Complex biliary stones: treatment with removable self-expandable metal stents: a new approach

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In this single center study from Charlottesville, Virginia, USA, the authors have tried to evaluate the efﬁcacy and safety of covered self-expanding metal stents (CSEMSs) in patients with retained complex biliary stones. Complex biliary stones often require temporary stent placement between repeat attempts at extraction. The authors hypothesized that CSEMSs could have an advantage over plastic stents in improving the success rates of subsequent duct clearance.

This was a retrospective case series of 36 patients (24 women) who underwent endoscopic retrograde cholangiography (ERC) with biliary sphincterotomy, between November 2003 and June 2009. All of these patients had ‘difﬁcult stones’, and had incomplete stone clearance. The authors deﬁned ‘difﬁcult stone cases’ by the presence of complex stone(s) and/or cases marked by challenging anatomy. Complex stones were large stones (diameter >15 mm), multiple stones (> 3), or a stone that was ﬁxed or contained hard concretions. Technically challenging biliary anatomy was deﬁned as difﬁculties with biliary access (i.e., peri-ampullary diverticula), discrepancy of stone size greater than distal bile duct orifice (i.e., biliary strictures), and choledochal ﬁstula.

After failed duct clearance in these cases, a CSEMS was deployed across the ampulla, ending below the cystic duct insertion when the gallbladder was in situ. In 7 cases, the proximal end of the CSEMS was placed distal to the retained stone burden located within the common hepatic duct. The CSEMS used included partially covered metal stents with Peralume (Wallstent; Boston Scientiﬁc, Natick, Mass), or fully covered stents with anchoring ﬁns (Viabil; ConMed Corp, Utica, NY). All stent had a 10-mm diameter with variable lengths (40, 60, 80, or 100 mm).

Repeat ERC for attempt at stone extraction was scheduled 2 to 16 weeks after CSEMS placement. At the time of repeat ERC, the CSEMSs were removed using a polypectomy snare or rat-tooth forceps. A second attempt at stone extraction was made using a retrieval balloon with or without mechanical lithotripsy, laser lithotripsy, and papillary balloon dilatation, at the discretion of the endoscopist.

Twenty-three cases had large stones, 19 cases had multiple stones, 1 case had a ﬁxed stone, and in 1 case the stone could not be fragmented and removed because of hard concretions. The mean stone size was 19.4 mm (range 8-31 mm), and the mean number of stones was 2.6 (range 1-7 stones). Technically challenging biliary anatomy was present in 13 of 36 patients.

As expected, CSEMS placement was successful in establishing immediate biliary drainage in all 36 patients. Complete duct clearance at repeat ERC was achieved in 29 of 35 patients after a mean duration of 6.4 weeks. Four of the remaining 6 patients underwent sequential CSEMS placement, with eventual duct clearance after multiple ERCPs. There were no complications related to biliary obstruction. One patient died of a non-biliary cause. Of the total 42 CSEMSs placed, there were 4 cases (9.5%) of clinically insigniﬁcant stent migration. All CSEMS could be removed at the subsequent ERC.

The authors conclude that CSEMSs permit management of complex biliary stones. They admit that multiple sessions may be required, and cost-effectiveness of this technique needs further investigation.

Discussion

The initial success rates for stone extraction during ERC are approximately 80% to 90% of all cases. It has been estimated that 20% of all cases require a repeat procedure, or fail complete ductal clearance by using standard techniques. These difﬁcult cases are marked by large, multiple, or impacted stones; stones with hard concretions; difﬁcult ampullary access (peri-ampullary diverticula) or biliary anatomy (duct tortuosity, strictures); or high-risk patient characteristics. In the included cohort of patients, 60% had undergone mechanical / and or laser lithotripsy, and 38.8% had undergone EPBD at initial ERC before CSEMS placement.

There are previous studies that support a role of temporary plastic biliary stent placement for retained bile duct stones. It has been hypothesized that indwelling biliary endoprostheses produce constant mechanical friction forces that assist in stone fragmentation. Katsinelos et al reported reduction in stone size in the majority of cases with plastic
biliary stenting alongside large retained biliary stones. However, actual duct clearance with the assistance of mechanical lithotripsy was only achieved in 44% of their patients. The mean indwelling stent duration in this study was 11.3 months[1]. Similar results were published by Horiuchi et al, showing a decrease in both size and number of retained stones, with mean indwelling plastic stent duration of 2 months[2].

