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Case report

Extraskeletal conventional chondrosarcoma of genitalia in a child- An unusual pathology for a rare tumor

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ABSTRACT

Introduction and importance: Chondrosarcoma is a rare malignant tumor considered as the second common sarcoma of bone following osteosarcoma. Less than 5 % of chondrosarcomas occur in children. Conventional chondrosarcoma is the most common type observed as skeletal tumors. Extraskeletal chondrosarcomas account for about 1 % of chondrosarcomas. They are almost always of myxoid or mesenchymal subtypes.

Case presentation: A 4-year-old girl was referred with pain and palpable mass in the labia majora since 2 years of age for which she had undergone twice biopsies, reported as soft tissue enchondroma. At this time, complete excision of the lesion with negative margins was carried out. The pathology was in favor of extraskeletal chondrosarcoma of conventional type without any evidence of bone involvement.

Clinical discussion: Our case was a very young child with extraskeletal conventional chondrosarcoma, not reported yet in the literature. The vast majority of extraskeletal myxoid chondrosarcomas arise in the soft tissues of the extremities. The lesion in this case was located within the subcutaneous tissue of the labia majora; however, the tumor was not compatible with myxoid chondrosarcoma. Mesenchymal chondrosarcoma is another type of extraskeletal chondrosarcoma but the histopathologic patterns observed in our patient were not compatible even with the mesenchymal chondrosarcoma.

Conclusion: We present a unique case of extraskeletal chondrosarcoma in a child with conventional subtype which has not been reported in the literature. In addition, the lesion was assumed to arise from a previous soft tissue enchondroma of the labia majora since infancy which makes the case distinctive.

1. Introduction

Chondrosarcoma (CS) is considered the second most common sarcoma of bone following osteosarcoma, accounting for 20–30 % of all skeletal sarcomas. CSs have an estimated incidence of 1 in 200,000 per year in the United States [1]. CS is a heterogeneous malignant tumor that produce cartilage matrix showing hyaline cartilage differentiation. CSs are categorized as primary when arise de novo; however, if they arise from preexisting benign cartilaginous neoplasms such as enchondroma or osteochondroma are referred to as secondary chondrosarcomas [2]. The risk of chondrosarcoma arising in a solitary osteochondroma has been reported to be <1 %, though the risk increases to 5 % in multiple osteochondromatosis [3]. CS occurs mostly in adult with the peak of incidence occurring in the fifth to seventh decades of life.

Chondrosarcomas in children and adolescents are uncommon and constitute <5 % of all chondrosarcomas. The pelvis, followed by the proximal femur is the most common site of skeletal involvement in CS irrespective of the age group [3]. CS most commonly presents in the bony skeleton, although a small percentage present as a primary soft tissue mass [4].

Conventional chondrosarcomas are locally aggressive tumors that constitute the most common form of CS observed only as skeletal tumors (85 % of cases) [5]. Chondrosarcomas, based on the osseous location in which they arise are classified as central (within the intramedullary cavity), peripheral (within the cartilage cap of a pre-existing

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osteochondroma), or periosteal (juxtacortical; on the surface of the bone) [6]. Extraskeletal chondrosarcomas account for about 1 % of all chondrosarcomas with the majority being of the myxoid (most common) or mesenchymal subtypes [2]. Here, we report a 4-year-girl with an extraskeletal chondrosarcoma of genitalia (vulva) which did not fulfill either criteria for mesenchymal or myxoid chondrosarcoma but showed the pathologic features of the conventional type. This pathologic subtype has not been reported in the extraskeletal CS so far.

This work has been reported in line with the SCARE criteria [7].

2. Presentation of case

A 4-year-old girl, born to consanguineous parents was referred to pediatric oncology clinic with complaints of pain and palpable lumps in labia majora on the right side since the age of two for which she had gone through fine needle aspiration and core needle biopsy twice before. The pathologic examinations were in favor of enchondroma without any malignant features.

