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SHORT COMMENTARY

Endometrial Sarcoidosis Presenting as Postmenopausal Bleeding

Anju Shukla[1] · **Himani Negi**[2] · **Surbhi Gupta**[1]

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Introduction

Sarcoidosis is an enigmatic entity, a chronic multisystem disorder with worldwide distribution. Any organ of the body can be involved in sarcoidosis, but the most common site of involvement is the lung and hilar lymph nodes which is seen in 90% of cases [1]. Involvement is other sites including peripheral lymph nodes, liver, skin and eye comprised 10–30% of cases [2]. Most of the cases of extrapulmonary involvement have concomitant pulmonary involvement. Involvement of the female genital tract in sarcoidosis is very rare, accounting for less than 1% of total cases and can affect the uterus, cervix, fallopian tubes or the ovaries [3]. Uterine involvement is generally seen in patients of reproductive age and presents clinically as menorrhagia or metrorrhagia. Diagnosis is based on endometrial biopsy and is typically a diagnosis of exclusion. In this paper, we discuss a case of endometrial sarcoid present clinically as postmenopausal bleeding.

Case Report

A 47-year-old nulliparous female of Indian origin presented with single episode of bleeding P/V, 4 years after menopause. Three years prior, she presented with axillary lymph node enlargement, mild hepatomegaly on ultrasound and hilar lymphadenopathy as detected on high-resolution CT (HRCT). Routine hematological parameters were normal at that time, while liver function test showed increase gamma glutamyl transferase 599 U/L (normal range 6–42), alkaline phosphatase 67 IU/L (0–33) and ALT 67 IU/L (0–33). Serum ACE was not increased 61.8 U/L (65.8–114.4). Biopsy from axillary lymph node revealed many discrete, non-necrotizing granulomas consistent with sarcoidosis, as they were negative for any infectious pathology (Fig. 1). A diagnosis of extrapulmonary sarcoidosis was made with lymph node and liver involvement, and she was put on steroids and immunosuppressive drugs. She responded well to treatment with complete remission as monitored by serial biochemical and radiological investigations. Later on, she lost follow-up for about a year and now presented with single episode of postmenopausal bleeding. Her pelvic examination was normal, and on ultrasound the endometrial thickness was 7.0 mm. Pap smear examination was negative for intraepithelial lesion or malignancy, and all routine parameters were within normal range. An endometrial biopsy was performed which showed many discrete non-caseating granulomas (Fig. 2a, b). Sections were subject of Ziehl–Neelsen (ZN), periodic acid–Schiff (PAS) and Grocott's methenamine silver (GMS) stains which were negative for acid fast bacilli or fungal elements. Myobacterial PCR of tissue sample was negative. Antinuclear antibody (ANA) and cytoplasmic antineutrophilic cytoplasmic antibodies (c-ANCA) were performed and found to be negative, and no foreign body was demonstrated on polarized microscopy. In the absence of any infective pathology, an autoimmune condition or foreign body and in view of previous history, a diagnosis of endometrial sarcoid was made and no active management was given to the patient. Now after 9 month of follow-up, there is no further episode of vaginal bleeding and follow-up ultrasounds are normal.

Anju Shukla, MD (Pathology), Senior Consultant, Department of Lab Medicine, Sahara hospital, Lucknow, UP, India. Himani Negi, MS (Gynae and Obs), Senior Consultant, Department of Gynaecology and Obstetrics, Sahara hospital, Lucknow, UP, India. Surbhi Gupta, MD (Pathology), Senior Consultant, Department of Lab Medicine, Sahara hospital, Lucknow, UP, India.

✉ Anju Shukla
anjushukla2012@gmail.com

[1] Department of Lab Medicine, Sahara Hospital, Lucknow, UP, India

[2] Department of Gynaecology and Obstetrics, Sahara Hospital, Lucknow, UP, India

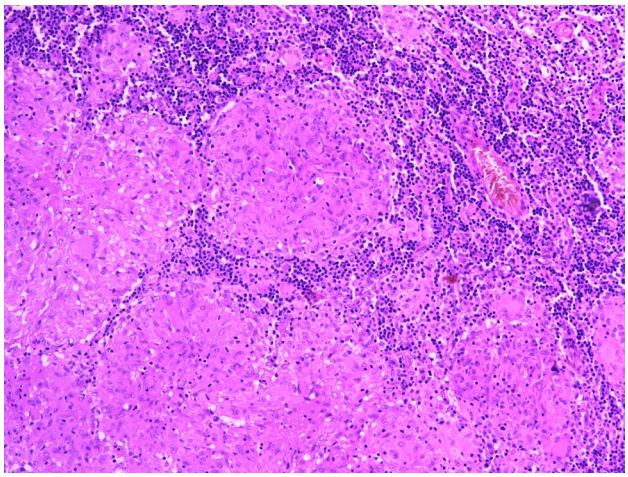

Fig. 1 Tissue section of axillary lymph node showing many discrete non-caseating granulomas (H & E, ×20)

