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PRIMARNI ANGISARKOM DOJKE KOD ŽENE U POSTMENOPAUSI SA SLIKOM NALIK NA KASABACH-MERRITTOV SINDROM - PRIKAZ SLUČAJA

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Abstract

**Introduction.** Primary breast angiosarcoma is a very rare tumor and accounts for 0.04% of all breast malignant tumors and most commonly occur in young women. Kasabach-Merritt syndrome (KMS) is described as consumption coagulopathy with thrombocytopenia, and without adequate therapy almost certainly leads to a very fast lethal outcome. **Case report.** We present a rare case of 60-year-old postmenopausal woman with metastatic primary angiosarcoma of the breast associated with a picture like Kasabach-Merritt's syndrome (thrombocytopenia and anemia without the coagulation factor disorder with massive bleeding in the tumor). **Conclusion.** Primary breast angiosarcoma in postmenopausal women is a very rare tumor, and may be associated with anemia and thrombocytopenia without other laboratory parameters for Kasabach-Merritt's syndrome. Anemia and thrombocytopenia are refractory to standard treatment protocols, and also significantly reduces the quality of life of these patients. The literature contains only a few cases of PAB associated with thrombocytopenia or with KMS and there are no clear defined protocols for the treatment of these patients, which requires the presentation of as many cases as possible.

**Key words:**

anemia, angiosarcoma, breast, kasabach-merritt, syndrome, thrombocytopenia

Apstrakt.

**Uvod.** Primarni angiosarkom dojke je vrlo redak tumor koji čini 0,04% svih malignih tumora dojke i najčešće se javlja kod mladih žena. Kasabach-Merrittov sindrom (KMS) je opisan kao potrošna koagulopatija sa trombocitopenijom i gotovo sigurno dovodi do veoma brzog letalnog ishoda bez adekvatne terapije. **Prikaz slučaja.** Predstavljamo redak slučaj postmenopauzalne žene starosti 60 godina sa metastatskim primarnim angiosarkomom dojke udruženim sa slikom sličnom Kasabach-Merrittovom sindromu (trombocitopenija i anemija bez poremećaja faktora koagulacije, sa masivnim krvarenjem u tumoru).
**Zaključak.** Primarni angiosarkom dojke kod žena u postmenopauzi je vrlo redak tumor i može biti povezan sa anemijom i trombocitopenijom bez drugih laboratorijskih parametara za Kasabach-Merrittov sindrom. Anemija i trombocitopenija su otporne na standardne protokole lečenja, a takođe značajno smanjuju kvalitet života ovih pacijenata. Literatura sadrži samo nekoliko slučajeva PAB-a povezanih sa trombocitopenijom ili sa KMS-om i nema jasno definisanih protokola za lečenje ovih pacijenata, što zahteva prezentaciju što većeg broja slučajeva.

**Ključne reči:**

anemija, angiosarkom, dojka, kasabach-merritt, sindrom, trombocitopenija

**Introduction**

Primary angiosarcoma of the breast (PAB) is a very rare, soft tissue tumor, and makes less than 0.04% of all malignant breast tumors and about 1% of all soft tissue breast tumors \(^1\). The etiology of this tumor is unknown. It usually occurs in the third and fourth decade of life as opposed to other malignant tumors of the breast \(^2\). Secondary angiosarcoma of the breast (SAB) is more likely to occur in elderly women patients as a result of previous radiotherapy and mastectomy \(^3\). Kasabach-Merritt syndrome (KMS) is described as consumption coagulopathy with thrombocytopenia, first detected in children with benign tumors of vascular genesis, and recently has also been described in adults usually in association with malignant tumors of vascular genesis \(^4\).