She was referred due to recurrence of pain and firm masses in the genitalia. Upon physical examination, an ill-defined mass with firm consistency was identified within the skin fold of right labia majora. Magnetic resonance imaging revealed a lobulated lesion measuring 35 × 20 × 19 mm, high signal in T2-weighted images on right side of prepubic space with extension into the suprapubic area and retzius space without evidence of bone involvement (Fig. 1 A, B). T1-weighted image showed patchy and peripheral enhancement of the prepubic mass after contrast administration (Fig. 2). A whole-body scan was performed for the patient which was negative for increased bone activity.

Wide surgical excision of the tumor was carried out under general anesthesia. Pubic area, bladder, and the space between them was completely explored extraperitoneally through a low midline incision. A soft tissue mass was found at the right side of the prepubic space with extension into the suprapubic area and deeply into the retzius space. During the surgery, the surgeon observed that the tumor was confined to the soft tissue without involvement of the adjacent bony structures; however, biopsies were taken from ramus and symphysis of pubis. The pathologic examination revealed a cartilaginous neoplasm composed of chondroid nodules of varying sizes permeating through fibrous stroma. The lesion also exhibited relatively atypical chondrocytes with hyperchromatic or vesicular nuclei, with some binucleated or multinucleated forms, accompanied by myxoid areas. There were also foci of chondrocytes in the periphery with spindle and epithelioid pattern. The neoplastic chondrocyte nodules were encapsulated by a thin fibrous capsule (Figs. 3-5). All surgical margins and biopsy from bony structures were reported to be negative. Immunohistochemistry study demonstrated positive staining for S-100, desmin, and vimentin, while negative staining was observed for CD99, FLI-1, myogenin, NKX2.2, and pancytokeratin. The histopathological findings were indicative of a conventional chondrosarcoma (grade II) of soft tissue, since the lesion was located in the soft tissue of the labia majora.

3. Discussion

Chondrosarcomas are a various group of malignant cartilaginous matrix-producing neoplasms. Based on the biologic activity of the tumor, chondrosarcomas are a spectrum ranging from relatively benign low-grade tumors or intermediate atypical cartilaginous tumors (ACTs) to malignant, aggressive high-grade tumors [1]. Most chondrosarcomas are of low-grade, conventional type. Other rarer subtypes include dedifferentiated, periosteal, mesenchymal, myxoid and clear cell variants [1].

The 2020 WHO classification categorizes malignant chondrosarcoma as grade 1 to 3 based on the nuclear size, mitotic activity, and degree of cellularity. The majority of chondrosarcomas are conventional and are classified as grade 1 or 2 [8].

Extraskeletal chondrosarcomas comprise 1–2 % of soft-tissue sarcomas and about 1 % of all chondrosarcomas. They tend to be of higher grade than conventional chondrosarcomas, with the majority being of the myxoid (most common) or mesenchymal varieties [2]. Our case was a very young child with extraskeletal chondrosarcoma of conventional type not reported in the literature.

Extraskeletal myxoid CS is the most common type of soft-tissue chondrosarcoma with an incidence of <1/1,000,000/year. It usually occurs in adults, with a median age of onset in the fifth decade and only a few cases have been reported in childhood and adolescence [9–11]. The vast majority of the lesions arise in the soft tissues of the extremities,