The authors of the present study extended this view, and postulated that CSEMSs, because of their stronger outward radial force applied to the adjacent stone, could be more efficient in this role compared with plastic stenting. However, they failed to compare the actual stone numbers and size before and after CSEMS placement. They proposed that the stones would fragment by stent expansion besides the stent-stone friction, and eventual clearance would be further facilitated by the papillary dilation from the stent expansion. This study demonstrated a relatively high success rate of 83% for biliary duct clearance after initial placement of CSEMSs with shorter mean stent duration of 1.5 months. Balloon sweep alone was required in 65.5% patients for achieving final duct clearance. This suggests that CSEMSs may promote resolution of the retained stone burden.

Minami et al initially described the concept of SEMS placement as a means of dilating the papilla and lower bile duct. They described their technique as “expandable metal stent lithotripsy.” They used covered or uncovered Diamond stents (Boston Scientific, Natick, Mass) in the initial 14 cases. In the subsequent 15 cases they used covered or uncovered Wallstent’s (Boston Scientific) because of their greater radial force. They exploited the radial force of the SEMSs for transient intra-procedure papillary dilation to facilitate stone extraction in a single endoscopic session. Even mechanical lithotripsy could be performed through the stent in the same session, followed by SEMS removal. Single-session stone extraction was successful in 82% of their patients[3].

What about the risk of cholangitis with prolonged biliary stenting for choledolithiasis? Kubota et al placed one or two 7Fr endoprosthesis in 34 high-risk patients, with bile duct stones too large to be extracted by conventional endoscopic means. Cholangitis occurred in 3 patients between 18 and 28 months. The stent had dislodged in 2 of these patients. Of the 21 patients who underwent a second endoscopic intervention after 4-30 months of indwelling plastic biliary stents, the endoprotheses were found to be universally blocked but without any signs of biliary obstruction. The authors suggest that a lumen remains in the bile duct after endoprotheses placement alongside the stones, which allows biliary drainage. Stone fragmentation was achieved in 19/25 patients, with complete stone clearance in 10 of them by stenting alone[4].

Finally, placement and removal of CSEMSs in this setting was safe. In this study, the placement and removal of CSEMSs did not result in any complications. The CSEMS migrated in 4 patients. Although the authors state that this rate of migration is comparable to that of plastic stents, it is important to note that migration of SEMS has been associated with complications including serious ones like bleeding and perforation. One patient had cholecystitis, and needed cholecystectomy within 24 hours.

It is unlikely that CSEMS placement will become the standard of care for patients with difficult stones. However this study provides proof of concept that for selected patients in whom initial stone extraction has failed, placement of a CSEMS can safely and effectively provide temporary biliary drainage, and may improve the subsequent success of duct clearance.

References

EUS-FNA with rescue fluorescence in situ hybridization for the diagnosis of pancreatic carcinoma in patients with inconclusive on-site cytopathology results


The detection of chromosomal abnormalities by fluorescence in situ hybridization (FISH) analysis has not been well studied in FNA samples of pancreatic masses. This study evaluated whether the selective use of FISH in patients with inconclusive on-site cytopathology results may improve the sensitivity of EUS for pancreatic malignancy.

This was a nonrandomized cohort study, carried out at a single tertiary-care referral cancer center (University of Miami, Florida). Consecutive patients with suspected
pancreatic malignancy were included over a 24-month period (January 2009-December 2010). The final diagnosis was based on either surgical biopsy or disease progression on extended follow-up, or death. Cytology results reported as “abnormal cells,” “suggestive of malignancy,” or “atypical cells” were classified as negative cytological results for analytical purposes. Only diagnoses of carcinoma on cytology were considered as true positives. A standard 22G FNA needle was used. If on-site pathology was not definitively able to confirm a diagnosis of carcinoma after 4 FNA passes, additional passes were done for cytology, and 2 FNA passes were submitted for FISH analysis. The mean number of needle passes, including the samples sent for FISH, was 7 (range 4-11). Probes for the peri-centromeric regions of chromosomes 3 (CEP3), 7 (CEP7), and 17 (CEP17) and a probe for the 9p21 region (LSI p16) (VysisUroVysion) were used for FISH. The authors laid down the criteria for a positive test in the study.

