Case Report
Primary popliteal granulocytic sarcoma: a case report and review of literature

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Abstract: Primary granulocytic sarcoma (PGS), also known as chloroma, is a type of malignant tumour that forms in extramedullary tissues by proliferating myeloblasts or immature granulocytes. Here, we reported a 63-year-old female case of PGS that primarily emerged in the popliteal fossa. Macroscopically, a greyish white and greyish yellow mass was observed, with 7.5 × 6 × 3 cm in size. Microscopically, the mass was cystic and necrotic tissue was present within the cyst, which was uniformly infiltrated with small- or medium-sized round cells with basophilic cytoplasm and fine chromatin. The immunohistochemical staining showed positive for MPO, LSZ and CD43. Additionally, we reviewed the relevant literature in order to improve our understanding of the disease.

Keywords: Primary popliteal granulocytic sarcoma, clinical pathology, case report

Introduction

Primary granulocytic sarcoma (PGS), with another name as chloroma, forms in extramedullary tissues by proliferating myeloblasts or immature granulocytes. PGS is extremely unusual and has rarely been reported in the literature. Furthermore, PGS is clinically prone to misdiagnosis due to the challenge in the differentiation of its morphology from that of non-Hodgkin’s lymphoma, also due to no abnormalities in the patient’s blood. Here, we reported a case of PGS who primarily emerged in the popliteal fossa and was diagnosed in 2016 in our institute, and we also reviewed the related literature to improve our understanding of the disease.

Case report

This patient was a 63-year-old female who experienced pain in the left knee with movement impairment, but no obvious cause for more than one month. After treatment at other hospitals, her symptoms did not remit. On the contrary, the swelling and pain worsened, and movement impairment was exacerbated. An examination revealed that the patient’s left knee joint was swollen and that significant tenderness and bruises were present along with a high skin temperature. In the patient’s popliteal fossa, a mass could be palpated, which was soft and movable. Clear boundary along the surrounding soft tissues and tenderness were present without fluctuation, bleeding or ulceration. Despite a good blood supply in the left foot, movement of the patient’s left knee joint was limited. An ultrasound examination revealed a hypoechoic mass of 8.1 × 3.6 cm that had clear borders and uneven internal echo in the left popliteal subcutaneous tissue (Figure 1). Colour Doppler flow imaging (CDFI) showed that the blood flow signal was absent in the mass, and thus, the mass was considered a cyst or haematoma. Magnetic resonance imaging (MRI) of the left knee revealed a thickened left popliteal synovial membrane and a synovial cyst 7.9 × 4.0 × 8.8 cm in size, with long T1 and T2 signals and a high signal under the fat-suppressed sequence. The synovial membrane was slightly thickened, and a noticeable amount of effusion was present in the suprapatellar bursa and joint cavity (Figures 2 and 3), which was diagnosed as effusion in the capsule of the
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Figure 1. Popliteal ultrasound examination. An ultrasound examination revealed a hypoechoic mass of 8.1 × 3.6 cm that had clear boundaries and uneven internal echo in the left popliteal subcutaneous tissue.

Figure 2. Magnetic resonance imaging (MRI) of the left knee. The synovial membrane was slightly thickened, and a noticeable amount of effusion was present in the suprapatellar bursa and joint cavity.

Figure 3. Magnetic resonance imaging (MRI) of the left knee. The synovial membrane was slightly thickened, and a noticeable amount of effusion was present in the suprapatellar bursa and joint cavity.

Figure 4. Gross morphology of the tumor. A greyish white and greyish yellow mass (7.5 × 6 × 3 cm) was observed, with a smooth surface and a smooth internal cystic wall 0.2-0.3 cm in thickness. The unilocular cyst was filled with greyish, greenish and yellowish jelly-like or pus-like material.