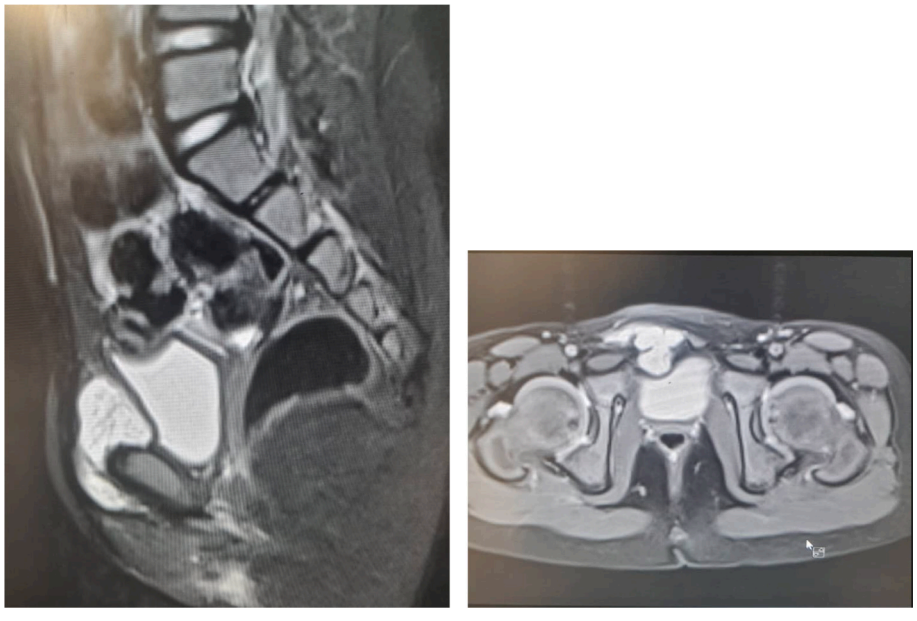

Fig. 1. Sagital (A) and Axial T2 (B) Fat saturated images show a lobulated high signal mass in T2 sequence in prepubic soft tissue with extension to the retzius space via suprapubic without evidence of bony involvement.

