Successful Localization of Abnormal Parathyroid Gland Using Ultrasound-Guided Methylene Blue Dye Injection in the Reoperative Neck

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Received: 30 April 2014 / Accepted: 11 September 2014 / Published online: 20 September 2014
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Abstract Persistent or recurrent hyperparathyroidism is a challenging problem for endocrine surgeons. The aim of this study was to review our experience using ultrasound-guided (US-G) methylene blue dye injection for the localization and removal of abnormal parathyroid glands in patients having primary hyperparathyroidism and previous neck surgery. Between January 2012 and May 2013, six consecutive patients with primary hyperparathyroidism (PHPT) and previous neck surgery underwent focused parathyroidectomy with the use of US-G methylene blue dye injections to localize the presumed parathyroid adenoma were included in the study. We analyzed the data of six patients who underwent reoperative parathyroid surgery using US-G methylene blue dye injection retrospectively. The dye injection was performed just prior to surgery. All patients were successfully treated for their hyperparathyroidism which was confirmed by at least 50 % drop in intraoperative parathormone level 10 min after resection. There were no complications related with US-G dye injection or with surgery. US-G methylene blue dye injection is a cheap, safe, and effective method for localization of diseased parathyroid glands and guiding surgery in the reoperative neck.

This paper was presented in the National Endocrine Surgery Congress, April 22–24, 2013, Antalya, Turkey.

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Keywords Hyperparathyroidism · Methylene blue · Neck · Reoperative

Introduction

Persistent or recurrent hyperparathyroidism is a challenging problem as a reoperation carries higher complication and failure rates. Reoperations can often be performed via an image-guided approach by experienced surgeons after localization using requisite imaging techniques [1]. Localization of the abnormal parathyroid gland(s), particularly in previously operated areas, can be challenging to perform in an accurate, efficient, and safe manner. Preoperative imaging with ultrasonography, sestamibi scintigraphy, computed tomography, magnetic resonance, and/or ultrasound-guided fine-needle aspiration biopsy and parathormone (PTH) determination in aspirate (US-G-FNABx) are typical tools used to identify a hyperfunctioning parathyroid tumor and if it needs excision or not [2]. Ultrasound (US) provides the surgeon with direct and dynamic information about the location of the targeted tumor in relation to other identifiable anatomic landmarks as coordinates. Even in an US performed as preoperative preparation prior to incision, localizing certain tumors can still be confounded because of the disorientation of dissection in scar tissue, especially when it comes to small tumors [1, 3]. Hook-needle guidance, systemic radioactivity uptake/gamma probe guidance, US-guided (US-G) injection of radioisotope (ROLL), or blue dye have all been identified especially for residual thyroid cancer as solutions to localization, each with advantages and disadvantages [1, 4].

The same group of authors previously identified the use of US-G methylene blue dye injection for localization and removal of recurrent thyroid cancer [5, 6]. Because of their success in localizing recurrent thyroid cancer, it can be

hypothesized that a similar technique might also be helpful for localization of parathyroid adenomas in reoperative neck.

They recently published their initial experience using the novel technique and declared that it was the first case series using the technique for the treatment of PHPT in the reoperative neck setting [6]. We have also used the technique successfully with some modifications. The purpose of this article is to report our experience using the novel technique as the second case series.

Materials and Methods

Institutional review board approval was obtained for the retrospective chart review to identify consecutive patients who underwent parathyroidectomy and having previous neck surgery, using US-G methylene blue dye injection at our tertiary referral center, Izmir Katip Celebi University Atatürk Training and Research Hospital.

All patients had neck US and Tc99m sestamibi scintigraphy as preoperative localization study and had concordant studies. All patients had a preoperative laryngoscopy to evaluate vocal cord function. All patients had a preoperative PTH assay in US-G-FNABx with biochemical diagnosis and confirmation of the tumor as parathyroid gland. PTH values of $>1,500$ pg/mL were considered diagnostic of parathyroid tissue [7].

Technique

The technique used to inject blue dye was the one described by Harari et al. [6]. The blue dye was injected by one of the two expert neck radiologists (MBK, NKE) at our institution. In each case, the guiding radiologist carefully reviewed the previous images before coming to the operating room for injection, to ensure that the same lesion was being localized.

In brief, just prior to operation, the radiologist perform preoperative US to the patient in the supine position with a shoulder roll to extend the neck. Once the abnormal parathyroid tissue was identified, the neck was cleaned with betadine solution and the needle tip location was confirmed inside the area of recurrence; 0.2 mL of the 1:5 diluted 1 % methylene blue solution was injected directly into the adenoma during real-time ultrasound guidance. A tuberculin syringe (1 cc) and 26-gauge needle were used for the injection. Typically, only one injection was done, directly into the suspected adenoma. The needle is then removed from the mass, and previous to the removal from the body, 0.1 mL of the dye was injected just under the skin to guide the incision (Fig. 1). After the injection, during the dissection, the blue color helps guide the direction of dissection and the extent of the excision. Following injection of methylene blue dye, the patient

Fig. 1 Preincision view of the dye-injected area

underwent a focused parathyroidectomy in standard manner. Figure 2 shows an injected blue dye adenoma in situ. Figure 3 shows an excised dye-injected adenoma.