Laboratory tests indicated that the peripheral hemogram was normal. Surgical resection of the popliteal cyst was then performed. Macroscopic examination revealed a greyish white and greyish yellow mass, with 7.5 × 6 × 3 cm in size. It had a smooth surface and a smooth internal cystic wall 0.2-0.3 cm in thickness. The unilocular cyst was filled with greyish, greenish and yellowish jelly-like or pus-like material (Figure 4). Specimens were fixed in 4% neutral formalin, dehydrated and then embedded in paraffin according to routine pathology methods. From each paraffin block, sections with 4 µm in thickness were generated and subjected to haematoxylin-eosin (HE) staining and immunohistochemistry. Under light microscopy, the mass was cystic with a wall composed of loose connective tissue, but it was not lined with epithelium. Necrotic tissue was present within the cyst, which was uniformly infiltrated with small- or medium-sized round cells with basophilic cytoplasm and fine chromatin, but without clear nucleoli (Figures 5 and 6). Moreover, a small number of mature neutrophils were also observed in some areas of the cyst. The immunohistochemical staining results were as follows: MPO (+) (Figure 7), LSZ (+), CD43 (+) (Figure 8), CD68 (+), CD34 (+), CD3 (-), CD20 (-), PAX-5 (-), CD99 (-), CD56 (-), FLI-1 (-) and TDT (-), with all antibodies purchased from Fuzhou
Thus, granulocytic sarcoma (GS, popliteal mass) was primarily composed of young-middle-stage and earlier-stage granulocytic series.

Discussion

Primary granulocytic sarcoma (PGS), which is also known as myeloid sarcoma or chloroma, is a type of malignant tumour formed in extramedullary tissues as a result of the proliferation of myeloblasts or immature granulocytes. In 1811, Burns, a British scholar, first noticed cases of green lumps on the head and neck of his patients, and in 1853, King found that particles with myeloperoxidase activity in tumour cells caused the green colour of the tumour; thus, the name of “chloroma” was given to this tumour type. In 1893, Dock found that chloroma was associated with acute leukaemia, and in 1988, Davey proposed the concept of extramedullary myeloid tumours, including isolated GS (non-leukemic GS) and those with leukemic extramedullary infiltration (leukemic GS) [1]. PGS is rare, with a prevalence of 2/100,000 among adults. Clinically, PGS has no specific manifestations and is often discovered inadvertently as isolated extramedullary lumps. PGS can occur in any anatomical site, but the most common sites are the skull, paranasal sinus, sternum, ribs, vertebrae, periosteum of the pelvic bones, lymph nodes and skin; this tumour type has also been observed in the brain, mouth, mediastinum, intestine, breast, ovary, cervix, testis and epididymis, among other sites [2-12]. The tumour may arise prior to or concurrently with acute or chronic myeloid leukaemia or other types of myeloproliferative diseases (MPDs) or myelodysplastic syndromes.
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(MDSs), or as the primary manifestation of relapse after the treatment-induced remission of acute myeloid leukaemia (AML). In some cases, the tumour does not progress and can persist for 10 years [10]. The case reported in this study occurred in the popliteal fossa, which has never been reported in the literature. Therefore, PGS is prone to clinical misdiagnosis; in a retrospective analysis, Zhou et al. showed that the misdiagnosis rate of this tumour has ranged from 75-86% [5].

PGS generally manifests as isolated extramedullary lumps; most of which demonstrate invasive growth and, in some cases, may have an envelope. Most of the tumour is a solid mass with homogeneous sections and a fine, fishmeat-like texture. These tumours are greyish or reddish brown, but some parts of the tumour are often light green, which is why they are referred to as “chloromas”. Parts of the tumour may also display cystic degeneration.

GS is composed of myeloblasts, neutrophils and myeloid precursor cells. Tumour cells are often present as uniformly dispersed small round cells that are medium or small in size with little basophilic cytoplasm, round or irregular nuclei with fine chromatin but inconspicuous nucleoli. According to the maturity of the tumour cells, GS may be divided into three types [13]: (1) the primordial cell-type, which is mainly composed of primordial cells; (2) the immature cell-type, which is composed of myeloblastic and promyelocytic cells; and (3) the mature cell-type, which is composed of promyelocytic and partially mature neutrophils. In mature cell-type GS, young eosinophils are often present, and their quantity is associated with the differentiation level of the tumour. Therefore, in cases where the histological morphology is atypical, the presence of young eosinophils may be an indicator for the diagnosis of PGS, which can be further confirmed by the presence of aniline blue particles or Auer bodies.