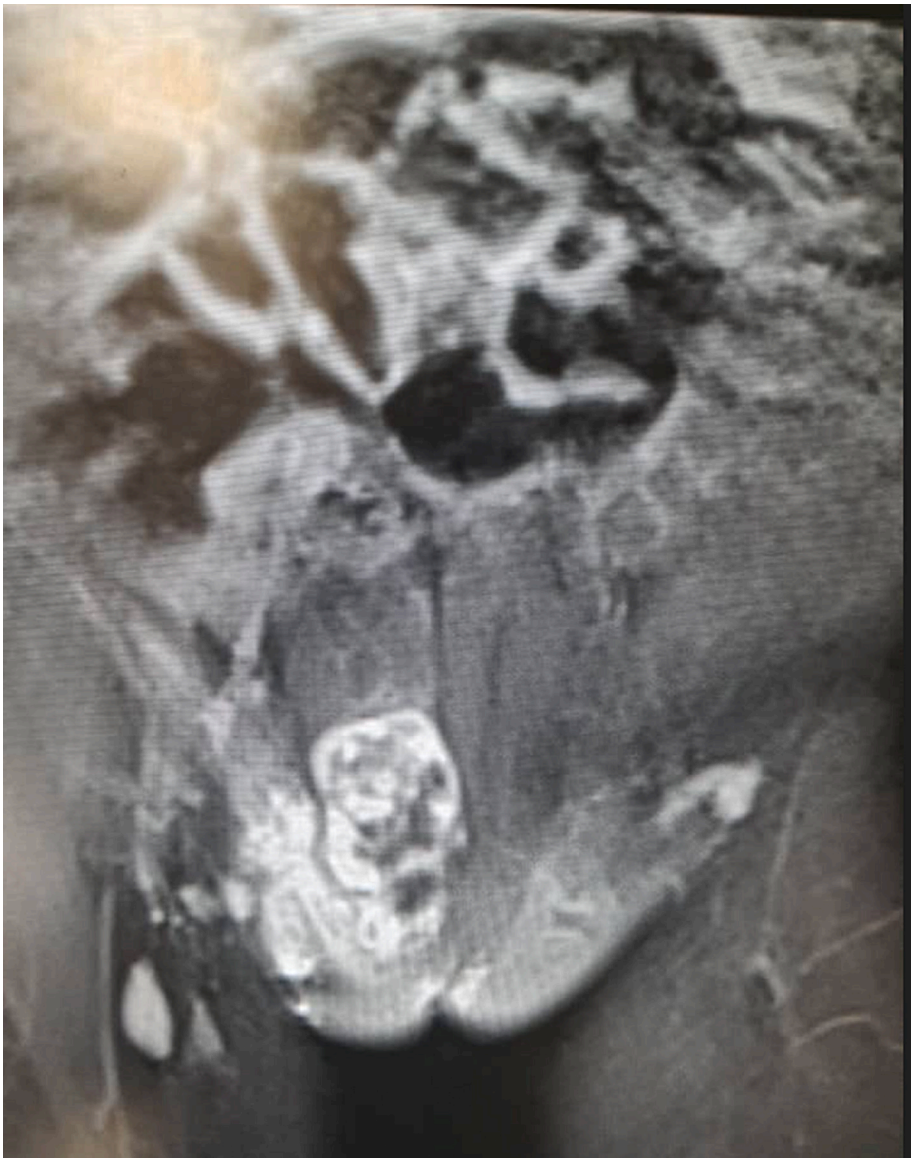

Fig. 2. T1 weighted image with contrast. Patchy and peripheral enhancement of prepubic mass is seen after contrast administration.

with the thigh being the most common location. Most lesions are in the deep soft tissue, but approximately 25 %–33 % are located in subcutaneous tissues [11]. Extraskeletal myxoid chondrosarcoma of the vulva is extremely rare, with only 15 adult cases reported in the literature [12].

Although myxoid chondrosarcoma is a soft-tissue malignancy with chondrocytic differentiation, most do not show chondroid tissue formation [13]. The tumor in our case showed typical chondroid nodules of varying sizes permeating through a fibrous stroma along with atypical chondrocytes which was not compatible with myxoid chondrosarcoma.

Regarding the IHC, there is no specific marker for diagnosis of chondrosarcoma subtypes since the pathology itself is conclusive enough. It is noteworthy that Alpha-methylacyl-CoA racemase and periostin are proposed as new biomarkers for differential diagnosis of enchondroma from chondrosarcoma [14]. Although in our case due to the observation of malignant features, enchondroma was not considered and we did not apply the new mentioned biomarkers for her.

Extraskeletal mesenchymal chondrosarcoma typically affects young adults between 15 and 35 years of age, with a female predilection. Lesions in soft tissue account for 30 %–75 % of all mesenchymal chondrosarcomas, although osseous sites are more common in some series [15–17]. Extraskeletal mesenchymal chondrosarcoma is histologically distinguished by its characteristic biphasic pattern, consisting of small cells and clusters of hyaline cartilage [18]. None of these histopathologic patterns were observed in our patient.

In a study from Italy, the clinical, radiological, and pathological features of patients with chondrosarcoma referring to a single institution (Istituto Ortopedico Rizzoli) has been reported. There were 17 patients ranging from 13 to 17 years (median 15 years). The tumors were central, periosteal and peripheral, the latter arising from multiple exostoses. They involved the femur, tibia, pelvic bones, humerus and metacarpal bones. A 17-year-old male with Maffucci disease developed CS originating from a metacarpal bone who died of disease with rib and lung metastases. There was also a 17-year-old female with peripheral CS of pubic bone [19]. Our patient had been symptomatic since the age of two, for which had gone through twice biopsies, and both were reported as soft tissue enchondroma. It can be assumed that malignant transformation of the enchondroma to the soft tissue chondrosarcoma has been occurred in our patient.

According to some authors reporting small series of CS in children, CS mainly involves head and neck in children and seem to affect craniofacial structures four times as frequently as in adults [19,20]. The

