ORIGINAL ARTICLE

Congenital anomalies in surgical oncology practice

Shanmugam Subbiah, Rajaraman, Noushad Navin

ABSTRACT

Aims: Congenital anomalies are defects present at birth. The etiology is frequently multi factorial with interaction between genetic and environmental factors. Most anomalies are innocuous but some assume clinical significance that includes cancer risks, diagnostic dilemmas or surgical challenges. In this article, we present our experience with congenital anomalies, and review their embryological basis with emphasis on clinical significance and overcoming surgical challenges posed. Methods: Case records of 12,538 patients attending surgical oncology department were screened for congenital anomalies. Those with obvious congenital malformations and others with anatomical variations documented at surgery were included in the study. Results: Overall 21 anomalies were noted with a prevalence rate of less than 1%. The genitourinary system was the most affected 42% (n = 8) and multiple neurofibromatosis the most common disorder (n = 4). Pelvic kidney was the most common anomaly. In 57% (n = 12) patients, the defect was recognized at surgery, a preoperative suspicion based on imaging was possible only in two cases (pelvic kidney and situs inversus). Conclusion: Congenital Anomalies are rare, but present

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Received: 29 June 2015 Accepted: 06 October 2015 Published: 23 January 2016 diverse problems to the oncologist. A majority are anatomical variations noticed at surgery an awareness and early recognition prevents surgical morbidity.

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INTRODUCTION

Congenital anomalies are defined as structural or functional defects which are present at the time of birth. Worldwide they affect 1 in 33 infants and produces disability in 3.2 million individuals each year (WHO factsheet 370). The etiology of these defects includes genetic, environmental or infectious causes although most (50%) are idiopathic. The term congenital malformation is restricted to the description of a structural defect at birth and signifies a defective embryogenesis. The malformations vary from innocuous defects without clinical sequelae to severe multisystem defects that lead to death in 13.6% of live births [1].

Congenital anomalies in surgical practice range from life-threatening defects (e.g., cardiac defect) that require surgical correction to minor abnormalities that cause diagnostic dilemmas or impact surgical morbidity by altering anatomy. An association between congenital anomalies and pediatric malignancies has been well reported, in adults apart from isolated case reports of cancers in a particular congenital anomaly no dedicated multisystem anomaly reporting in cancer patients have been published. Traditionally, an organ oriented approach has been adopted to describe anomalies [2]. In this article we report a wide range of subtle congenital malformations in the setting of contemporary surgical oncology practice and their clinical implications.

MATERIALS AND METHODS

A total of 12, 538 patients attending surgical oncology department with a diagnosis of malignancy were screened for congenital anomalies. Those with obvious congenital malformations and others with anatomical variations documented at surgery were included in the study. All patients were thoroughly evaluated with physical examination and primary cancer appropriate imaging studies. A detailed family history was taken for patients with obvious congenital disorders (neurofibromatosis, Albinism) and specialist consultations obtained for confirming the diagnosis. Primary cancer specific and stage appropriate multimodal treatment was done confirming to standard treatment recommendations.

RESULTS

Overall 21 anomalies were noted, a prevalence rate of less than 1%. The genitourinary system was the most affected 42% (n = 8) and multiple neurofibromatosis the most common disorder (n = 3). The average age of the patients was 52 years. Female patients predominated (n = 12) with an average age of 48 years and the group included nine (n = 9) males with an average age of 56 years. Pelvic kidney was the most common anomaly noticed in females and the anomalies among males were spread out evenly with none appearing to predominate, due to the small sample size. In 57% (n = 12), patients the defect was recognized at surgery, a preoperative suspicion based on imaging was possible only in two types of anomalies (pelvic kidney and situs inversus). The anatomical anomalies presented surgical surprises and management challenges but none resulted in adverse surgical outcome. Table 1 gives a list of the congenital anomalies noted in the study.

DISCUSSSION

Genito Urinary System

Duplex Ureters

Ureteric duplication (Figure 1) was the second most common genitourinary anomaly encountered in

Table 1: congenital anomalies noted among cancer patients in the study.

S. No	Congenital Anomaly	Malignancy	n=21
Genito Urinary System			
1	Ureteric Duplication	Cervical Carcinoma	3 (Figure 1)
2	Pelvic Kidney	Cervical Carcinoma	4 (Figure 2)
3	Anomalous Internal Iliac Vein	Cervical Carcinoma	1
4	Inter Sex Disorder	Germ Cell Tumor	1
Gastro Intestinal System			
5	Situs Inversus	SCC-Esophagus	1 (Figure 3)
6	Anomalous Left Hepatic Artery	Pancreatic Adenocarcinoma	1 (Figure 4)
Head and Neck			
7	Non-recurrent Laryngeal Nerve	Papillary Thyroid Cancer	1 (Figure 5)
8	Anomalous Spinal Accessory	SCC-Alveolus	1
Breast			
9	Sternalis Muscle	IDC -Breast	1
10	Pectoralis Major- Anomaly	IDC- Breast	1 (Figure 6)
Musculoskeletal System			
11	Brachydactyly	Osteosarcoma	1
12	Syndactyly	Osteosarcoma	1
OTHERS			
13	Neurofibromatosis	Malignant Peripheral Nerve Sheath Tumor	3
14	Albinism	Cutaneous Cancers	1