Discussion

Very limited information is available on uterine sarcoidosis derived from isolated case reports, and no case series are found on the literature search. Most of these cases are seen in reproductive age group (21–40 years), and only few has been described in postmenopausal age group [3]. These cases are of varying presentations as endometrial polypoidal lesion, recurrent serometra and cervical erosion. Menstrual irregularities are most common as menorrhagia, metrorrhagia and postmenopausal bleeding. Amenorrhoea is rarely reported in uterine sarcoidosis. Diagnosis can only be made on histology. Characteristic sarcoid histology is shared by many infectious, non-infectious and even neoplastic pathology. Tuberculosis, which is most prevalent in developing countries including India, should be excluded first followed by fungal infections. Large, coalescing, necrotizing granulomas are seen in tuberculosis while discrete, non-necrotizing, naked granulomas with only few surrounding lymphocytes are observed in sarcoidosis. Demonstration of Acid fast bacilli either by ZN stain, culture or by molecular method on tissue is required to confirm the diagnosis [4, 5]. In our case, histology was in favour of sarcoidosis and we were not able to demonstrate any infectious pathology by special stain or by molecular methods. Similar granulomas can be found in Crohn's disease, foreign body reaction and even in lymphoma [6]. All these conditions should also be ruled out before making a diagnosis of sarcoidosis because a premature diagnosis and administration of steroids and other immunosuppressive drugs will be life-threatening in the presence of the infection.

We discovered the first diagnostic clue on observing the patient's previous biopsy and other biochemical reports which irrefutably confirmed the presence of sarcoid granulomas in the lymph node and elevated liver enzymes, alkaline phosphatase, alanine aminotransferase and gamma-glutamyl transferase suggestive of previous liver involvement, although a liver biopsy was not performed at that time.

Thus, it is mandatory to provide a full clinical history to the pathologist to escape diagnostic and therapeutic dilemma. If not for the fortunate discovery of the previous patient reports, the final histopathology report would have only stated the presence of granulomatous inflammation without necrosis.

This report adds to the handful reports of uterine sarcoidosis available currently and also delivers a crucial message to clinicians that sarcoidosis can be a cause of postmenopausal bleeding and should be considered in the differential diagnosis of the granulomatous disease in the endometrium.

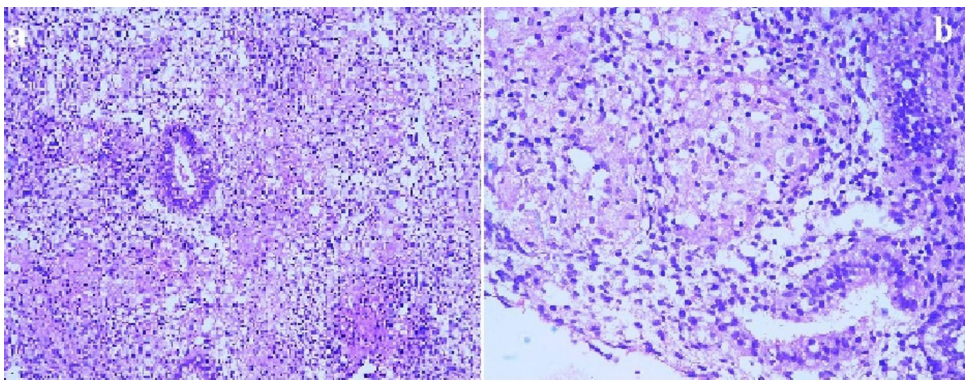

Fig. 2 **a** Tissue section of endometrial biopsy showing an endometrial gland and many granulomas (H &E, ×10). **b** Tissue section of endometrial biopsy showing non-caseating granuloma with surrounding lymphocytes (H& E, ×40)

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Compliance with Ethical Standards

Conflict of interest The authors declare that they have no conflict of interest.

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About the Author

Dr. Anju Shukla has obtained MD (Pathology) from University of Allahabad, Allahabad, in year 1999, has received various gold medals during MBBS and Best oral presentation award in conferences, published various case reports and review articles in index journals, is a research coguide in 24 DNB thesis, actively participated in workshop, conferences and delivered lectures in different forums and interested in histopathology, cytology, neuropathology and gynaepathology.