Skin Anergy and Its Significance to Predict Post-operative Sepsis In Benign Prostatic Hyperplasia

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Introduction

No drug has proved effective to cure Benign Prostatic Hyperplasia (BPH). At present, surgery is the only effective treatment of BPH. Less than fifty grams of BPH adenomas are treated by transurethral resection, whereas those larger than fifty grams are reserved for open surgery. Cryosurgery of BPH is restricted only to high-risk patients. Unfortunately surgical treatment of BPH has also different complications including sepsis. It is proved that host immunity plays great role in the development of sepsis (Gurewich, Barsukov, 1980; Morgan, Bailey, 1978). We studied the significance of skin testing to predict complications in surgical treatment of Benign Prostatic Hyperplasia.

1. Patients and Methods

Hundred and fourteen patients with BPH, admitted to the First City Hospital, Moscow, participated in the study. Patients ranged in age from 52 to 95 years. Out of them 102 (89.48%) patients were above 60 years.

Forty one (35.97%) patients were admitted with acute urinary retention; 14(12.28%) patients had suprapubic cystostomy; 17(14.91%) patients had vesical stone; 39(34.24%) patients had fever; 19 (16.67%) patients had symptoms of chronic renal failure; and 9 (7.9%) patients had hematuria.

According to the clinical course 24(21.05%) patients were at the stage I, 79

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(69.30%) patients were at stage II and 11 (9.65%) patients were at stage III of the disease (Lopatkin 1982).

The diagnosis was confirmed by history, physical examination, urinalysis, haematological and biochemical investigations, urine culture, roentgenographic examinations, radioisotopic study, ultrasonographic evaluation, urodynamic study and if necessary, instrumental examination of the bladder. Cellular and humeral immunity were also studied. Delayed hypersensitivity skin testing to bacterial antigens and tuberculin Purified Protein Derivative (PPD) were carried out.

Skin testing - Bacterial antigens prepared from *Staphylococci haemolytici*, *Streptococci faecalis*, *Bacterii diphtheroids*, *Bacterii pseudodiphtheriae*, *Proteus Mirabilis* and *Escherichia Coli* as well as Tuberculin Purified Protein Derivative were injected into the forearm (0.1ml of each of the three to six antigens) on admission to the hospital. Reaction was considered positive when induration at each injection site was greater than 5mm in diameter at 24-48 hours. The patients were classified as anergic if no positive reactions to skin tests were present.

The differences observed were evaluated by students 't' test.

All patients had undergone surgery. First stage Suprapubic Transvesical Adenectomy was carried on 59 (51.75%) patients. Second stage suprapubic transvesical adenectomy was carried on 10 (8.77%) patients. 12 (10.53%) patients had only epicystostomy. Transurethral Resection of the Prostate (TURP) was carried on 33 (28.95%) patients.

Adenectomy was always completed with 3 to 5 sutures on bed of the enucleated adenoma of the prostate. Bladder was drained by epicystostomic tube and silicone urethral catheter. After TURP bladder was drained with silicone urethral foley catheter and catheter irrigation was instituted.

2. Results

Out of 114 patients 67 (58.77%) had cutaneous anergy. There was a significant dependence between skin anergy and clinical stage of the disease (Table I). The higher the clinical stage of the disease the greater the percent of the anergic patients.

Table I
Skin tests and clinical stage of BPH

Clinical state of Normal BPH	Skin test		Total
	N (%)*	Anergy N (%)	
I	19(79.2)	5(20.8)	24(100.0)
II	28(35.4)	51(64.6)	79(100.0)
III	-	11(100.0)	11(100.0)
Total (%)	47(41.23)	67(58.77)	112(100.0)

*Figures are numbers of patients (percentage in parenthesis)

Haemoglobin concentration was 145.7 g/l for normoenergetic patients and 124.5 g/l for anergic patients. The difference was significant ($p < 0.001$). The peripheral lymphocytes count was markedly low in anergic patients ($P < 0.001$). Anergy was more often among the elder patients ($P < 0.001$). Table II shows the relation between haemoglobin concentration, peripheral lymphocytes count, age of the patients and reactions to skin tests.

Table II
Relation between haemoglobin, lymphocytes, age and reaction
to skin tests

Skin Tests	Haemoglobin g/l $\pm$ S.E.M*	Lymphocytes Count per cu $\pm$ mm S.E.M	Age years $\pm$ S.E.M.
Normal (47)	145.7 $\pm$ 4.10	1684 $\pm$ 70	87.34 $\pm$ 101
Anergy (67)	124.5 $\pm$ 3.22	1174 $\pm$ 81	74.26 $\pm$ 1.02
P**	0.001	0.001	0.001

*S.E.M - Standard Error of Mean

** Differs by P less than..... by the student's "t" test.

Number of cases examined in parenthesis.