Since the tumour cells of GS are complex in their composition and are imbalanced in their differentiation, as they vary from the myeloblasts to mature granulocytes, it becomes a challenge to diagnose it based on only histology information. Therefore, the immunohistochemical detection of MPO, LSZ and chloroacetate esterase is crucial for the correct diagnosis. Myeloblasts express MPO, CD13, CD33 and CD117. Of these, MPO is expressed in almost all myeloid cells and is thus a biomarker specific to these cells. It has also been reported that the positive rate of MPO in PGS ranges from 85% to 100% [2, 3]. LSZ is an enzyme that is mainly present in the cytoplasm of granulocytes and is the most sensitive marker for the detection of myeloid cells. Chloroacetate esterase is an excellent marker for neutrophils. CD68 is another important marker of PGS and is also a marker of monocyte-macrophage cell lines and CD68 is expressed in AML and chronic myelogenous leukaemia (CML). Most CD34-positive cells do not express CD68, and although CD68 is less sensitive than MPO, its positive expression rate in PGS can be as high as 83% [2]. Thus, these two markers are significant in the diagnosis of PGS. In addition, in most cases, PGS, CD43 is expressed, and thus, for any tumour of unknown origin, once the tumour cells are determined to be CD43-positive and CD3-negative, myeloid sarcoma should immediately be considered. However, due to the low sensitivity and specificity of CD43 and CD3, they cannot serve as the basis of PGS diagnosis, and consequently, the role of MPO, LSZ, chloroacetate esterase and CD68 in the diagnosis of PGS should be further examined. One-third of PGS cases also express CD34, which is a haematopoietic progenitor cell-associated antigen that is specifically expressed in haematopoietic stem cells, but its expression is progressively weakened or absent as haematopoietic stem cells differentiate and mature. Therefore, it is necessary for this marker to be combined with the analysis of MPO, LSZ, CD68 and chloroacetate esterase. Recently, a CD33 antibody for use in paraffin-embedded specimens was developed and was deemed supportive in the diagnosis of myeloid sarcoma [14].

GS should be distinguished primarily from non-Hodgkin’s lymphoblastic lymphoma, Burkitt lymphoma, large-cell lymphoma and small round-cell tumours (e.g., neuroblastoma, Ewing/PNET, embryonal rhabdomyosarcoma and medulloblastoma), which is challenging to achieve based on morphology alone. The primary means of identification include flow cytometry and the immunohistochemical detection of granulocyte antigens, mononuclear antigens, myeloid-associated peroxidase and chloroacetate esterase.
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Molecular pathological techniques are advancing quickly and are extensively applied in the diagnosis of PGS. Recently, a variety of chromosomal abnormalities (e.g., t (8; 21) (q22; q22), inv (16) (p13; q22), t (16; 16) (p13; q22), 11q23, +8; 8q) [13] and fusion genes (e.g., CBFB/MYH11, AML/MTG8, bcr-abl) [15, 16] have been discovered. Of these, 25% of children with AML concurrent with t (8; 21) (q22; q22) have GS, while approximately 10% of adults with AML concurrent with t (8; 21) have GS; moreover, skin lesions are often associated with chromosomal abnormalities in 11q23 and chromosome 16 [14]. These findings will enable a more accurate diagnosis of GS. It was found that the abovementioned chromosomal and genetic abnormalities are also present in AML, and since most cases of PGS progress to AML, this suggests that the two may have the same pathogenic mechanism and may provide ideas for the treatment of PGS.

PGS has a poor prognosis, with an average survival of 2.5 to 22 months. If untreated before the onset of leukaemia symptoms or if it is treated as a lymphoma, PGS almost always progresses to AML [2], and approximately 90% of patients develop AML. Therefore, the correct diagnosis of PGS is critical for the therapeutic effect and for the prolonging of the patients’ survival time. Surgical resection is the preferred treatment modality, while postoperative local radiotherapy is also effective for some PGS patients, but the application of postoperative conventional chemotherapy is still in dispute. Liu et al. [2] and Chelly et al. [17] argued that the active application of postoperative AML treatment regimens in PGS patients could delay the onset of AML, which would enable longer patient survival. For PGS, most clinical teams have agreed on the use of whole-body comprehensive therapy of surgical resection + local radiotherapy + combined chemotherapy + bone marrow transplant, which has been successfully applied in countries outside China [18]. The patient reported here was transferred to a higher-grade hospital for treatment after surgery but was lost to follow-up.

Although PGS is rare and has no specific clinical manifestations, cautious examination of the cell morphology in combination with the results of immunohistochemical staining can lead to a correct diagnosis so that patients can receive timely and effective treatment and thus survive longer.

Disclosure of conflict of interest

None.

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