Obstructive uropathy associated with myelomonocytic infiltration of the prostate

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Abstract

A 72 year old man was diagnosed with chronic myelomonocytic leukaemia (CMML) according to the FAB group classification. He presented with symptoms of anaemia, urinary frequency, hesitancy, and nocturia. He was later admitted with acute urinary retention and acute renal failure, which resolved with treatment. A transurethral resection of the prostate was performed. Histological examination showed fibromuscular hyperplasia with dense infiltration by myelomonocytes which stained positively with chloroacetate esterase; immunohistochemical staining was positive for lysozyme, CD43, CD45, and CD68. Following treatment with oral etoposide he transformed to acute myeloid leukaemia and eventually died. Myelomonocytic infiltration of the prostate has not been reported before. This case extends the spectrum of disease previously recognised in CMML.


Keywords: chronic myelomonocytic leukaemia; prostate; urinary retention; myelomonocytes

The bone marrow showed myeloid and monocytic hyperplasia and myeloid precursors were hypogranular. There was no excess of blast cells. Micromegakaryocytes were identified in marrow smears.

In the context of a persistent peripheral blood monocytosis of $>1.0 \times 10^9$/litre, these findings were consistent with a diagnosis of chronic myelomonocytic leukaemia as defined by the FAB criteria. Elective admission was arranged for a three unit transfusion of packed red cells a few days later.

While awaiting admission he became increasingly lethargic and nauseous. Examination revealed a distended bladder and a smooth, tender, moderately enlarged prostate; when catheterised, 2300 ml of urine were drained. He had not previously experienced any symptoms of urinary obstruction until two weeks before admission. Investigations at this stage revealed Na 131 mmol/litre, K 5.9 mmol/litre, HCO3 21 mmol/litre, urea 30 mmol/litre, HCO3 21 mmol/litre, urea 30 mmol/litre, creatinine 995 µmol/litre.

Treatment with intravenous fluids was started and a blood transfusion was given. He developed postcatheterisation diuresis and his serum biochemistry improved such that the creatinine had fallen to 126 µmol/litre two days later. He was discharged with a urethral catheter in situ to await an elective transurethral resection of the prostate. Subsequently a 30 g prostate was resected and histological examination revealed dense infiltration with myelomonocytes.

Postoperatively, he required multiple packed red cell and platelet transfusions owing to heavy haematuria.

Chronic monomyelocytic leukaemia (CMML) as defined by the FAB group is classified as a myelodysplastic disorder characterised by a peripheral monocytosis and particular bone marrow features. Cytopenia, hepatospleno-megaly, and lymphadenopathy are common. Skin infiltration and serous effusions are also recognised, and gingival infiltration occasionally occurs, particularly if accompanied by a high peripheral monocytosis ($>2.6 \times 10^9$/litre). However, myelomonocytic infiltration of other tissues is not reported.

Case report

A 72 year old man was referred to our department in September 1995 with two weeks of increasing exertional shortness of breath. He also had a four week history of urinary frequency, hesitancy, and nocturia.

The general practitioner had performed a full blood count—haemoglobin 5.7 g/dl (MCV 90.8 fl), white blood cell count $5.6 \times 10^9$/litre (neutrophils 0.6, lymphocytes 3.1, monocytes 1.7), platelet count $69 \times 10^9$/litre—and urea and electrolyte determinations—sodium 138 mmol/litre, potassium 4.2 mmol/litre, HCO3 25 mmol/litre, urea 8.9 mmol/litre, creatinine 143 µmol/litre. Prostate specific antigen was 12.1 ng/ml. The blood film and bone marrow smears both showed morphological abnormalities with abnormal dysplastic granulopoiesis.

Cytopenia, hepatospleno-megaly, and lymphadenopathy are common. Skin infiltration and serous effusions are also recognised, and gingival infiltration occasionally occurs, particularly if accompanied by a high peripheral monocytosis ($>2.6 \times 10^9$/litre). However, myelomonocytic infiltration of other tissues is not reported.

