Limited polyarteritis nodosa of the male and female reproductive systems: diagnostic and therapeutic approach

M Fraenkel-Rubin, D Ergas, Z M Sthoeger

Background: Polyarteritis nodosa (PAN) is a multisystem necrotising small and medium sized vasculitis that when left untreated carries a grave prognosis, with a five year survival of 10–15%. Prolonged immunosuppressive treatment with cyclophosphamide and steroids leads to high remission rates while carrying the risk of life threatening complications. The diagnostic and therapeutic approach for patients with isolated genital tract PAN is not well defined.

Objective: To present the management and follow up of two patients with limited PAN localised to the male and female reproductive system.

Case reports: A 26 year old man presented with an “acute scrotum”. He was afebrile and had no other sign or symptom. Laboratory tests, including complete blood count, erythrocyte sedimentation rate, liver and renal function tests, C reactive protein, rheumatoid factor, cryoglobulins, complement levels, antineutrophil cytoplasmic antibodies, and hepatitis B surface antigen, were all normal. His left testis was excised. Histopathology disclosed PAN of medium sized arteries with testicular infarction but no signs of torsion or infection. The other patient was a 51 year old woman who had had a total hysterectomy for a uterine myoma; incidentally PAN of the uterus and fallopian tubes was discovered. Neither patient received any immunosuppressive treatment after surgical removal of the affected organ. On prolonged follow up (clinical and laboratory evaluation) both patients are healthy with no sign of local recurrence or systemic PAN.

Polyarteritis nodosa (PAN), first described by Kussmaul and Maier in 1866, is a multisystem necrotising vasculitis affecting medium and small sized arteries of multiple organs, including the skin, peripheral and central nervous system, joints, kidneys, gastrointestinal tract, and the heart. Systemic manifestations such as fever, fatigue, and weight loss are not uncommon. Unlike microscopic polyangiitis, which is a small vessel systemic vasculitis, PAN is not associated with the presence of antineutrophil cytoplasmic antibodies (ANCA); rather there is an association between classic PAN and infection with hepatitis B virus. PAN carries a grave prognosis when left untreated, but treatment with a combination of steroids and cyclophosphamide increases the five year survival from 10% to 80%. However, the treatment may lead to severe complications, such as marrow suppression, sterility, and a high rate of secondary malignancies.

There are numerous reports of isolated PAN affecting a single organ with no systemic involvement. Isolated PAN can affect any single organ. Most cases of isolated PAN were discovered incidentally when an organ was surgically removed for unexplained symptoms or by misdiagnosis. The major dilemma is whether single organ PAN is really an isolated form of the disease (in this case removal of the affected organ will be curative) or just the presenting symptom of a multisystem vasculitis, for which aggressive immunosuppressive treatment is indicated.

We present two cases of limited PAN of the reproductive system: a man with PAN of his testis and a female with PAN of the uterus and adnexa. Neither patient received any additional treatment after the affected organs were removed. After several years of follow up there has been no recurrence of the disease. We review other published reports and present a diagnostic and therapeutic approach to limited PAN of the reproductive system.

CASE REPORTS

Case 1

A 26 year old man was admitted to the urology department owing to three weeks of pain in his left testis. On examination he was normotensive and afebrile. A complete physical examination was unremarkable, except for his left testis which was tender on palpation without other signs of inflammation. No mass was palpated and the right testis was normal. Laboratory tests, including complete blood count, cryoglobuline sedimentation rate (ESR), sugar, liver and renal function tests, electrolytes, and urine analysis, were all normal. A chest x ray examination and films of frontal and maxillary sinuses were also normal. Ultrasound of his left testis showed diffuse damage consistent with an interstitial process. Diagnosis of an acute scrotum was made, and the patient’s left testicle was excised.

A pathological examination showed fibrinoid necrosis of medium and small sized arteries together with an acute transmural inflammation with lymphoplasmacytic and eosinophilic infiltrates. A few of the arteries were obliterated with mural thrombi, focal testicular infarcts, and recent bleeding, consistent with a diagnosis of polyarteritis nodosa (fig 1). Additional laboratory evaluations, including antinuclear antibodies, rheumatoid factor (RF), C reactive protein (CRP), Venereal Disease Research Laboratory (VDRL) test, hepatitis B surface antigen (HBsAg), hepatitis C virus antibodies, cryoglobulins, perinuclear and cytoplasmic ANCA, and HIV, were all negative. Complement levels were normal. His Birmingham vasculitis activity score (BVAS) was 0.

After surgery the patient was discharged with no additional treatment. On follow up of more than 2.5 years he is doing...
Well with no signs of systemic illness. Sequential blood tests and repeated ultrasound of his right testis were normal.

Case 2

A 51 year old woman presented to the medical ward with a febrile illness of two weeks’ duration. The fever was accompanied by a mild arthralgia of the distal joints of both hands and legs, lethargy, and a non-specific rash. Her past history included poliomyelitis in her childhood with no residual neurological deficits. Her physical examination was unremarkable except for a 10 cm abdominal mass, suggesting a uterine myoma. Blood tests carried out at that time showed a raised ESR of 80 mm/1st h, mild anaemia, thrombocytosis of $441 \times 10^9/l$, CRP of 45 mg/l (normal <8), and RF of 370 IU/ml (normal <20). Liver and renal function tests were normal.