our series after pelvic kidney. Although incomplete duplication is more common (1 in 500), in this series we had one bifid and two duplex ureters. Bifid ureters (incomplete) are more likely to be symptomatic but both can produce vesico-ureteric reflux, or ureterocele, ectopic ureters occur when the drainage orifice is extravesical [3]. The ureters develop from the Wolffian ducts that appear at about the fifth week of intrauterine life [3]. The embryological basis postulated for the development of bifid ureters is the premature division of a single ureteric bud before fusion with the metanephric blastema [3]. The complete duplication is the result of formation of a double ureteric bud or very early splitting of the bud. Ureteric budding is induced primarily by Glial derived neurotropic factor and other factors like Wnt-4 and 11, bmp-2, activin, HGF, TGF alpha mediate early, late branching and tubule maintenance [3]. The upper pole ureter is the anomalous one and inserts inferomedial to the normal ureter into the bladder (Weigert–Meyer law) [3].

A literature search failed to reveal a predisposition of duplex ureters to any malignancy. However, it poses several challenges to the surgeon. Awareness and early recognition of the anomaly is required to prevent injury during pelvic and retroperitoneal surgeries [4–6]. The risk is obvious at the infundibulopelvic ligaments and ureteric tunnel regions at radical hysterectomy [4, 5]. Identification of this anomaly is paramount in performance of an ileal conduit for advanced carcinoma cervix with vesico-vaginal fistula as this requires implantation of three rather than the usual two ureters into the conduit (personal experience).

Pelvic Kidney

Ectopic kidney (Figure 2) is a common anomaly with incidence of pelvic kidney varying from 1 in 2200 to 1 in 3000 [7]. Renal ectopia may be iliac, abdominal or pelvic and crossed if contralateral. Most are asymptomatic but some develop hydroureteronephrosis and calculi [7].The kidneys develop from the mesenchyme of the metanephros in the pelvis and migrate cephalad to reach the posterior abdominal wall and rotate 90 degrees such that the renal pelvis achieves a medial position. During ascent the kidneys receives blood supply from adjacent vessels like the external, internal iliac vessels and finally



Figure 1: Duplex ureters.

from the aorta [7]. Factors like genetic abnormalities, ureteric bud maldevelopment, teratogens and maternal illnesses can produce an arrest of normal development and result in ectopic kidney [7–10].

A literature search of PubMed database revealed isolated reports of renal cell carcinoma arising from a pelvic ectopic kidney. Presently, there is no evidence to suggest the anomaly predisposes to malignancy at any site. For the surgeon this anomaly poses several problems. It simulates a mass lesion, creates imaging misdiagnosis, and makes pelvic surgery hazardous [11, 12]. The surgical problems stem from a short ureter, anomalous blood supply from pelvic vessels and misidentification with retroperitoneal or pelvic nodes [10, 11]. For laparoscopic approaches an accurate preoperative diagnosis helps in better planning of port sites [12]. Finally, the pelvic kidney has been traditionally considered an absolute contraindication to radiotherapy for pelvic cancers though recent IMRT techniques may overcome this issue [8].

Anomalous internal iliac vein

Minor anomalies of the pelvic veins are common events but those of major veins are rare. These are frequently associated with abnormalities of IVC [13]. Awareness is required to prevent retroperitoneal, pelvic surgical morbidity and in planning interventional vascular procedures [14]. The retroperitoneal venous system develops from three embryonic venous structures the subcardinal veins, posterior and supracardinal veins. The iliac veins develop from the posterior cardinal veins and several abnormalities have been described [13]. Absent common iliac veins, internal iliac fusing in midline then ascending to empty at the confluence of common iliac or forming an annulus around the internal iliac artery, absent external iliac or iliac veins lateral to



Figure 2: Pelvic kidney.

external iliac artery are some major anomalies described in literature [13, 14]. The internal iliac may drain into the external iliac or directly into the IVC. Contrast CT scan has been reliably shown to predict these anomalies than venography [15–16]. Anomalous pelvic venous drainage has been shown to assume significance during obstetric, pelvic laparoscopic and orthopedic surgery [16]. However, troublesome hemorrhage from these anomalies vessels can always be controlled by adhering to good surgical principles [17–18].

