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Invited Commentary

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Despite the fact that pheochromocytomas are relatively rare, occurring in approximately 2 of 100,000 adults, they are important because they can be diagnosed with great accuracy if suspected and are usually fatal if not detected and appropriately managed [1]. In 90% of primary cases, modern management results in a successful outcome with cure of the patient. Brennan and Keiser in the present report relate their experience in managing a small but important group of patients in which the initial operation failed, either because an ectopic tumor was not found, the tumor was malignant or there were multiple tumors present. They also emphasize that aggressive surgical treatment of malignant pheochromocytomas in conjunction with adrenergic blocking agents may result in some long-term survivals.

One preventable cause of persistent or recurrent pheochromocytoma is the failure to excise both adrenal glands in patients with MEA II syndromes. When adrenal medullary disease is present in the MEA II syndrome, it is always bilateral [2–4]. In some patients, however, the adrenal contralateral to one with an obviously palpable tumor may show only medullary hyperplasia (the precursor to the development of pheochromocytoma in these syndromes). Any attempt to leave functioning adrenal tissue will inevitably result in recurrence. Our experience is in complete agreement with that at the Mayo Clinic where they have concluded that total adrenalectomy is the treatment of choice in patients when the adrenal component of the MEA II syndrome has been diagnosed [1, 4]. Scintigraphy of the adrenal medulla using I^{131} metaiodobenzylguanidine (MIBG) has recently demonstrated that bilateral adrenal medullary hyperplasia can be diagnosed at a very early stage before biochemical evidence of hyperplasia or pheochromocytoma is diagnostic [5]. Of 6 MEA II family members who were found to have the adrenal component of the syndrome by MIBG scanning, none had CT scan

evidence of adrenal disease. At operation, all 6 patients had either adrenal medullary hyperplasia or pheochromocytomas less than a centimeter in diameter. Although it is controversial as to when these asymptomatic patients should undergo bilateral adrenalectomy, it is further evidence that bilateral changes are present even when the adrenal glands appear normal.

The authors utilized CT scanning as their first localizing study just as they would in patients undergoing localization for primary explorations. Currently CT should be considered the best means of localizing a pheochromocytoma. Utilizing present generation CT scanners, more than 90% of adrenal pheochromocytomas can be identified [1]. Invasive localization studies including selective aortography and selective venous sampling for catecholamines are no longer needed in most primary cases. Although CT scanning is accurate in demonstrating pheochromocytomas arising from the adrenal glands, this technique has been less successful in identifying extra-adrenal tumors. The authors have utilized both selective arteriography and selective venous sampling in these circumstances. Invasive localization studies should be performed only after the patients have been blocked with alpha adrenergic agents. Despite the benefit of all 3 types of localization procedures, some pheochromocytomas will not be identified [6, 7]. Furthermore, false/positive localization may result from the interpretation of both CT and venous sampling studies. This is less likely with aortography when a definite tumor blush has been seen. Unfortunately, some extra-adrenal tumors may not be sufficiently vascular to be identified by this method.

Since August, 1980, we have utilized I^{131} MIBG for localization of pheochromocytomas in all patients in whom this disease was strongly suspected on the basis of biochemical studies. The preliminary results with this agent showed that even small extra-adrenal pheochromocytomas as well as malignant tumors and their metastases could be demonstrated [8]. More than 40 patients with surgically proven pheochromocytomas have now been evaluated. Only 3 pheochromocytomas were not demonstrated by scintigraphy within 48 hours following the administration of this agent. The 3 tumors which failed to image were all solitary, extra-adrenal tumors located in the right renal hilum. Two were subsequently localized by selective arteriography and the other by CT scan. With the exception of primary tumors within the adrenal gland, CT scans and selective venous sampling were frequently negative or misleading in the other cases. Fourteen patients had malignant pheochromocytomas. Some of these patients had multiple metastases to lymph nodes, liver, lungs and bone which were readily demonstrated by I^{131} MIBG. Extra-adrenal pheochromocytomas were successfully imaged in 7 patients whose lesions were apparently benign. Three local recurrences, believed caused by previous operative implantation, were also identified by this method. At present, 5 patients with metastatic pheochromocytomas have received therapeutic doses of I^{131} MIBG. We are encouraged by the preliminary results, although it is too early to determine whether this will be the most effective means of managing malignant lesions not amenable to surgical extirpation. For localization, however, we consider I^{131} MIBG to be the most accurate technique for identifying extra-adrenal, malignant or recurrent pheochromocytomas. Furthermore, even when CT scanning is positive in demonstrating a mass, it does not verify its function which I^{131} MIBG does. Also scintigraphy may identify occult metastases in patients unsuspected of having a malignancy. Finally, some patients with adrenal primary tumors also have synchronous benign extra-adrenal tumors which can be a cause of persistent disease if unrecognized. It is hoped that I^{131} MIBG imaging will appreciably decrease the occurrence of failed operations for pheochromocytomas in the future. This agent will be available for multicenter evaluation during this year.

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