Blood and urine cultures were negative. An ultrasound examination suggested the presence of a uterine myoma. The patient was referred to the gynaecological department and underwent total abdominal hysterectomy with no complications. Pathological examination confirmed the diagnosis of a uterine myoma; however, further evaluation of medium sized arteries of the cervix, ovaries, and fallopian tubes showed fibrinoid necrosis with lymphoplasmacytic infiltrate. Some of the arteries were obliterated by endothelial proliferation. The histopathological picture was consistent with the diagnosis of PAN of the cervix and adnexa. Sequential blood tests, including antinuclear antibodies, extractable nuclear antigens, anti-double-stranded DNA, VDRL test, cryoglobulins, and complement, were all normal. Tests for pANCA and cANCA and HBsAg were not carried out at that time. Her BVAS was 2–3. After surgery the patient felt well, ESR, CRP, and RF returned to normal, and the patient was discharged with no additional treatment. Her BVAS after surgery was 0. Six and a half years later she is well, and her physical examination and routine blood tests, including repeated HBsAg and ANCA (p/c) tests, are all normal.

DISCUSSION

We present here two cases of isolated PAN of the male and female reproductive (genital) system. In both cases the diagnosis of PAN was made incidentally after the excision of the diseased organ (testis; uterus and adnexa) for another preoperative diagnosis. Neither patient received any further specific treatment for PAN. Prolonged follow-up did not disclose any recurrence or systemic PAN involvement.

According to various studies, pathological involvement of the testis is quite common in systemic PAN (up to 85%). However, only a limited number of patients with systemic PAN had significant clinical testicular involvement. Very rarely systemic PAN presents with testicular disease as the first sign. In previous reports only eight patients with isolated testicular PAN, but no systemic involvement, have been described. In seven of those patients the affected testicle was surgically removed and the patients did not receive any additional treatment. None of those patients developed systemic PAN or local recurrence in the contralateral testis. In contrast, Warfield et al described a 19 year old man who underwent testicular excision with a preoperative diagnosis of tumour, but the
pathological examination demonstrated testicular PAN. During the follow up period the disease relapsed in the remaining testis, as was proved by biopsy. Complete longlasting remission was achieved with high dose steroids, Warfield et al recommended the use of a repeat testicular ultrasound examination (or preferably, magnetic resonance imaging) as a part of the clinical follow up of patients who underwent orchectomy because of limited testicular PAN. As in the case of isolated testicular PAN, most patients with localised PAN of the gastrointestinal tract have a favourable outcome and remain in remission without immunosuppressive treatment, but some may relapse, and thus, a close follow up is obligatory.

The clinical presentation of testicular PAN may include pain, swelling, or local mass, thus leading to a preoperative diagnosis of acute orchitis, torsion, or tumour. The symptoms and signs are similar in isolated testicular PAN and systemic PAN with testicular involvement. Muhamad and Epstein showed that although the histology of testicular PAN is similar in the limited and systemic forms, the existence of infarcts in the affected testis correlates more with systemic rather than isolated PAN. Nevertheless, our patient had infarcts in the affected testis (fig 1) but no systemic involvement.

No reports of any clinical involvement of the female genital tracts in systemic PAN have been published. About 50 cases of isolated PAN of the female genitalia were previously reported. All these cases were discovered incidentally when hysterectomy was done for other indications such as uterine myoma or menorrhagia. As shown in our report and review of the literature, J Urol 1990;144:1236–8. The cervix was found to be affected in all cases, whereas the uterus and adnexa were involved in only a few patients. As was shown in our patient, prolonged follow up (6.5 years) did not show any systemic PAN involvement, despite the fact that none of the patients received any immunosuppressive treatment.

The BVAS is currently used to assess disease activity in systemic vasculitis. This score relies on clinical judgment, laboratory tests, and x ray studies. The BVAS is very useful in the evaluation of patients presenting with localised gut PAN. Although most published reports on limited PAN have focused on vasculitis of the gastrointestinal tract, a similar therapeutic approach can be employed in limited PAN of the genital system. Thus, a low BVAS, like the scores of our two patients, points to the presence of a localised disease. In such patients, close follow up (physical examination, laboratory tests, ultrasound/magnetic resonance imaging) but no immunosuppressive treatment is indicated, after the removal of the affected organ.

The aetiopathogenesis of PAN is not yet defined. It is not clear whether limited PAN of a single organ has the same cause as systemic PAN. Moreover, the natural history of limited PAN of a single organ like the testis or uterus without any treatment (including surgical removal) is not known. Nevertheless, we recommend the use of the BVAS for assessment of systemic involvement in all patients with isolated genital tract PAN. Once systemic PAN has been ruled out, surgical resection of the affected organ should be carried out, followed by close clinical and laboratory follow up without any further immunosuppressive treatment.

Authors’ affiliations
M Fraenkel-Rubin, D Ergas, Z M Sthoeger, Department of Medicine “B”, Kaplan Medical Centre, Rehovot, affiliated to the Hebrew University Hadassah Medical School, Jerusalem, Israel
Correspondence to: Dr Z M Sthoeger, Department of Internal Medicine “B”, Kaplan Medical Centre, Rehovot 76100, Israel; sthoeger@inter.net.il
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REFERENCES
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