During the study period, a total of 212 EUS examinations were performed in 206 patients for solid pancreatic lesions. The authors excluded patients with positive-on-site cytology (n=110), neuroendocrine tumors (n=22), insufficient follow-up (n=1), FISH not obtained (n=3), and renal cancer with pancreatic metastasis (n=1). FISH analysis was done for 69 patients with inconclusive or non-available on-site cytology results, who comprised the study cohort. Of these patients, 54 had a final diagnosis of malignancy and 15 had benign disease. Among the 50 patients with malignancy and evaluable FISH results, deletion of 9p21 was the most common finding in 29 (58%) patients, followed by polysomy of chromosome 7 in 23 (46%) patients. Sensitivity for malignancy of cytology, FISH analysis, and their combination were 61%, 74%, and 85%, respectively (p = 0.009). FISH detected an additional 13 cases of pancreatic adenocarcinoma missed by cytology. There was no false-positive FISH analysis in 15 patients with benign disease. No major complications occurred from EUS-FNA.

The authors conclude that in patients with suspected pancreatic cancer, FISH analysis can detect additional cases missed by cytology without compromising specificity. They suggest that FISH analysis to detect polysomy of chromosomes 3, 7, and 17 and deletion of 9p21 should be considered when cytology is negative for malignancy in patients with a known pancreatic mass.

Discussion

The diagnostic accuracy of EUS-guided FNA (EUS-FNA) with cytological analysis for pancreatic carcinoma varies from 60% to 90% with nearly 100% specificity. The yield of EUS-FNA can be negatively influenced by inaccurate needle placement, excessive blood on the slides obscuring the cancer cells, well-differentiated tumor morphology, extensive tumor necrosis, presence of chronic pancreatitis, and inexperience of the cytopathologist. Nearly 20% of patients with pancreatic cancer are left with an inconclusive cytopathological diagnosis after EUS-FNA[5-7]. In the present study, only two-thirds of patients with malignancy had an on-site cytological diagnosis of carcinoma. Hence we need further adjunctive tests on the aspirate from a pancreatic mass to improve its sensitivity for malignancy, but without increasing false positive results.

FISH is a technique that uses fluorescently labeled deoxyribonucleic acid (DNA) probes to chromosomal centromeres or unique loci to detect cells that have numeric or structural abnormalities indicative of malignancy. Specifically, the probe set used in this study (UroVysion, Abbott Molecular, Des Plaines, Ill) targets centromeres of chromosomes 3 (CEP3), 7 (CEP7), and 17 (CEP17) and band 9p21 (P16 / CDKN2A gene). It is now known that several genomic regions are amplified in most cancers, irrespective of the histologic diagnosis. In addition although specific mutations may be unique to certain cancers, use of a panel of markers in FISH usually permits identification of the malignant cells. The assumption of the FISH technique is that finding of aneuploidy is equivalent to malignancy[8]. While this is usually true, it is not a universal finding in all cancers. Colonic cancers associated with the hereditary non-polyposis colon cancer syndromes may not demonstrate aneuploidy. Some premalignant lesions such as colonic adenomas may also demonstrate aneuploidy, risking a false-positive diagnosis. Furthermore, although inflammatory processes usually do not produce aneuploid cell populations, this occurrence has rarely been reported. Lastly, success of any advanced cytological or molecular technique depends on the ability to harvest enough tumor cells. Four patients in the present study had inconclusive FISH results because of lack of cellular material in the EUS-FNA aspirate.

In a previous smaller study based on EUS-FNA, Levy et al compared routine cytology with digital image analysis (DIA) and FISH in 39 patients with known or suspected extra-luminal malignancy, including 19 pancreatic masses. The authors reported an increase in sensitivity from 87% to 97%, maintaining a specificity of 100%, with the addition of DIA and FISH. The overall sensitivity and specificity of FISH alone was 77% and 100%, respectively[9].