**Case report**

We present a 60-year-old postmenopausal woman who was admitted to our hospital because of the pain in the lumbar region of the spine. 18 months ago the patient noticed swelling and induration in the right breast, without pain and without nipple discharge from. Previous surgical procedures and radiation are denied. When examining the right breast, it was enlarged, occupied by a tumor mass of the largest diameter of 15 cm with the presence of fluctuations in the tumor. The skin of the breast above the tumor is livid and tense. Physical findings in the left breast and both axillary regions are neat. In laboratory findings, accelerated sedimentation of 50/87 values is noticeable, elevated values of LDH – 303 U/L as well as moderate anemia and mild thrombocytopenia: white blood cells (WBC) – 4.6 x 10\(^9\)/L; red blood cells (RBC) – 3.14 x 10\(^12\)/L; haemoglobin (Hgb) – 88 g/L; hematocrit
(Hct) – 0.27; platelets (PLT) – 122 x 10^9/L. Other laboratory findings were within the limits of the reference values: fibrinogen – 7.2 µmol/L; coagulation time – 430 seconds; bleeding time – 110 seconds; prothrombine time – 12 seconds; prothrombine index – 100%; international normalized ratio (INR) – 1; aspartate aminotransferase (AST) – 19 U/L; alanine aminotransferase (ALT) – 18 U/L; creatinine – 111 µmol/L; urea – 6.2 mmol/L; glucose – 4.95 mmol/L; cholesterol – 4.85 mmol/L; triglyceride – 1.61 mmol/L; electrolytes (Na – 143 mmol/L; K – 4.7 mmol/L; Cl – 100 mm/L; Ca^{2+} – 1.31 mmol/L).

Core tumor biopsy resulted in fragments of necrotic detritus and blood. Computerized tomography (CT) confirmed metastatic deposits in the lungs, liver, spinal vertebrae and ribs. During hospitalization, the right breast was rapidly enlarged with severe pain and tension of the skin. Because of the skin tear, above the tumor, mastectomy is performed without the extirpation of the axillary region. Intraoperatively, rupture of the tumor node occurs with evident abundant central bleeding area. By macroscopic examination, the tumor tissue mostly appears to be coagulated blood, dilapidated, and only on the periphery underneath the skin there is a narrow area of grayish-white, highly-vascularized tumor tissue of firm consistency. A microscopic examination of the tumor tissue recorded a colorful picture. The tumor was composed of solid areas of atypical spindle cells, capillary vessels of irregular shape incorporated in collagen stroma, and focal papillary proliferation of atypical, spindle and polygonal tumor cells with necrosis zones (Picture 1.). Mitoses are numerous, more than 80 to 10 HPF. Positive immunohistochemical reaction was present on endothelium specific antibodies: CD31, CD34 and factor VIII, and negative on S100. A definitive diagnosis was set: Angiosarcoma of the breast, grade III (Picture 2.).

Preoperatively and postoperatively the patient was given two doses of deplasmated erythrocytes. After the surgery, improvement with anemia and thrombocytopenia was noticed: WBC – 3.3 x 10^9/L; RBC – 3.37 x 10^{12}/L; Hgb – 92 g/L; Hct – 0.28; PLT – 156 x 10^9/L. This patient was presented to Oncology Advisory Board one month after the surgery with laboratory findings of blood count: WBC – 3,5 x 10^9/L; RBC – 2,74 x 10^{12}/L; Hgb – 81 g/L; Hct – 0.23; PLT – 104 x 10^9/L. Supportive and symptomatic therapy was indicated, as well as bisphosphonate therapy. Because of the progressive anemia and thrombocytopenia, the patient was admitted to the hospital again very soon. Deplasmated erythrocytes and methylprednisolone were ordinated. Blood count was: (WBC: 3.2 ... 4.4 ... 4.7... 4.4 ... 5.1 ... 6.2 x 10^9/L), (RBC: 1.84 ... 2.07 ... 2.50 ... 2.64 ... 2.76... 3.32 x 10^{12}/L),
(Hgb: 57 ... 58 ... 74 ... 76 ... 78 ... 95 g/L), (Hct: 0,18 ... 0,19 ... 0,23 ... 0,24 ... 0,25 ... 0,31), (PLT: 87 ... 89 ... 74 ... 58 ... 64 ... 67 x 10^9/L). After the improvement of anemia, the patient was sent to home treatment with recommendation to continue with supportive, symptomatic and oral corticosteroid therapy. However, the patient visited us again because of the prominent symptoms of general weakness. During the hospitalisation on a daily basis she was given deplasmated erythrocytes and methylprednisolone. (WBC: 5,6 ... 5,8 ... 5,0 ... 5,0 ... 5,1 x 10^9/L), (RBC: 1,34 ... 1,71 ... 1,69 ... 2,07 ... 2,09 x 10^{12}/L), (Hgb: 41 ... 51 ... 52 ... 60 ... 62 g/L), (Hct: 0,13 ... 0,16 ... 0,16 ... 0,19 ... 0,19), (PLT: 59 ... 53 ... 51 ... 44 ... 39 x 10^9/L). The improvement with anemia and progression of thrombocytopenia was noticed. Fibrinogen and coagulation factors were still within reference values. The patient died four months after the surgery.