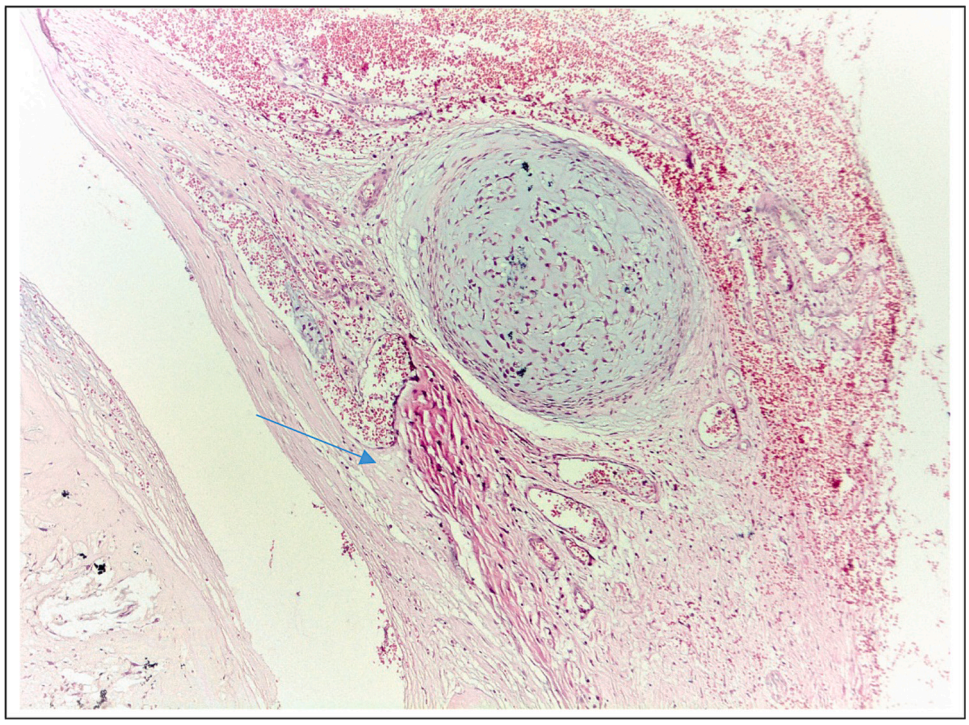

Fig. 3. Neoplastic chondroid nodule associated with vascular invasion in the periphery, showed with blue arrow (H&E, X200). (For interpretation of the references to colour in this figure legend, the reader is referred to the web version of this article.)

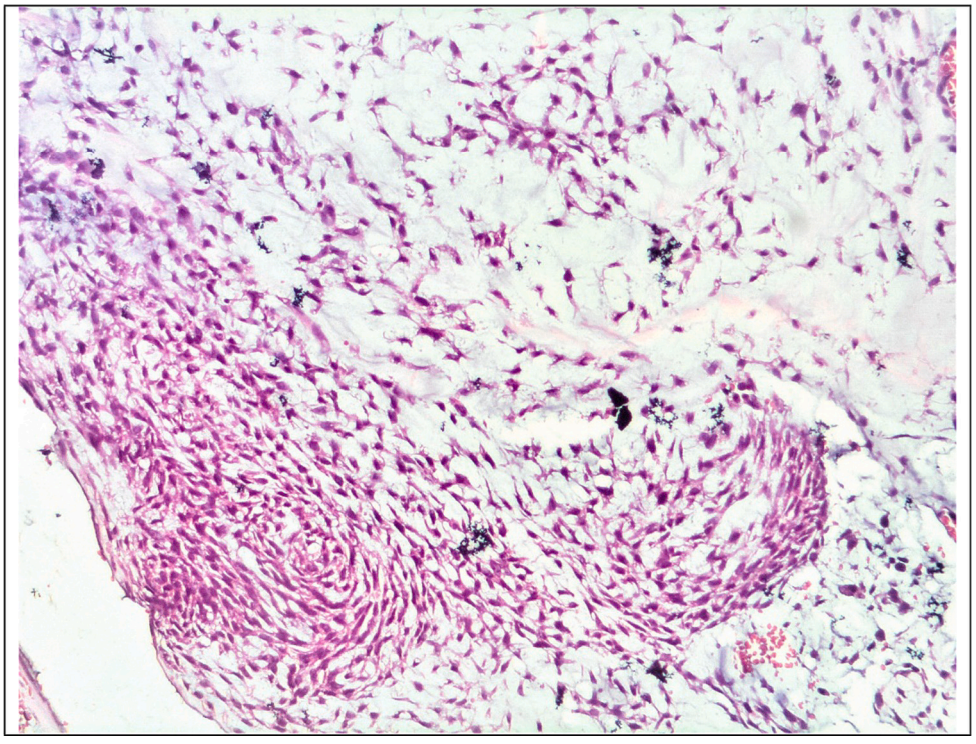

Fig. 4. Chondroid stroma with myxoid areas and atypical chondrocytes with spindle pattern (H&E, X200).

youngest reported child with CS is a 11-month-old female with myxoid CS of nasal cavity who presented with swelling near the inner canthus of her left eye since 2 months of age [21].