It seems logical that if other molecular and advanced cytological techniques are combined with FISH and cytology, accuracy may further improve, as demonstrated in patients with pancreaticobiliary strictures[10,11]. What are the other molecular tests that have been evaluated for the diagnosis of pancreatic cancer in EUS-FNA aspirates? Takahashi et al performed K-ras point mutation analysis in 77 patients (62 with pancreatic cancer and 15 with focal pancreatitis). The authors noted a 10% increase in the sensitivity of EUS-FNA for the diagnosis of pancreatic malignancy from 82% to 94%. Interestingly, K-ras point mutation was not present in any of the 15 cases of focal pancreatitis. Telomerase is a ribonucleoprotein enzyme that catalyzes the addition of repeats of the nucleotide sequence TTAGGG to the ends of the chromosomal DNA. Telomerase activity is virtually absent from normal human somatic cells but is up regulated in germ-line cells and neoplastic cells of many different types. Telomerase activity is not regulated in...
approximately 85% of solid tumors in humans. Furthermore, telomerase activity is not detected in chronic pancreatitis.[12]. Mishra et al studied the presence or absence of telomerase activity in EUS-FNA specimens, and found positive telomerase results in 6 of the 7 patients (86%) with pancreatic malignancy that had negative cytology results. Used in combination with cytology, telomerase increased the sensitivity from 85% to 98% while maintaining the specificity at 100%. Salek et al used a more comprehensive molecular analysis in 101 patients with pancreatic masses (81 carcinoma and 20 chronic pancreatitis). These authors examined K-ras, p16, and p53 mutations plus allelic losses of 9p and 18q. In this study, the sensitivity was greatly improved by molecular tests, but false positive results for either a p53 mutation or a loss of heterozygosity of 9p and 18q were seen in 13 patients with chronic pancreatitis.[14].

What were the limitations of this study? Only a small number of patients with benign diagnosis (15 patients) were included for comparison. The FISH criteria to diagnose malignancy differ in the literature, and are not standardized. A larger number of patients will be required to validate those criteria in patients with pancreatic masses.

The authors appropriately suggest that specimens for FISH be obtained when immediate cytological reading is inconclusive or not available, and that the test should be performed only if the final cytological diagnosis is negative. With this algorithm, this costly test would be appropriately utilized.

References


Randomized, controlled trial of standard-definition white-light, high-definition white-light, and narrow-band imaging colonoscopy for the detection of colon polyps and prediction of polyp histology


Missing adenomas and the inability to accurately differentiate between polyp histology remain the main limitations of standard-definition white-light (SD-WL) colonoscopy. The objective of the present study was to compare the adenoma detection rates of SD-WL with those of high-definition white-light (HD-WL) and narrow band imaging (NBI), as well as the accuracy of predicting polyp histology.

This was a multicenter, prospective, randomized, controlled trial, conducted at 2 tertiary referral centers. A total of 6 experienced endoscopists (3 at each center) participated in the study. Subjects referred and scheduled for...
screening or surveillance colonoscopy were prospectively enrolled between August 2008 and November 2009. The subjects were randomized to undergo colonoscopy with one of the following: SD-WL, HD-WL, or NBI. The randomization was stratified by site, and each of the two sites recruited equal participants.

No effort was made to detect polyps during the insertion phase. In patients randomized to the NBI arm, the colonoscope was inserted to the cecum under white light, and the NBI mode was switched on at the start of the withdrawal phase. The entire withdrawal phase was performed with the allocated imaging type.

The authors used the polyp morphology classification system described by the Japanese Society for Cancer of the Colon and Rectum. For the NBI classification, the authors divided the polyp into 2 types as follows: Type A (suggestive of hyperplastic polyp), when a fine capillary network alone with absent mucosal pattern was seen, or presence of a circular pattern with dots (pattern with central dark area surrounded by clear lighter area) was present. Type B (suggestive of adenoma), when a round / oval surface pattern (central light area surrounded by dark outer area), or a tubulogyrus pattern with presence of linear or convoluted tubules was seen. The polyp histology was predicted in real time during the procedure based on the surface pattern identified by the respective imaging type. After this, polyps were removed and sent in separate jars for histopathological examination by pathologists who were blinded to the colonoscopy findings. The histopathological diagnosis served as the reference standard for comparisons.

The main outcome measurements were the proportion of subjects detected with adenomas, adenomas detected per subject, and the accuracy of predicting polyp histology real time.