Successful resection of adenoma was defined as a 50 % drop in 10 min post excision intraoperative PTH level than the baseline; a resection in which postoperative pathology identified adenoma and normocalcemia achieved postoperative morning and patients remained normocalcemic during the 6 months postoperatively.

Results

Between January 2012 and May 2013, six consecutive patients with PHPT and previous neck surgery underwent focused parathyroidectomy with the use of US-G methylene blue dye injections to localize the presumed parathyroid adenoma were included in the study. Table 1 displays a summary of patient characteristics.

Fig. 2 A blue dye-injected adenoma in situ

Fig. 3 An excised dye-injected adenoma

Using US-G needle injection with methylene blue dye, six of six (100 %) of cases were successful in retrieving the target tumor. Four of six (66 %) dissections were revision cases through scar. The other two excisions were done using other small incisions.

All patients had successful operations. All had more than 50 % decreases in their intraoperative parathormone (IOPTH) level at 10 min post resection with a mean of 81 % (58–90) when compared to their highest preresection PTH level (Table 2).

None of the patients experienced any sign of allergic reaction against the methylene blue dye injection. There were no needle-related complications such as hematoma or nerve injury. There were no complications related with the operations (e.g., no permanent hypoparathyroidism or recurrent nerve palsy).

In all cases, the blue dye remained long enough to be present and useful. No patient had permanent discoloration of the skin. In all cases, we found the blue dye color to increase visual differentiation of tissue and thus saved time during dissection, particularly at reoperative neck. Since we

Table 1 Patient characteristics ($n=6$)

	Mean	Range
Age (years)	51	46–62
Preoperative calcium (mg/dL)	11.6	11.1–14.3
Preoperative PTH (pg/mL)	221	125–481
Decrease in IOPTH	81 %	58–90 %

PTH parathormone, IOPTH intraoperative parathormone measurement

Table 2 Previous operations

	Number	Percent
Female/male	4/2	66/33
Previous neck operation		
Thyroidectomy	3	50
Bilateral neck exploration and failed parathyroidectomy ^a	2	33
Focused neck exploration and failed parathyroidectomy	1	17

^a Both patients had two previous operations

injected a very small amount of dye (0.2 mL) and immediately operated on the patient after injection, the blue dye was not scattered around and confused the anatomy.

Two patients experienced transient temporary hypocalcemia and were treated with temporary oral calcium and vitamin D supplementation until hypocalcemia resolved.

All patients were normocalcemic, but one had persistent PTH elevation without any obvious reason at a mean follow-up of 14.6 months (range 6–23 months). All extracted parathyroid tissues were confirmed pathologically as hypercellular parathyroid glands, and four of them had microscopic features of typical adenoma.

Discussion

Parathyroidectomy in the reoperative neck might be very challenging due to extensive and dense scar tissue, distorted anatomy, and ectopically located gland. Ultrasound guidance and localization with dye injection shortened the operative times and decreased the complication and failure rates [5, 6, 8, 9] especially in reoperative thyroid cancer surgery. The technique was adopted to parathyroidectomy in the reoperative neck by Harari et al. and Candell et al., who reported the first case series using US-G blue dye injection for localization to perform parathyroidectomy in those difficult groups of patients [6, 10]. To our knowledge, our series is the second one in this manner. We successfully identified and resected the abnormal parathyroid gland without any complication in those six patients. Previous studies of reoperative parathyroidectomy have permanent hypoparathyroidism in 10–20 % and recurrent laryngeal nerve paralysis in 3–10 % of patients [11, 12]. We should especially mention that those tumors we injected were small tumors (diameters ranging 5.1 to 12 mm), and the technique was the most useful in that group of patients since the identification of the small tumor can be extremely difficult among the scar tissue.

Our high success rate and no complication rate were directly related to the use of neck US and Tc99m sestamibi scintigraphy as preoperative localization studies and a preoperative

PTH assay in US-G-FNABx with biochemical diagnosis and confirmation of the tumor as parathyroid gland. We also tested the adequacy of the resection using IOPTH determination. As reported before, IOPTH increases the success rate of parathyroid surgery [13].

Blue dyes and especially methylene blue are used intravenously for the localization of parathyroid tumors [14]. It is considered safe for humans, and side effects like local skin necrosis or systemic toxicity were directly related with the volume and concentration used [5]. We and others used the 1:5 dilution of the dye without a significant decline in its efficacy. We should specifically emphasize that we did the injection just prior to incision to prevent the dye from washing out of the tissues, although it cannot do it rapidly [5, 6, 10].

In conclusion, a preincision US-G blue dye injection is a safe, easy, and useful tool even in small abnormal parathyroid glands when performing parathyroidectomy in the reoperative neck. Methylene blue dye localization facilitates the identification and successful removal of those small abnormal parathyroid glands, even in the densely scarred reoperative field. There were no systemic or local complications related to the dye injection.

Acknowledgments The authors specifically thank Prof. Orlo H. Clark for the critical revision of the manuscript.

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