4. Conclusion

This was a unique case of extraskeletal conventional chondrosarcoma in a 4-year-old female most probable arising from a previous soft tissue enchondroma. The typical chondroid nodules and cartilaginous differentiation excluded myxoid chondrosarcoma and lack of small

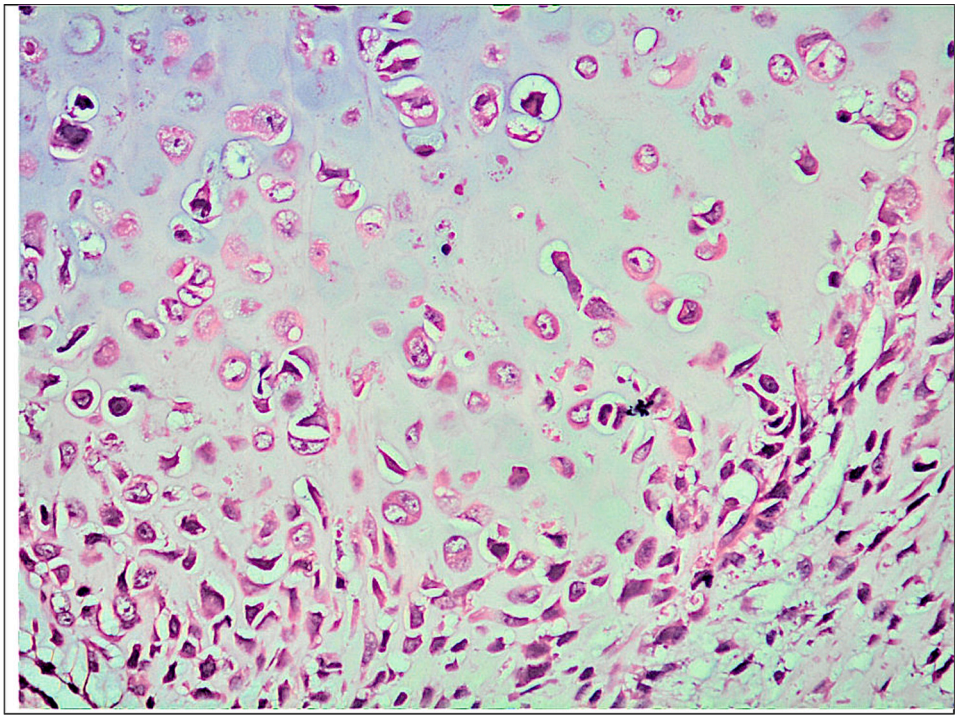

Fig. 5. Atypical chondrocytes with hyperchromatic and vesicular nuclei (H&E, X400).

round cell appearance made mesenchymal chondrosarcoma an unlikely diagnosis.

Ethical approval

The case report was approved by ethical committee of "shahid Beheshti University of Medical Sciences, school of Medicine, Tehran, Iran."

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Registration of research studies

N/A.

CRediT authorship contribution statement

Gholamreza Sarajebrahimi: study concept.

Samin Alavi: Study design and literature review and writing the case report.

Maryam Kazemi Aghdam: Pathology review of the patient and literature review on pathology.

Mitra Khalili: Radiographic analysis and interpretation of the imagings.

Zahra Khaffafpour: Analysis of clinical and pathological and data analysis.

Manoochehr Ebrahimian: writing the paper.

Guarantor

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Patient consent

Written informed consent was obtained from the patients' legal guardians to let us for publication. This report does not include any personal information that could lead to the identification of the patient.

Declaration of competing interest

No conflict of interest existed.

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