A total of 630 subjects were included in the study, and a total of 998 polyps were detected. The proportion of subjects with adenomas was 38.6% with SD-WL compared with 45.7% with HD-WL and 46.2% with NBI (p =0.17 and p=0.14, respectively). Adenomas detected per subject were 0.69 with SD-WL compared with 1.12 with HD-WL and 1.13 with NBI (p =0.016 and p=0.014, respectively). HD-WL and NBI detected more subjects with flat and right-sided adenomas compared with SD-WL (all p values < 0.005). NBI had a superior sensitivity (90%) and accuracy (82%) to predict adenomas compared with SD-WL and HD-WL (all p values < 0.005).

The study concluded that there was no difference in the proportion of subjects with adenomas detected with SD-WL, HD-WL, and NBI. However, HD-WL and NBI detected significantly more adenomas per subject (> 60%) compared with SD-WL. In addition, NBI had the highest accuracy in predicting adenomas in real time during colonoscopy.

Discussion

This was a very well conducted study. Before study initiation, the lead investigator (A.R.) reviewed the polyp surface mucosal and vascular patterns with NBI with all the study endoscopists. Narrow band images of 50 polyps as representative of the different surface patterns were discussed in detail in a structured teaching session until all investigators were confident in their recognition. In addition, a standardized bowel preparation classification was discussed and agreed on, by all the endoscopists before the start of enrollment[15]. Subjects with inadequate bowel preparation (<90% mucosa seen, mixture of semisolid and solid colonic contents that could not be suctioned or washed) were excluded. During the procedure polypectomy was performed under the same imaging modality to which the subject was randomized, and switching from NBI to white light and vice versa was not permitted. This ensured that the investigator was not influenced by the other imaging modality. A standard case report form was used for each procedure.

The withdrawal time in the NBI group was longer compared with SD-WL group (p =0.003), but this was only a mean difference of 0.6 minutes. The mean withdrawal time in the NBI arm was 7.5 minutes compared with 6.9 minutes in the SD-WL arm.

There was no significant difference in the proportion of subjects detected with adenomas (primary outcome) among SD-WL, HD-WL, and NBI. Both HD-WL and NBI detected a 7% higher proportion of subjects with adenomas compared with SD-WL, a difference that was not statistically significant. However, the number of adenomas detected per subject was significantly higher with HD-WL (1.11) and NBI (1.12) compared with SD-WL (0.69). This represents a > 60% higher yield of adenomas with HD-WL and NBI over SD-WL. In addition, both HD-WL and NBI detected significantly more subjects with flat and right-sided adenomas, as well as total number of flat and right-sided adenomas compared with SD-WL. Previous studies comparing SD-WL with NBI for adenoma detection have shown that NBI is either superior or equivalent and may induce a learning effect for adenoma detection[16,17].

With regards to polyp histology, NBI had superior sensitivity (90%) and accuracy (82%) to predict adenomas compared with SD-WL and HD-WL. Only 10% of adenomas were misclassified by NBI compared with 33% by HD-WL and 48% by SD-WL.

Of note, for adenomas smaller than 1 cm, the sensitivity and accuracy of NBI (89% and 81%, respectively) were significantly superior to those of SD-WL (45% and 67%, respectively) and HD-WL (62% and 72%, respectively).

Although chromoendoscopy has been shown to be an accurate method for in vivo histology prediction of polyps, it has not been routinely used in clinical practice outside of Japan. Recently, there has been a renewed interest in the real-time prediction of polyp histology, with the development of NBI or electronic chromoendoscopy. The real-time identification of polyp histology has several potential applications. It can help avoid unnecessary polypectomies of
small hyperplastic polyps, thus improving the efficiency of colonoscopy by decreasing the procedure duration, costs, and risk of complications. Another new paradigm, as recently proposed, would be to not send small polyps (<1 cm) for formal histopathological evaluation after polypectomy (resect-and-discard strategy), and use the real-time histology prediction by NBI to guide the surveillance intervals[18].

The limitation of this study is that both sites were tertiary referral centers with experienced endoscopists, and the results may not be generalizable to the community settings or to less experienced endoscopists. In the NBI arm, the colonoscopy was inserted under HD-WL, and NBI was activated at the start of the withdrawal phase. Although no attempt was made to detect polyps during the insertion phase, some could have been inadvertently detected by HD-WL and thus introduce a bias in favor of NBI. In practical terms, in everyday practice, the use of NBI will be combined with white light by switching back and forth between the two when required, and this could add to the potential benefits of NBI. Whether these increased adenoma detection rates ultimately translate into a decreased incidence of colorectal cancer and mortality needs further evaluation.