Histology report

Numerous prostate fragments were received fixed in formalin. These showed bladder neck and prostate, with hyperplasia of prostate...
glands and particularly of the fibromuscular stroma. Prostatic stromal elements were infiltrated by dense masses and cords of cells (fig 1). These were of medium size with slight pleomorphism. The nucleus was ovoid to rounded and vesicular cytoplasm varied in extent; in some it was granular. Chloroacetate esterase staining was positive in many of these cells. Immunohistochemical staining was positive in most cells for lysozyme, in many for CD43 and CD45, and in many for CD68 (fig 2).

Discussion
Case reports concerning leukaemic infiltration of the prostate are uncommon. Dajani and Burke reviewed 57 cases and we have found four more cases in other published reports (table 1). The majority presented with the onset of or worsening of symptoms of urinary outflow obstruction. The best documented and most recent cases occurred with chronic lymphocytic leukaemia, in which 20 cases of 29 presented with acute urinary retention; subsequent investigation and treatment of this revealed leukaemic infiltration of the prostate.

A necropsy study of 503 leukaemic patients showed that the actual incidence of metastases to the prostate is higher than the number of case reports would suggest. Necropsy revealed up to 40% prostatic infiltration in acute lymphoblastic leukaemia (ALL), 11–20% in chronic lymphocytic leukaemia (CLL), 11–20% in acute myeloblastic leukaemia (AML), and between 1% and 10% in chronic myelocytic leukaemia (CML). These frequencies reflect the tendencies of the different leukaemias to metastasise to non-reticuloendothelial tissues. The discrepancy between the frequency of case reports and incidence of prostatic involvement found at necropsy reflects the fact that unless urinary symptoms develop prostatic involvement is unlikely to be detected.

The extent to which the leukaemic infiltrate contributes to urinary obstruction is unknown. The best documented cases of CLL infiltration of the prostate associated with urinary retention were combined with histological evidence of benign prostatic hypertrophy or with bladder trabeculation, suggesting chronic obstruction. Certainly others suggest that the presence of benign prostatic hypertrophy is necessary to precipitate retention, and not all cases with leukaemic infiltration of the prostate develop obstructive symptoms. Cases of acute retention in acute leukaemia may be explained by other mechanisms, such as leukaemic meningitis.

Patients present with typical symptoms of urinary outflow obstruction. The prostate is uniformly enlarged and smooth, as in benign prostatic hypertrophy. In CLL, lymphocytic infiltration is irregular in distribution, so that preoperative needle biopsy is unreliable. There are insufficient published data to show whether this is also true for granulocytic leukaemias. It has been suggested that patients who present with acute granulocytic leukaemia and urinary retention tolerate surgical transurethral resection of the prostate for alleviation of symptoms less well than patients with CLL, in whom the five year survival is good. Therefore, where the diagnosis is known in advance, preoperative prostatic needle biopsy is warranted in these patients and other treatment options should be considered. This patient responded to surgical transurethral resection of the prostate and he subsequently died after transformation to AML.

Dajani and Burke reported five previous cases of granulocytic leukaemia (table 1) causing urinary retention. However, precise defined subtyping of the granulocytic infiltrate is lacking. We were unable to find a conclusive report in the English language literature of myelomonocytic infiltration of the prostate more recently than 1982, when the diagnostic criteria for CMM were defined by the FAB
group. This illustrates the highly unusual nature of this particular case.

Interestingly, bladder outlet obstructive symptoms developed while the peripheral monocyte count was lower than $2.6 \times 10^9/litre$—monocytosis greater than this is associated with non-reticuloendothelial tissue infiltration.\(^2\)

Eleven of 12 cases of myelomonocytic skin infiltration occurred with a high peripheral myelomonocyte count.\(^2\) None of the published reviews has addressed tissue infiltration by monocytes other than in the sites previously mentioned, which may be because the possibility has not been recognised. This case shows that the spectrum of disease seen in CMML is wider than has been appreciated and lends support to the premise that the peripheral monocyte count is not a wholly reliable indicator of clinical disease.


