Review Article Medical Science

Aggressive Angiomyxoma: a Diagnostic Dilemma

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ABSTRACT

Aggressive angiomyxoma (AA) is a rare, slow-growing mesenchymal neoplasm of vulvo-perineal region, occurring usually in women of reproductive age during the third to fifth decades. It carries a marked tendency for local recurrence but with a low tendency to metastasize. The high recurrence rate may partially be due to inadequate excision, which may be due to an incorrect preoperative diagnosis. The diagnosis of AA is a difficult one to make with preoperative misdiagnosis occurring in >82% of cases. AA clinically simulates as Bartholin cyst, Gartner duct cyst, vaginal polyp, vaginal cyst, vaginal prolapse, abscess, pelvic floor hernia, fibromatosis, lipoma and other soft tissue neoplasm

Keywords : Aggressive angiomyxoma, Pregnancy, Vulva, Mesenchymal neoplasm

Introduction:
Aggressive angiomyxoma was first described by Steeper and Rosai in 1983[1]. AA is a rare, slow-growing and locally aggressive mesenchymal neoplasm that commonly involves the vulvo-perineal region of premenopausal women. It carries a marked tendency for local recurrence but with a low tendency to metastasize [2,3,4]. The high recurrence rate may partially be due to inadequate excision, which may be due to an incorrect preoperative diagnosis [5]. The diagnosis of AA is a difficult one to make with preoperative misdiagnosis occurring in >82% of cases [6]

Epidemiology:
This is rare tumor with approximately 150 cases reported in the literature [7]. The AA commonly occurs in the women of reproductive age, but can be seen between age 16 to 70 year (median 34 years) [8,9]. However, it can occur in children and males also [10].

Clinical behavior:
The term “aggressive” emphasizes the tumor’s often infiltrative nature and its association with local recurrence in about 30-72% cases in spite of wide excision [11]. Usually AA does not metastasize but out of 150 published cases, only 3 cases presented with distal metastasis (approximately 2% of reported cases in literature) [2,3,4].

Clinical Feature:
AA commonly presents as a large (usually larger than 10cm), painless, slow-growing, partly circumscribed, gelatinous soft mass or ill-defined swelling with infiltrating margins. Patients often present with a visible mass or vague symptoms secondary to pressure effects on the adjacent urogenital or anorectal tracts and pain in the vulvo-perineal, or pelvic region [9]. Vulvar region is the most common site of involvement, however its occurrence in vagina, retroperitoneum, buttock, urinary bladder [12], scrotum, epididymis [13], testis, spermatic cord [14], inguinal region [15], larynx [16], lungs [17], maxillary sinus [18], jejunum [19], has also been documented in the literature [8]. AA clinically simulates as Bartholin cyst, Gartner duct cyst, vaginal polyp, vaginal cyst, vaginal prolapse, abscess, pelvic floor hernia, fibromatosis, lipoma and other soft tissue neoplasm [11,20].

Radiological feature:
On CT-scan, AA has well-defined margin with attenuation less than that of the muscles. On MRI, AA show high signal intensity on T2 weighted image and low signal intensity on T1-weighted image [21,22]. A whorled pattern of signal intensity on T2-weighted images has been reported as a typical feature of AA [23,24]. The possible differential diagnoses to consider include lipomas, bartholin cyst, vaginal myomas, endometriomas, and other malignant tumors. Lipomas would be expected to show signal intensity dropout on fat-suppressed images. Bartholin cysts do not typically show strong enhancement after contrast agent administration. Vaginal myomas tend to have low signal intensity on T2-weighted images with uniform enhancement [25]. Endometriomas show high signal intensity on T1-weighted images because of contained methemoglobin, blood products, or concentrated proteins [26]. Malignant tumors like melanomas, rhabdomyosarcomas, and squamous cell carcinomas, can also occur in the perineal region but would not be expected to demonstrate whorled T2-weighted high signal intensity. MRI is invaluable for assessing tumor extent and determining the best surgical approach [5].

Pathological feature:
Grossly, the AA appear lobulated, soft to rubbery, solid and poorly demarcated mass of varying size, measuring between 3 and 60 cm [9]. The cut surface has a gray-white glittering smooth homogenous appearance with or without area of necrosis and hemorrhage. Microscopically, the AA is usually hypocellular to moderate cellular tumor which is composed of bland stellate and spindle cells with round to ovoid nuclei and palely eosinophilic cytoplasm in myxoid background. Presence of blood vessels of variable calibers and condensation of delicate fibrillary collagen around blood vessels are characteristic features [11]. Histopathologically, AA must be distinguished from the more common myxoid tumors including myxoma, myxoid neurofibroma, myxolipoma, myxoid liposarcoma, myxoid variant of malignant fibrous histiocytoma and

other soft tissue tumor with myxoid changes [27]. The distinctively striking vascular component in AA helps in ruling out most of the above mentioned neoplasms as differentials [27]

The neoplastic cells of AA exhibit fibroblastic and myofibroblastic features and appear to be hormonally influenced [3]. The tumor cells are immunoreactive to vimentin, desmin and smooth muscle actin (SMA) but negative to S100 protein [28]. Most tumors exhibit estrogen receptor (ER) and progesterone receptor (PR) positivity in females [29]. AA from male patients was positive for androgen and progesterone receptors [30].

There are only few cases reported about its coexistence with pregnancy [5,7,10,31,32]. The presence of ER and PR in the AA and its enlargement or recurrence in pregnancy suggest the possibility of hormone dependence of this neoplasm. Recurrence may occur during the ongoing pregnancy or during subsequent pregnancy [10].

Pathogenesis:

The pathogenesis of AA is unclear, but recently a translocation of chromosome 12 with a consequent aberrant expression of the high mobility group protein isoform I-C (HMGIC) protein involved in DNA transcription has been demonstrated [8]. The role of estrogen and progesterone has been elucidated in the pathogenesis of this tumor, as it has been reported that there is rapid growth of the tumor in pregnant women.

Treatment:

Resection of tumor with wide tumor-free margin is the treatment of choice. However, radical surgery does not lead to a significant lower recurrence rate of AA when compared to incomplete resection [10,11]. Laparoscopic removal of AA was not uncommon [33]. Some adjuvant treatments such as hormone therapy with tamoxifen, raloxifene and gonadotrophin releasing hormone (GnRH) agonists have been used for primary treatment in cases where an extensive surgical procedure will lead to great morbidity and for treatment against tumor recurrence [5,11,31,34,35]. These have been shown to reduce the tumor size and may help to make complete excision feasible in large tumors. Vascular embolization is also used for recurrence [11]. Radiotherapy and chemotherapy are considered less suitable option due to low mitotic activity [36].

Despite high recurrence rate, the prognosis for patients with AA is generally considered good. Long-term follow-up and careful monitoring with imaging techniques are essential for timely identification of recurrence and prompt resection [27].

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