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Pancreatic Duct Compliance After Secretin Stimulation: A Novel Endoscopic Ultrasound Diagnostic Tool for Chronic Pancreatitis

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Chronic pancreatitis (CP) is an irreversible and progressive inflammatory disease leading on to destruction of exocrine and endocrine pancreatic tissue. Endoscopic ultrasonography (EUS) has a unique ability to image both the pancreatic parenchyma as well as pancreatic duct and detect both early and late changes of chronic pancreatitis. The pancreas is well assessed by EUS due to its high resolution and the proximity of the transducer to the pancreas. Although the morphologic changes seen on EUS have been well characterized, poor inter observer agreement and disagreement about which features are physiologic versus pathologic have led to concerns over the accuracy of EUS to diagnose CP, especially the early CP[1,2]. The development of the endoscopic pancreatic function test (ePFT) using secretin stimulation has refocused the attention on direct pancreatic function testing for diagnosis of CP. Although promising ePFT is time consuming and is available only at selected specialized centers. Therefore, there is need for developing a quick, sensitive and specific diagnostic method for the diagnosis of CP especially the early CP. Determination of the main pancreatic duct compliance after intravenous administration of secretin has been reported as a useful surrogate marker for pancreatic function during undergoing secretin enhanced magnetic resonance cholangiopancreatography (MRCP)[3]. This test is based on the fact that secretin stimulation causes a transient increase in the intraductal fluid volume by stimulating secretion by the ductal cells. This transient secretion would cause an increase in the diameter of the main pancreatic duct and thus by measuring the change in the main pancreatic duct diameter from baseline, inferences can be made about the exocrine function of the pancreas.

The authors of the current study evaluated the feasibility of performing EUS morphologic examination, EUS secretin enhanced ductal compliance measurements, and secretin-enhanced duodenal fluid [HCO3-] measurement in a single endoscopic session in 35 patients who were referred to them for evaluation for possible CP. They also evaluated the correlation between pancreatic ductal compliance and duodenal fluid [HCO3-] after secretin stimulation as a measurement of pancreatic exocrine function. The patients first underwent EUS examination of the pancreas using radial echoendoscope from the gastric and duodenal stations. The standard parenchymal (hyperechoic foci, hyperechoic strands, lobular contour, cysts, and calculi) and ductal (main duct dilatation, irregularity, hyperechoic...

The authors have demonstrated that there is a positive correlation between pancreatic ductal compliance and duodenal fluid bicarbonate concentration. However, the current study has several limitations. This is a feasibility study with small number of patients. The variability in degree of fibrosis in various regions of CP needs to be determined and thus know which region of the pancreatic duct (head, body, or tail) is most representative of the degree of gland fibrosis and to what degree regional variation in gland fibrosis affects ductal changes. Also not known is what time from baseline is most representative of maximum ductal diameter change. The inter observer variability also needs to be determined as in the current study all the procedures were done by a single endoscopist. Also it is possible that ductal measurements would have been taken at different locations at each point of time and this will be important when the changes in the diameter are in millimeters. We also need to compare the results of this technique with changes in ductal compliance during secretin MRCP, which is less invasive then EUS. Still this study does demonstrate the potential for a simple, safe and novel mean of characterizing pancreatic structure and function in a single endoscopic session and further multi centre studies with large sample size are needed to validate these initial results. Till then the search for an ideal diagnostic test for CP continues!

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**Granulomatous mediastinal adenopathy: can endoscopic ultrasound-guided fine-needle aspiration differentiate between tuberculosis and sarcoidosis?**

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Granulomatous mediastinal adenopathy: can endoscopic ultrasound-guided fine-needle aspiration differentiate between tuberculosis and sarcoidosis?

Tuberculosis and sarcoidosis, both chronic granulomatous diseases, pose a diagnostic dilemma as they have a high degree of overlapping clinical and diagnostic features with completely different therapeutic measures. EUS has revolutionized the evaluation of mediastinal lesions with EUS FNA having a sensitivity of more than 90% (range 88%–96%) and a specificity approaching 100% for diagnosis of mediastinal lymphadenopathy[4,5]. There are also reports of EUS FNA helping in achieving diagnosis of sarcoidosis and tuberculosis in patients with unexplained mediastinal lymphadenopathy[6,7]. However, there is still paucity of data on whether EUS FNA can differentiate between these two disorders.

