Chondroblastic Osteosarcoma in Adolescent: Crucial Decision of Site of Biopsy to Avoid Diagnostic Adversity.

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Title: Chondroblastic Osteosarcoma in Adolescent: Crucial Decision of Site of Biopsy to Avoid Diagnostic Adversity.

Key Clinical Message

Proliferating intraoral mass, biopsy of which twice revealed benign fibromatous lesion. But excisional biopsy of involved bone confirmed chondroblastic osteosarcoma. Considering this deviation from actual diagnosis, this article is an attempt to answer the age old question of biopsy site determination and its impact on patient diagnosis, treatment and prognosis.

Key words

Chondroblastic Osteosarcoma, biopsy site, differential diagnosis, chemoresistance

Introduction

Aggressively proliferating intraoral mass with extraoral facial swelling clinically points towards malignant pathology which needs urgent intervention, but at times so called diagnostic 'gold standard' histopathology can differ from actual pathology due to poorly representative biopsy site.

Some pathologies show higher risk of such misdiagnosis. Comprising of only 5-8% of jaw tumours[1], Chondroblastic osteosarcoma is being one of the such pathologies with many clusters of representative tissues. It generally consists of variants like osteoblastic, chondroblastic and fibrous,[2] small cell[3] but single pathology can have areas dominant in proliferating chondroblasts, or hyalinized areas with proliferating fibroblasts or myxoid and osteoid areas each prone to be confused with separate pathologies. As site of biopsy governs the final diagnosis and management protocol, maxillofacial surgeons should be attentive to the delusional manifestations of Chondrogenic Osteosarcoma and have a high index of suspicion to start prompt treatment to increase chances of a favourable outcome.

Case Report

A 19 year old female presented with history of rapidly-growing, non-resolving swelling over right lower face region since 2 months. Clinically this tumorous growth was sessile, bright pink in colour resembling fibromatosis gingivae but rapid growth rate had caused almost complete coverage of posterior teeth.(Figure 1) Extraoral facial swelling near right body of mandible was bony hard and slow growing.(Figure 2) Despite of striking differences both were painless which was contrary to previous reports from literature[4,5,6].

Panoramic radiograph showed a diffuse radiolucent lesion overlying right body of mandible and empty alveolus of first molar (Figure 3). A subsequent computed tomography scan (Figure 4) revealed a hyper-

attenuated diffuse exophytic lesion extending from external oblique ridge till alveolus of first mandibular right first molar. The bony mass was more towards lingual aspect of mandible.

Bright pink, tough, fibrous tissue was obtained from incisional biopsy, microscopy of which revealed ossifying fibroma(Figure 5), but due to sheer rate of growth and radiographic findings biopsy report was found to be inconsistent with clinical findings. Hence repeat biopsy was performed which revealed fibrous hyperplasia(Figure 6). With both biopsies pointing towards a benign pathology excisional biopsy was planned under general anaesthesia. Pre-anaesthetic workup showed low haemoglobin levels with normal bleeding & clotting times, ESR, serum electrolytes and liver function tests.

Under all aseptic precautions, intraoperatively complete excision of intraoral soft tissue lesion was performed and buccal and lingual mucoperiosteal flaps were raised to expose the bony lesion. By preserving mental nerve complete excision of exophytic bony mass was done(Figure 7) and closure was done with 3-0 vicryl. Soft and hard tissue specimens were sent separately for histopathological analysis.

Histopathology:

The Hematoxylin and eosin stained sections revealed superficial stratified squamous epithelium and underlying connective tissue. The lesion appeared to be well encapsulated(Figure 8E). Focal areas of connective tissue stroma was myxomatous (Figure 8C), collagenous and hyalinized. Areas of spindle and stellate shaped fibroblastic cells (Figure 8D) and atypical, hyperchromatic, fusiform chondroblastic cells proliferation (Figure 8A), bizarrely shaped mitotic figures along with adjacent malignant osteoid tissue was evident (Figure 8B). Osteoid was scanty and immature. Chondroblastic proliferation was dominant and aggressively proliferating with areas showing pleomorphism. Hence, histopathological diagnosis of chondroblastic osteosarcoma was made.

Discussion: Osteosarcomas are difficult to diagnose even with immunohistochemistry and advanced radiography as single lesion may show osteoid in one region along with scattered chondroid, myxoid, fibrous areas. Superficial layers may show benign fibrous growth with epithelial hyperplasia which is the most common site of biopsy. Such diversity of histopathology in various areas of lesion pose a challenge to surgeon to procure representative biopsy specimen. When suspecting a osteosarcomatous lesion surgeon should prefer deeper hard tissue biopsies preferably the hard tissue growing beyond the confines of cortices. These sites are more representative of actual pathology rather than superficial fungating tumour mass which is comparatively easier to excise.

In this case final histopathology of excised hard tissue specimen was confirmative of very rare mixed form of chondrogenic osteosarcoma. The role of neo-adjuvant chemotherapy in chondroblastic osteosarcoma is limited to tumour mass shrinkage and to achieve negative tumour margins[7]. But due to its rapid metastasis, before definitive surgery patient was advised neo-adjuvant chemotherapy with doxorubicin 80 mg and cisplatin 140 mg, but even after 2 cycles there was no considerable decrease in size of tumour mass which was in accordance with chemoresistance mechanisms in osteosarcoma. Altered deoxyribonucleic acid (DNA) repair activity[8], overexpression of resistance-related proteins such as metallothioneins, glutathione-S-transferase π, heat shock protein 27, and lung resistance-related protein[9] and alterations in cell cycle[10] are the probable factors for chemoresistance.

As definitive surgery patient underwent right side supra-omohyoid neck dissection and right hemimandibulectomy(Figure 9) followed by reconstruction with anterolateral thigh flap(Figure 10,11) in Department of Surgical Oncology. Following which patient was referred to radiotherapy.

Low and intermediate grade osteosarcomas are juxtacortical, medullary or periosteal in nature. Whereas aggressive high grade osteosarcomas are classified by World Health Organization (WHO) in 4 histopathological types as per predominance of tissue found. Osteoblastic, chondroblastic, fibroblastic and small cell types as the name suggests show predominance of respective tissue. Yet another telangiectatic form is also described in the literature[11].

Conclusion:

Even though clinical presentation points directly towards malignant pathology, non-representative biopsy specimen can divert surgeons mind, into completely different management plan jeopardizing final prognosis. Hence it is crucial to take representative tissue biopsy which pin-points the diagnosis and appropriate treatment can commence as early as possible, which is critical in osteosarcoma cases to increase overall survival rate.

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Figure Legends:

Figure 1: Pre-operative Intraoral clinical picture.

Figure 2: Pre-operative Extraoral clinical picture.

Figure 3: Pre-operative orthopantomogram.

Figure 4: Pre-operative computer tomographic scan.

Figure 5: First biopsy showing ossifying fibroma.

Figure 6: Repeat biopsy showing Epithelial Hyperplasia.

Figure 7: Excisional biopsy gross histopathology specimen.

Figure 8: Histopathologic picture of Chondroblastic Osteosarcoma.

A: Chondroblastic proliferation with atypical, hyperchromatic, fusiform cells.

B: Malignant Osteoblastic proliferation with atypical mitotic figures.

C: Myxomatous stoma.

D: Fibroblastic proliferation.

E: Well defined capsule with epithelium.

Figure 9: Post-operative orthopantomogram showing right hemi-mandibulectomy.

Figure 10: Postoperative Intraoral picture showing Healthy Anterolateral thigh flap.

Figure 11: Postoperative Extraoral picture showing Healthy Anterolateral thigh flap.