A Case of Wegener's Granulomatosis with Necrosis of the Penis

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MATSUDA, S., MITSUKAWA, S., ISHI, N. and SHIRAI, M. A Case of Wegener's Granulomatosis with Necrosis of the Penis. Tohoku J. exp. Med., 1976, 118 (2), 145-151 — A 31-year-old male had a sudden onset of painful swelling in the penile root region. He then developed necrosis of the penis and further a progressive, chemotherapy-resistant ulcer which involved the perineal region also. Histologically there was evidence of neither malignancy nor specific inflammation, but there were granulomatous tissues with cellular infiltration and scattered vascular necrosis. Examination of the nose suggested gangrenous rhinitis with perforation of the nasal septum. X-ray examination revealed that the nasal septum and conchae had disappeared. Chest roentgenogram also revealed increased hilar shadows in both fields of the chest. Routine laboratory examinations showed slight albuminuria and a normal BUN level. Positive findings included leucocytosis, hyper-gamma-globulinemia, accelerated ESR, positive RA and CRP tests. The patient's death was caused by bleeding from gastric ulcer and pulmonary failure.

Wegener's granulomatosis (abbreviated WG) had been recognized as an independent pathological entity since Wegener first reported it in 1936. This disease is known to have a poor prognosis with the onset of necrotic changes in the air way, the upper air way in particular. This is followed by general dissemination of the disease throughout the body with corresponding symptoms, and the morbid process finally terminates in death. Development of an ulcer or necrosis in the reproductive system or in the perineum as part of this dissemination has been rare. Stewart (1933) reported an ulcer in the perineum of a female patient and Osada et al. (1974) reported necrosis of the penis.

The present paper deals with a case suggestive of Wegener's granulomatosis associated with necrosis of the penis, and some of the pertinent literature are reviewed.

CASE REPORT

Patient: 31 years of age, male.
Chief complaint: Necrosis of the penis.
Family history: Non-contributory.

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Past history: When he was 21 years old, he received surgery for sinusitis. In the same year intercostal neuralgia was diagnosed and at 27 years of age he had ischias.

Present history: In January 1974 he had general malaise, pollakisuria, pain at urination, a high temperature and coughing. He was then treated by a physician for two months and his symptoms were ameliorated. But in March of the same year he had a recurrence of the pollakisuria and pain at urination and was treated as an out-patient. In June, however, he had a sudden onset of painful swelling at the root of the penis and was referred to urologic clinic. About that time the penis became necrotic. His illness was progressive and refractory to various kinds of treatment. He was then referred to our Department and admitted on 21, January 1975.

Inventory by systems: BP: 140/84 mm mercury. Conjunctiva bulbi not icteric. Conjunctiva palpebrae not anemic. No ulcer in the oral cavity. Tonsils were normal. No lymph nodes were palpable in the neck. Auscultation of the chest evidenced no rales or pathologic cardiac murmurs. In the thoraco-abdominal regions the right kidney was slightly palpable but no other abnormal tumors were palpable anywhere.

In the urological systems, however, the penis was almost entirely necrotic with a complete disappearance of the corpus cavernosum and only the dorsal skin was left (Fig. 1). The testicles were almost normal, about hen’s egg in size. The epididymis was swollen bilaterally and very tender so that palpation was difficult to do. The prostate was slightly larger than a walnut in size and seemed

Fig. 1. The penis is almost entirely necrotic, the corpus spongiosum disappearing and only the dorsal skin of the penis is left.
Routine laboratory examinations on admission: Erythrocyte sedimentation rate was 105 mm/liter hr and 120 mm/2 hr. In the urinalysis numerous bacilli and leucocytes were found in the sediment with protein in the urine, 30 mg/100 ml. In the blood picture were RBC 449 × 10⁴, WBC 17,000, Hgb 13.7 g/100 ml, Hct 42%. Serum total protein was 7.4 g/100 ml. Serum protein fractions: Albumin 40.8%, alpha-1-globulin 6.4%, alpha-2-globulin 16.3%, beta-globulin 10.7%, gamma-globulin 24.8%. Serum electrolytes: Na 140 mEq/liter, Cl 101 mEq/liter, K 5.0 mEq/liter. Serum BUN 10 mg/100 ml, creatinine 1.1 mg/100 ml. Liver function: Icterus index 5, CCPT (–), ZTT 7.2, TTT 3.8, SGOT 51, SGPT 79, alk. phosphatase 5.3, LDH 330. Blood sugar at fasting 64 mg/100 ml. RA reaction positive, and CRP +6. Serologic tests for syphilis were negative. Urinary cell diagnosis was Class II without typical cells. Chest x-ray evidenced increased hilar shadows bilaterally (Fig. 2).

Clinical procedure after admission: From the time of admission the patient complained severe pain in the penis. On the seventh day resection of remnant penile skin was performed, which revealed granulation of the penile root and an absence of urethral mucosa, up to the pars membranacea. Postoperatively, the wound showed only retarded healing tendency even with intensive chemotherapy. Rather, the necrosis became progressively worse. A specimen for histological analysis was taken from the resected skin. Microscopically there was no evidence of malignancy or specific inflammation, but the tissue was granulated, infiltrated with lymphocytes, histiocytes, neutrophiles, and plasma cells, and the vessels showed swollen endothelial cells and cell infiltration in the adventitia (Fig. 3). Since admission the patient had a recurring fever of about 38°C, which did not fall.
Fig. 3. Pathological histological picture. H-E stain. Granulation tissue with infiltration of lymphocytes, neutrophiles, plasma cells etc. and the vascular endothelial cells are swollen and there is cellular infiltration in the adventitia.

