

Circulatory Biomarkers of Osteosarcoma: A Review

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Abstract

Osteosarcoma is a complex disease with various biological and clinical dissimilarities that further complicates the management as well as prognosis disease. Higher mortality and morbidity rate is also associated, because of late diagnosis, metastasis, due to chemo resistant and non-availability of alternative treatment. The clinic-radiological examinations having their own limitations and could not able to discriminate the micro changes due to treatment at an early stage. This mini review focused on the utility of biomarkers along with their advantages over conventional therapy of osteosarcoma. Till date, numerous fundamental, translational and clinical studies have acknowledged various biomarkers related to osteosarcoma. Furthermore, accomplishing the translating knowledge of biomarkers from benchside to bedside needs prudently distinct preclinical studies and randomized controlled studies.

Keywords: Osteosarcoma; Biomarkers; Diagnostic; Prognostic

Introduction

Osteosarcoma [OS], followed by chondrosarcoma and Ewing, is the most malignant bone neoplasm. Till date, the diagnosis of osteosarcoma is commonly confirmed by histological evaluation of a biopsy. Still, the clinical and radiological features are important in diagnosis, staging as well as treatment response in osteosarcoma [1]. Unfortunately, higher mortality and morbidity rate is also associated, because of late diagnosis, metastasis, due to chemo resistant and non-availability of alternative treatment. The clinic-radiological examinations having their own limitations and could not able to discriminate the micro changes due to treatment at an early stage. Till date, Several fundamental translation and clinical research to date have identified specific osteosarcoma-related biomarkers. In addition, to achieve translations of biomarkers from benchside to bedside, pre-clinical studies and correctly randomized controlled studies are required. This mini review focused on the utility of biomarkers along with their advantages over conventional therapy of osteosarcoma.

Osteosarcoma

Osteosarcoma is the utmost frequent primary malignancy of bone in teen-agers and young adults [1]. The primary skeletal sarcomas are 30 - 80 percent [2]. The affected population is predominantly male children, adolescents and young adults aged 10 - 30 years old [3]. The tumor is produced from cells that are mesenchymal and are distinguished by neoplastic osteoblasty differentiation [4]. It is essentially unknown the exact etiology of osteosarcoma [5]. In the bones around the knee, most tumours form in the distal femur (lower portion of the thigh bone) as well as the proximal tibia (upper portion of the shinbone). The long extremity bones close to the metaphysical growth plates often have osteosarcoma. The most common sites include femur (42%, 75% of distal femur tumors), tibia (19%,80%, proximal tibia), and humerus (10%,90% of tumors in the proximal humerus) [6]. But in any bone osteosarcoma can develop.

Osteosarcoma has a high degree of malignancy that tends to metastasize early: newly diagnosed patients are often diagnosed with lung metastasis, and pulmonary symptoms may develop without chemotherapy within a year [7]. For OS patients, the 5-year survival rate is 20% compared with 65% for localized patients and the bulk of the dead caused by the osteosarcoma were due to metastatic disease [8,9]. Consequently, the prognosis is often very poor [10,11].

Current diagnosis and treatment of osteosarcoma

Proper diagnosis is imperative for the appropriate management of musculoskeletal tumors. Triple diagnostic approach, i.e., clinical, radiological and histopathological is essential in all cases [12]. Till date, the histopathological examination is the gold standard method to confirm osteosarcoma.

After confirmed diagnosis, surgery with pre and post- chemotherapy is the first-line therapy used for most osteosarcoma patients [13]. Surgical resection of the primary tumor at an appropriate margin for the patient with localized osteosarcoma is a crucial component of the curative strategy. When full surgical resection is not possible or surgical margins are small, local control levels may be increased by radiation therapy. If it is not possible to remove the tumor with safe margins, amputation as a further option should be taken into consideration.

Challenges in treatment

For 20 years, the 5-year survival rate in localized patients is at least 70 percent, however, following intensive treatment, the chance of long-term survival in metastatic patients is lower than 20 percent [14,15]. These disappointing survival rates are mainly due to following challenges in osteosarcoma treatment are: 1) Unable to diagnose at an early stage, before clinical compliance, 2) Not able to identifying responders to current neo-adjuvant therapy from non-responders prior to initiation of treatment. 3) No alternative therapies for responders as well as non-responders.

Biomarkers as a key solution

It is extremely critical to develop novel strategies not only for early diagnosis but also for the prognosis of osteosarcoma so that most effective treatment to achieve a better clinical outcome can be selected for the patients. Now days, the biomarkers are only the key solution for that, especially the circulatory biomarkers. The non-invasive nature may ease for multiple sampling and can be done at any time. Thus, they may able to provide the treatment response in real time at earliest possible. No matter what are the biomarkers types, it may be a nucleic acid biomarker, proteomic biomarkers, enzyme biomarkers miRNA etc [16].

Biomarkers may have the potential to change the trend of osteosarcoma treatment as they facilitate the molecular approach to the treatment protocol by developing therapies focussed on the molecular profile of tumors at the time of diagnosis and deals with adjuvant therapies target for a specific molecular pathway rather than the use of broad cytotoxic chemical strategies. The circulatory biomarkers (blood) have another advantage that the impact of the chemotherapy will be analysed throughout the treatment follow-up very easily and at the molecular level, that is impossible to found with the clinic-radiological examinations at a very early stage. Prior categorization of patients based on, will likely or will likely not respond to current chemotherapeutic regimens will definitely have a significant benefit as the responding patients to standard therapy may be able to receive and respond to a low treatment dose. Similarly, patients likely to not respond to the current therapy may undergo alternative therapies. Furthermore, by determining the nature of the metastatic phenotype of osteosarcoma at the molecular level, metastasizes can be prevented, especially the pulmonary metastasis. Biomarkers having significant roles in Ezrin and FAS/FASL signaling may be important in understanding these critical aspects of osteosarcoma micro-metastases to the pulmonary region. The identification of a reliable, not invasive circulatory biomarker for early diagnosis/prognose is therefore, one such step to enhance osteosarcoma survival.

Conclusion

Osteosarcoma is the utmost malignant bone neoplasm, commonly confirmed by histological evaluation of a biopsy. The limitation of present clinic-radiological examination includes not able to discriminate the micro changes at the early stage of treatment. This mini review focused on the utility of circulatory biomarkers along with their advantages over conventional therapy of osteosarcoma. Furthermore, accomplishing the translating knowledge of biomarkers from benchside to bedside needs prudently distinct preclinical studies and randomized controlled studies.

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