The authors conducted a prospective study including 72 patients with mediastinal lymphadenopathy, negative endoscopic investigations including bronchoscopic procedures, and no radiological evidence of lung cancer or other malignancies on computed tomography of various ethnic
subgroups most affected by these two diseases, to determine the accuracy and utility of EUS–FNA in diagnosing and differentiating these two diseases. After EUS staging of the entire dorsal mediastinum, the most prominent suspicious nodes were selected for tissue sampling. “Suspicious” node was defined as hypoechoic, inhomogeneous or having a number of vessels coursing through the node. Differential diagnosis of sarcoidosis and tuberculosis on cytology was made on the basis of a variety of findings which included the presence of epithelioid cell granulomas on a “dirty background” representing debris (protein precipitates, caseating cell necrosis), which is suggestive for tuberculosis and sarcoidosis suggested by epithelioid cell granulomas on a “clear background”.

The final diagnosis of all patients not diagnosed with tuberculosis on culture was made only after 12 months of clinical follow-up, which included repeat hospital appointments for evaluation of clinical features, blood tests including erythrocyte sedimentation rate and C-reactive protein, tuberculin skin test, CT and, if considered necessary, repeat EUS–FNA. In the absence of these features and negative culture, the patients with EUS–FNA not suggestive of tuberculosis but positive for epithelioid cell granuloma were given the final diagnosis of sarcoidosis. If culture was negative, tuberculosis was still diagnosed if the patient had the typical clinical features of fever and night sweats, with/without cough or hemoptysis, moderately raised C-reactive protein, and a positive tuberculin skin test.

Adequate samples on EUS FNA were obtained in 71/72 patients. There were no complications of the procedure. The tubercular nodes were significantly smaller in size compared with those in sarcoidosis. All the nodes were well demarcated and isoechoic or moderately hypoechoic. Inhomogeneous, hyperechoic areas without acoustic shadowing were seen within nine of the active tuberculosis nodes. In eight of these, caseation was proved on cytology. Acoustic shadowing was seen in seven patients and was thought to represent calcifications. None of the sarcoid lymph nodes this feature was present. In 18/30 patients with sarcoidosis, small vessels were seen coursing through the nodes whereas this feature was seen in only 4/28 patients with tubercular nodes and in none of the others which also included malignancy. The final diagnosis after “clinical follow-up” of at least 12 months was tuberculosis in 28 patients and sarcoidosis stage I and II in 30. The cytological examination revealed tuberculosis in 24 patients, three further cases were detected as tuberculosis on culture of EUS–FNA. These had been misdiagnosed as sarcoidosis on cytology. In one case, earlier diagnosed as having non specific changes, follow-up showed an increase in symptoms and node size and repeat EUS–FNA culture performed 6 weeks later proved the diagnosis of tuberculosis. EUS–FNA with cytology and microbiology was able to diagnose a disease or condition in 71/72 cases (99 %) and led to a definite diagnosis in 64/72 cases (89 %). A kappa measure of agreement of 0.88 and a Pearson’s correlation coefficient of 0.89 suggests that tuberculosis and sarcoidosis can be reliably distinguished from one another by cytology obtained by EUS–FNA.

Commentary

The authors have brought out a good study that has demonstrated that EUS FNA has an excellent ability to differentiate between sarcoidosis and tuberculosis, both granulomatous diseases, and this would be of great help for treating clinicians as the treatment of both the diseases is different. It is generally believed that cytology may not be sufficient to differentiate between tuberculosis and sarcoidosis, as epithelioid cell granulomas are present in both scenarios and the differentiating feature of caseating necrosis and “dirty background” may not be present in all the cases of tuberculosis and also may be difficult to interpret. However, strength of association in this study within the whole cohort suggests that cytology obtained by EUS–FNA is a good method for reliably differentiating between these two diseases. It has also been suggested that patchy anechoic or hypoechoic areas and hyperechoic foci in the mediastinal lymph nodes on EUS are important EUS signs of mediastinal tuberculous lymphadenopathy[7,8]. Unexplained mediastinal lymphadenopathy: detailed EUS morphological examination of the lymph nodes and cytological examination of EUS FNA is the answer!

References


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