CLINICAL VIGNETTE

Localized Amyloidosis of the Uterine Cervix

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Clinical Case

An asymptomatic 43-year-old woman underwent a screening PAP smear. The results demonstrated atypical squamous cells of undetermined significance (ASCUS) and high-risk human papilloma virus HPV (not type 16 or 18) infection. A complete review of systems was negative for any significant complaints, prior medical or surgical issues. Her physical exam was unremarkable. Additional labs including anion gap panel, hepatic function panel, serum calcium, complete blood count (CBC), serum protein electrophoresis (SPEP) and quantitative immune globulins (QIG) were all within normal limits. She subsequently underwent a colposcopy including endocervical and ectocervical biopsies. The results of both identified specimens showed no dysplasia or malignancies but did identify benign squamous and endocervical tissue with acute and chronic inflammation. Of concern, focal amyloid deposition on Congo red staining was seen. Immunohistochemistry was positive for both kappa and lambda chains. Hematology-oncology consultation ensued given the amyloid deposition and recommended further amyloid analysis and mass spectroscopy with amyloid typing. The cervical specimen was sent out for liquid chromatography with tandem mass spectrometry, and amyloidosis was again identified, but the specific type could not be determined definitively. Based on her asymptomatic presentation, not having any comorbidity or lab abnormalities which suggested systemic amyloidosis, the patient was ultimately diagnosed with localized amyloidosis of the uterine cervix.

Discussion

Amyloidosis is the general term for a large family of rare diseases characterized by the extracellular deposition of insoluble fibrillar proteins that may be deposited in tissues in bundles with an abnormal conformation and can cause end-organ damage. The deposition of amyloid may occur because of the presence of an abnormally folded protein, caused by high plasma levels of a normal protein.[1] There are many different types of amyloidosis, one of them being localized amyloidosis, where amyloid deposition can be isolated to a single organ. In localized amyloidosis, amyloid deposits at the site of production, so only one organ is disrupted.[2] Localized amyloidosis are confined to one site and are generally nonlethal and sometimes referred to as a pseudotumor.[3]

Localized amyloidosis presents in several well-recognized forms, particularly involving localized AL (primary) amyloid. This condition is generally non-life-threatening, with rare progression to systemic AL amyloidosis but often associated with frequent local recurrences.[4] Accurately identifying the causal amyloid protein is essential for effective clinical management, as it helps prevent misdiagnosis, inappropriate or potentially harmful treatments, and allows for proper assessment of prognosis. To diagnose amyloidosis, a tissue biopsy of either an affected organ or an amyloid-containing, but clinically silent, site is required. The current preferred method for histological confirmation of amyloid deposits is the Congo red stain used in conjunction with polarized light microscopy. Once amyloidosis is confirmed, it is critical to identify the subtype accurately, as treatment differs substantially depending on the nature and source of the amyloid-forming protein. Subtyping of amyloidosis is done by an assessment of clinical phenotype, immunohistochemistry, genetic testing, tandem mass spectrometry (MS/MS), and associated diseases will allow identification of the type of amyloid.[5]

Localized amyloidosis of the uterine cervix is an exceptionally rare entity, but not completely unheard of. In a study done in 1998, there were only seven confirmed cases reported.[6] Very often it can be misdiagnosed.[7] It can even present as postmenopausal bleeding.[8] In some cases, it can be associated with prominent intratumoral deposition of amyloid.[9,10] A pregnant patient who was diagnosed with localized uterine cervical amyloidosis, in which the deposits mainly consisted of immunoglobulin light chain (kappa chain), underwent a normal delivery.[11] Although localized uterine cervical amyloidosis is extremely rare, most patients don't experience any morbidity with the correct treatment and observation.

Localized amyloidosis has an excellent prognosis with no reduction in life expectancy, and evolution into systemic immunoglobulin light chain amyloidosis is very rare.[12] The main principles of treatment are the same for any type of amyloidosis: (i) reduce the supply of amyloid-forming proteins; (ii) increase the clearance of amyloid deposits; and (iii) support affected organs.[13] Management of systemic amyloid light-chain amyloidosis often involves first-line treatment with combination chemotherapy. This includes the use of thalidomide in conjunction with cyclophosphamide and dexamethasone.[13] Localized AL amyloidosis is typically managed with either observation or localized surgical interventions. Radiotherapy and chemotherapy are not routinely recommended for these patients. However, in severe cases, such as unresectable airway obstruction, localized radiotherapy may be considered as a

treatment option[14]. The factors affecting long-term survival are generally unknown.[15]

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