Fig. 4. X-ray tomogram. Nasal septum is defective (arrow).
after surgery. About 23 days after hospitalization the leucocyte count was over 20,000, suggesting septicemia. On the 27th day he suffered massive bleeding and melena. Endoscopy revealed that there were several ulcers and erosions in the gastric wall. The bleeding and melena were recurrent, the leucocyte count elevated to over 30,000 and his general condition gradually deteriorated. At about this time Wegener's granulomatosis was suspected and he was examined by an otorhinolaryngologist, who discovered gangrenous rhinitis with septal perforation and ulceration in the oral cavity as well. Roentgenogram revealed absence of nasal septum and conchae as shown in Figs. 4 and 5. Ophthalmologically, the fundus was normal but there were granuloma in the conjunctiva bulbi. The above findings together appeared to justify the diagnosis of WG with penile necrosis as the chief complaint. At this time administration of steroids and immunosuppressors, which are thought to be effective in this pathology, was contemplated. But because of the gastric ulcer and liver impairment we could not use these agents. The patient continued to have recurrent gastrointestinal bleeding, and then an associated pulmonary failure occurred, and the patient died on his 110th hospital day.

**DISCUSSION**

At the present time Wegener's granulomatosis is conceived to have the following characteristics. Generally there are physical signs of septicemia which
are constantly progressive until death. In the beginning there is progressive necrosis of the upper or lower air way in which histological analysis shows necrotic giant cell granuloma. Subsequently there is a general dissemination of the disease throughout the body (with angitis and giant cell granuloma), which in the target organs produces variable indefinite symptoms. In particular, renal impairment occurs in almost all cases of WG, terminating in the patient’s death. To date no definite provocative agent is known.

In a review of 56 autopsy cases in Japan, Mizukoshi (1972) reported that the average age of patient when the disease was first noticed was 35.6 years, and there was no difference by sex. With respect to initial symptoms, nasal obstruction, discharge or pain were overwhelmingly frequent (64%), followed by ear (8%), and pulmonary symptoms (7%). Subjectively, the next symptoms reported by the patients were in the upper air way in 91% of the cases, followed by symptoms of the eye (73%), lung (54%), joint pain (46%), ear (32%) and skin rash (30%). Objectively, roentgenologic evidence of sinuitis was overwhelmingly frequent (91%), as were pulmonary shadows (90%), then saddle nose, ulcer of the palate, conjunctivitis, keratitis and peripheral neuritis ranging from 37 to 18%. Laboratory tests revealed a high occurence of albuminuria and hematuria; Walton (1958) reported that albuminuria was found in 88% and hematuria in 81% of his patients. The results of Mizuno and Kobayashi (1962) also confirmed this finding: they found albuminuria in 88% and hematuria in 80% of their patients. Other laboratory tests showed anemia, leucocytosis, increased eosinophiles, increased BUN, increased gamma-globulinemia, accelerated ESR, and positive RA and CRP tests are regarded as pathognomonic. The direct cause of death of the patients was most frequently pulmonary failure, followed by uremia, intestinal or upper air way bleeding, and uremia associated with pulmonary pathology, in decreasing order. In our own case, albuminuria was slight and there was no increase in BUN and the direct cause of death was pulmonary failure. This appears to be in agreement with the incomplete type, without renal symptoms, as proposed by Carrington and Liebow (1966).

Pathogenically, the collagen disease theory of Kataura et al. (1968) and immunologic hypersensitivity theory propounded by Walton (1958), Blatt et al. (1959), and Mizuno and Kobayashi (1962) independently, are presently favored, yet they are not decisive and the true cause of this disease has not yet been found. Regarding prognosis and therapy, the prognosis is very poor. Walton (1958) reported that many of this patients died within five months of diagnosis and 82% of them died within one year of the onset of clinical symptoms and 92% within two years. Therapeutically, steroids once drew attention. Yet while this agent may produce a temporary remission of symptoms, it is practically ineffective in patients with renal impairment. The influence of steroids on a two-year mortality rate was examined by Hollander and Manning (1967) in over 90% of their cases, and there have been few reports in favor of steroid effect. With immunosuppressors Aungst and Lessmann reported in 1962 that the alkylating agent, nitrogen mustard,
was effective, and McIlvaine (1966) found in 1966 that chrombucil, a derivative of nitrogen mustard, was effective. Imuran, an antagonist of purine, has been used since Bounroncle et al.'s report in 1967 and appears to have yielded the most favorable results. Norton et al. (1968) with imuran and steroids, and Kaplan et al. (1968) with a combination of imuran predonine and duazomycin, an antagonist of glutamine, reported that favorable results were obtained even in patients with renal pathology. Capizzi and Bertino (1971) used methotrexate, an antagonist of folic acid, on patients whose condition had deteriorated, combined with imuran and steroid therapy. Because of the unknown pathogenesis of this disease, these therapies are all far from being appreciably effective. It is therefore hoped that the cause of this pathology soon may be clarified.

References