Table three shows the relation between post operative septic complications and reactions to skin tests. Patients with anergy had higher prevalences of postoperative septic complications (epididymitis, urethritis, secondary haemorrhage from the prostatic bed and delayed wound healing) than patients with normal reactions ($P < 0.001$).

Table III
Relations between postoperative septic complications and relation to skin tests

Skin Tests (n=114)	Delayed wound healing (n=22)	Epididymitis (n=18)	Urethritis (n=13)	Secondary haemorrhage (n=9)
Normal (47)	1 (2.1)	2 (4.3)	3 (6.4)	1 (2.1)
Anergy (67)	21 (31.3)	16 (23.9)	10 (14.9)	8 (11.9)

*Figures are numbers of patients (percentages in parenthesis).

3. Discussion

Delayed hypersensitivity skin tests in surgical patients were associated with increased morbidity from sepsis and non septic complications (Meakins et. al. 1979). However, the cause of cutaneous anergy in surgical patients is not known. It is believed that old age of the patients, anaemia, malnutrition, malignant tumor, and other factors play important role (Dely et.al. 1978, 1980; Meakins et, al 1979; Haffejee et al 1978). Above stated results suggest that skin anergy is seen very often in BPH patients with low haemoglobin concentration, with decreased number of circulating lymphocytes in peripheral blood, and among old patients. Patients with third clinical stage of BPH, who were most complicated and serious patients with complete impairment of the vesical bladder function, all had skin anergy. Clinically these patients often presented with ischuria paradoxa (overflow incontinence). The function of the upper urinary tract was also severely impaired. Chronic renal failure was always present.

Out of 79 patients with BPH with second clinical stage of disease, 51 (64.6%) had cutaneous anergy, whereas in first clinical stage of the disease only 5 (20.8%) out of twenty-four patients had anergy. In BPH patients the second and third clinical stages were charac-

terized by marked residual urine and secondary lower and upper urinary tract infection. The author believes that chronic pyelonephritis seen in BPH results in anemia, and uremia. At the same time, due to the accumulation of lymphocytes at the site of inflammation as well as because of bone marrow inhibition there is significant decrease in number of circulating peripheral blood lymphocytes. In this way skin anergy seen in BPH is obliged to secondary pyelonephritis and its sequels. This version of the author is supported by other works (Bhatta, Makhlin 1983, 1984).

As other authors (Johnson et. al 1979, Meakins et.al. 1979) in the present study a significant number of postoperative septic complications, among the anergy patients, is noted. The higher total septic rate in anergy patients with BPH was attributable to a higher incidence of pyelonephritis which was seen in this group of the patients. It is proved that surgery may cause transient immunodepression (Park et. al 1971; McCredie et al 1979 Muster et al 1981), which is suggested due to the presence of serum inhibitors of lymphocyte chemotaxis that also decrease neutrophil chemotaxis (Chistou, Meakins 1979). A patients with skin anergy (which means a patient with defective cellular element of immunity) like a patient with normal skin test undergoes marked immunodepression after surgery. This further immunodepression in anergic patients causes gross immune disturbance facilitating to development of underlying infection. Thus, we found significant septic complications among anergy patients. Therefore a BPH patient with skin anergy should be treated like other patients at a high surgical risk including intensive pre-and-post operative care and immunomodulating agents. Prophylaxis of the septic complications should be directed towards the normalisation of urodynamics and proper antibiotic treatment of pre-existing pyelonephritis.

Presently, immunologic screening is not a standard of preoperative patient evaluation. However, immune status study in urological patients was found to be a good guide to prognose postoperative septic complications (Guttmann et. al 1981; Bhatta 1983; Bhatta, Makhlin 1984). Above stated results reveal an overall depression of delayed hypersensitivity skin reactivity in BPH patients. It indicates that skin anergy to bacterial antigens and PPD in BPH patients has significant prognostic value to predict septic complications in surgical treatment of this disease.

Thus, delayed hypersensitivity skin testing is a valuable "in Vivo" immunologic test in BPH patients. This test is worth paying more attention but deserves more clinical investigations to be a standard part of preoperative patient evaluation in urogenital surgical centers.

4 Summary

Delayed hypersensitivity skin reactions to bacterial antigens and PPD were determined in 114 patients with BPH. Skin anergy was recorded in 67 (58.77%) patients. All patients with third clinical stage of BPH had skin anergy. Among the anergic patients early postoperative septic complications were very common. The higher total sepsis rate in anergy patients with BPH was attributable to a higher incidence of pyelonephritis. The author forwards a version that the cause of skin anergy in patients with BPH is mainly associated with secondary pyelonephritis and its sequels.

In the light of the available data patients with BPH, who have skin anergy, should be treated like other patients at a higher surgical risk. Prophylaxis of septic complications in BPH patients in postoperative period should be directed towards normalisation of urodynamics and proper antibiotic treatment of pre-existing pyelonephritis.

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