

Preliminary Communications

Urography in Myelomatosis

Brit. med. J., 1969, 1, 486

Summary: To investigate whether urographic contrast media might precipitate Bence Jones protein in the renal tubules and lead to renal failure in patients with myelomatosis, the reaction between the media and myeloma urine was studied in vitro. Appreciable precipitation was found only in urine at or below pH 4.5, and its occurrence did not correlate with the type or concentration of protein present. It is concluded that the risk of urography in myelomatosis is very small.

Introduction

It is now widely held that urography is contraindicated in myelomatosis (Leucutia, 1961). This view is based on 11 reported cases of acute renal failure following the administration of diodone or sodium acetrizoate (quoted by Rees and Waugh, 1965). In one of the cases where diodone was used the renal failure was secondary to circulatory collapse ensuing from a contrast-induced reaction. In the only case attributed to one of the newer contrast media (sodium and methylglucamine diatrizoate; Urografin) it would appear that the patient was almost certainly already in renal failure at the time of urography (Gross *et al.*, 1968). Thus renal failure following urography in cases of myelomatosis is infrequent. In addition, over 200 cases have been recorded where there were no renal complications (Lasser *et al.*, 1966; Morgan and Hammack, 1966; Vix, 1966). Indeed, Rees and Waugh (1965) pointed out that dehydration can cause anuria in myelomatosis and may be more important than contrast media in producing renal failure.

The belief that tubular casts in myeloma kidneys were due to precipitated Bence Jones protein led to the suggestion that the mode of action of contrast media was to accelerate this precipitation, with subsequent occlusion of the tubular lumen. This concept of the nature of the casts and their relation to Bence Jones protein needs careful reappraisal in the light of recent work (Levi *et al.*, 1968; Mackenzie *et al.*, 1968).

Lasser *et al.* (1966) studied the in-vitro interaction of contrast media and myeloma urine and concluded that urography with diatrizoates and iothalamates carried little risk; diodone, sodium acetrizoate, and Biligrafin (iodipamide methylglucamine) all caused precipitates and were potentially hazardous. We have undertaken further studies to see whether the reaction with media varies with the type of light chain (κ or λ), contrast, the concentration of the protein, or its electrophoretic mobility (and hence isoelectric point).

PRESENT STUDY

We used Uriodone (diodone) and Hypaque (sodium diatrizoate) in concentrations adjusted to give 3 g./100 ml. after mixing with an equal volume of urine. Biligrafin (1 drop to 0.5 ml. of urine) was used to test its practicability as a screening test. The results are summarized in the Table. Although each urine was tested through a wide pH range significant precipitation was noted only at or below pH 4.5.

Contrast Media.—At pH 4.5 of the three media used Biligrafin alone most consistently produced precipitation. Some precipitation was also recorded with Uriodone and Hypaque only on increasing the protein concentrations, though one urine even when tested at high concentrations (500 to 2,500 mg./100 ml.) showed precipitation only in the presence of Biligrafin.

Mobility of Bence Jones Protein.—Precipitation with Uriodone and Hypaque was seen only when using proteins having a fast mobility, but the number of proteins used of slow mobility was very much smaller.

Precipitation Patterns

No. of Cases	Type of Bence Jones Protein	Electrophoretic Mobility*	Precipitation		
			Uriodone	Hypaque	Biligrafin
Total Protein Concentration of 50 mg./100 ml.; pH 4.5					
7	κ	5 fast, 2 slow	0	0	5 (4 fast, 1 slow)
8		6 fast, 2 slow	0	0	4 (3 fast, 1 slow)
Total Protein Concentration of 230 mg./100 ml.; pH 4.5					
4	κ	3 fast, 1 slow	1 (fast)	1 (fast)	4 (3 fast, 1 slow)
6	λ	4 fast, 2 slow	3 (3 fast)	2 (2 fast)	5 (4 fast, 1 slow)

* Tested at pH 8.6 on cellulose acetate.

Type of Bence Jones Protein.—Precipitation was seen with both κ and λ proteins.

We were thus unable to demonstrate a correlation in these cases between type of Bence Jones protein, its concentration, or its mobility and ease of precipitation. Furthermore, the low pH needed for precipitation prevents any in-vivo significance being attached to these results. The presence of Bence Jones protein (and other urinary proteins) in the Biligrafin precipitates could be easily demonstrated by electrophoresis, and this method may well merit further study as a rapid means of concentrating urinary Bence Jones proteins. If the few recorded cases of renal failure were indeed due to interaction of contrast and protein, then it is likely that it occurs only with Bence Jones proteins having unusual physico-chemical properties, and we would be interested to receive urine specimens from any cases in which renal failure has been attributed to contrast media.

While it would be unreasonable to dismiss altogether the possible hazard of urography in myelomatosis, on the available evidence the risk must be very small, particularly with the iothalamates and diatrizoates now in use. It seems advisable to avoid preparatory dehydration or purgation, but with this proviso we no longer regard myelomatosis as a contraindication when there are good clinical indications for urography.

We wish to thank Professor S. Cohen for his guidance and encouragement during these investigations, and Drs. J. S. Cameron and C. S. Ogg for helpful discussion.

M. T. Cwynarski, M.B., B.S.,

Department of Chemical Pathology, Guy's Hospital
Medical School, London S.E.1.

H. M. Saxton, M.R.C.P., F.F.R.,

Department of Radiology, Guy's Hospital, London
S.E.1.

REFERENCES

- Gross, M., McDonald, H., and Waterhouse, K. (1968). *Radiology*, **90**, 780.
Lasser, E. C., Lang, J. H., and Zawadzki, Z. A. (1966). *J. Amer. med. Ass.*, **198**, 945.
Leucutia, T. (1961). *Amer. J. Roentgenol.*, **85**, 187.
Levi, D. F., Williams, R. C., jun., and Lindstrom, F. D. (1968). *Amer. J. Med.*, **44**, 922.
Mackenzie, M. R., Wuepper, K. D., Jordan, G., and Fudenberg, H. H. (1968). *Clin. exp. Immunol.*, **3**, 593.
Morgan, C., and Hammack, W. J. (1966). *New Engl. J. Med.*, **275**, 77.
Rees, E. D., and Waugh, W. H. (1965). *Arch. intern. Med.*, **116**, 400.
Vix, V. A. (1966). *Radiology*, **87**, 896.