**Discussion**

Primary breast angiosarcoma is a very rare tumor and most commonly occur in young women. Lei Wang et al. have shown that high grade PAB occur at a significantly younger age compared to intermediate and low grade PAB, 24:35:41, respectively. Diagnosis of PAB is most commonly rapid and accurate thanks to modern imaging techniques, and is confirmed by a definitive pathohistological analysis on core biopsy samples. Although the core biopsy has become the gold standard in breast tumor diagnosis, in cases like ours in which over 90% of the tumor mass is necrotic with massive central bleeding, this method is quite limited in obtaining representative samples. The diagnosis of primary angiosarcoma may be challenging even in cases without massive necrosis and bleeding. Differential diagnosis of low grade angiosarcoma includes benign vascular lesions: hemangiomas, papillary endothelial hyperplasia, and diffuse dermal angiomatosis. The main differential diagnostic problem in high grade angiosarcoma is sarcomatoid carcinoma. In setting up the diagnosis of sarcomatoid carcinoma, the most important parameter is the negativity of tumor cells to vascular markers, while the cells of the epithelioid subtype of PAB can express cytokeratin receptors on the surface.

Progressive thrombocytopenia in vascular tumors is often a sign of consumption coagulopathy associated with KMS. KMS is characterized with: rapidly enlarging vascular anomaly established, hypofibrinogenaemia, consumption coagulopathy, thrombocytopenia, prolonged prothrombin time and activated prothrombin time, presence of d-dimer and fibrin split products with or without microangiopathic haemolytic anemia.
Management of KMS includes high dose of corticosteroids and interferon alpha. Other therapeutic modalities include compression of the lesion, arterial embolization with bleomycin, laser therapy, sclerotherapy, radiotherapy and chemotherapy with vincristine, doxorubicin, paclitaxel and use of drugs such as pentoxyfylline, dipyridamole and propranolol. An unrecognized syndrome, without adequate therapy, almost certainly leads to a very fast lethal outcome. 

Conclusion

Our conclusion is that primary breast angiosarcoma in postmenopausal women is a very rare tumor, and may be associated with anemia and thrombocytopenia without other laboratory parameters for Kasabach-Merritt's syndrome. Anemia and thrombocytopenia is refractory to standard treatment protocols, and also significantly reduces the quality of life of these patients. The literature contains only a few cases of PAB associated with thrombocytopenia or with KMS and there are no clearly defined protocols for the treatment of these patients, which requires the presentation of as many cases as possible.

Informed Consent

Written informed consent was obtained from patient who participated in this study.

Conflicts of Interest

The authors have no conflicts of interest to declare.

Financial Disclosure

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References


Fig. 1 – Angiosarcoma of the breast: A) area with capillary pathohistological picture, H&E stain, x 400; B) area with papillary pathohistological picture, H&E stain, x 200; C) area with a solid pathohistological picture, H&E stain, x 200; D) area with a solid pathohistological picture, H&E stain, x 400.
Fig. 2 – Angiosarcoma of the breast: A) Von Willebrand (F VIII), x 400; B) S 100, x 400; C) CD34, x 400; D) CD31, x 400.

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