groin or neck were rare.[6] However it was significantly more common in lesion found in retroperitoneum, mediastinum, abdomen and pelvis. If surgery is not feasible, debulking surgery can be considered if patients present with local symptoms or risk of compression to surrounding structures. Previous case reports showed most patients underwent breast lump excision only with two patients required additional axillary dissection (Table I). Case reported by Rene Aloisio et al required breast lump excision and axillary dissection as patient presented with both axillary and breast node; while Fama F et al reported their patient required axillary dissection as frozen section of intramammary node showed lymphoid proliferation with germinal center hyalinisation. There was no study on optimal surveillance follow up for breast UCD post surgical resection. Most patients reported before remain disease free at 6 months to 2 years; only one case reported recurrence at supraclavicular adenopathy at 3 months post surgery where this patient was treated with cycles of prednisolone (Table I). Our patient was follow up post surgical resection with clinical assessment, at 1 year post surgery patient does not demonstrate any recurrence.

CONCLUSION

In conclusion, CD itself is a rare disease and may manifest in breast as breast UCD. Breast CD presentation is non specific and may mimic other benign or malignant breast disease thus making diagnosing breast CD a challenge. Prompt diagnosis and early surgical intervention is beneficial as most patients with breast CD showed good clinical outcome and prognosis.

CONFLICT OF INTEREST

The authors have no conflicts of interest

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