Gastrointestinal Anomalies

Hepatic Artery Anomalies

Arterial anomalies of the celiac artery branches are common and are important during gastric, pancreatic and hepatobiliary surgeries [19]. Of the three celiac artery branches the most anomaly prone is the common hepatic and its branches [19]. Deviations from normal anatomy have a reported prevalence rate of 25–75% [19]. In deviant anatomy the hepatic lobes receive blood from left gastric (Figure 4), superior mesenteric arteries or the aorta [19]. The abnormal artery may be true accessory or replace normal vasculature. Several classification systems like Michels's, Hiatt and Adachi are in vogue. Based on a study of 200 cadavers Michel's proposed a type 1–10 classification system which was later modified by Hiatt following observations made on hepatic artery anatomy on 1000 liver transplant patients [20]:

Type 1: Normal anatomy (75.7%).

Type 2: Replaced or accessory left hepatic artery arising from LT gastric artery (9.6%).

Type 3: Replaced or accessory right hepatic artery arising from superior mesenteric artery (10.7%).

Type 4: Double replaced pattern right hepatic originating from superior mesenteric artery and left hepatic artery arising from left gastric artery (2.3%).

Type 5: Entire common hepatic originating from superior mesenteric artery (1.7%).

Type 6: Common hepatic artery directly from the aorta (0.2%).

The above list does not include very rare patterns like the trifurcation anomaly (common hepatic divides to form right hepatic, left hepatic and gastroduodenal arteries).

For the gastric surgeon thorough knowledge of the vascular anatomy is essential to avoid visceral ischemic necrosis, peroperative bleeding, prolongation of surgery, devascularization of stomach remnant and postoperative morbidity [21, 22]. Type 5 anomaly is at high risk of injury during pancreatic transection during Whipple's procedure and Shukla et al. recommend careful palpation of posterior pancreatic head to recognize this anomaly and if division is required for oncological reasons an anastomosis of distal stump to left hepatic artery is advisable to avoid a biliary enteric leak. They also recommend early identification of vascular variations and

defer ligation until resectability is confirmed. Vascular anomalies of hepatic vessels present several problems to the liver transplant surgeon. Abnormal arteries are smaller, shorter and may be multiple demanding considerable skills in performing vascular anastomosis. These issues are vital for vascular patency and graft survival. Specific types like type 3 require appropriate modifications in donor selection and surgical technique. The use of preoperative MDCT and gadolinium enhanced MRI scan provide a vascular map of the anatomy and is considered essential prior to hepatobiliary surgery. Aberrant hepatic arteries may have to be occluded prior to intra arterial chemotherapy for treatment of hepatic cancers. The awareness of these anomalies prior to hepatic artery embolization procedures is obvious [23– 26].

Situs Inversus

Situs anomalies are rare with an estimated incidence of 1 in 8000 to 25000 live births [27–29]. Situs inversus (Figure 3) is defined as an anatomical arrangement that is a mirror image of situs solitus and situs ambiguous that result in dysmorphic and malpositioned arrangement of the viscera [27]. Situs inversus with dextrocardia is termed situs inversus totalis [27]. A pretreatment diagnosis is always possible with clinical examination and conventional imaging [27-29]. The exact etiology is unknown. It occurs sporadically or is inherited as autosomal dominant, X lined patterns [27]. The disorder is frequently associated with other abnormalities like primary ciliary dyskinesia and Kartagener syndrome [27, 28]. Cardiovascular system is the most commonly affected with single atrium, single ventricle, conotruncus anomalies and transposition of great vessels [27, 28]. Intraabdominal anomalies include duodenal, biliary atresia, asplenia, gastroschisis, congenital hepatic fibrosis, Currarino triad, tracheoesophageal fistula type



Figure 3: Situs inversus: Liver (yellow square) in the left hypochondrium.

C, and intestinal malrotation [27, 28]

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The relationship between situs disorders and malignancy is controversial with some reports arguing a sporadic association while others consider a possible correlation suggesting that the yet unidentified genes causing right to left disorientation to increase cancer susceptibility [27, 28]. Cancers of lung, thyroid, esophagus, stomach, duodenum, pancreas, liver, colon and rectum have been reported in situs inversus including double and triple malignancies both synchronous and metachronous [29]. Apart from the obvious right to left altered orientation situs inversus does not appear to increase surgical morbidity. A variety of conventional, laparoscopic and robotic assisted surgical procedures have been attempted successfully [30]. Some reports suggest a left-handed laparoscopic surgeon might find it easy to operate in situs inversus patients [30].

Head and Neck Cancer

Nonrecurrent laryngeal nerve

The nonrecurrent laryngeal nerve (RLN) is a rare but important anomaly to recognize in thyroid and anterior cervical surgeries [31]. Instead of the usual course by winding around the subclavian artery on the right and the arch of aorta on the left the nonrecurrent nerve as it originates from the vagus, traverses horizontally to enter larynx at the level of cricoid cartilage (Figure 5) [31]. It has been suggested the term inferior laryngeal nerve should replace RLN in such instances. The incidence varies from 0.3-1.6% for the right to 0.04% for the left RLN [31].It is usually associated with an anomalous retroesophageal right subclavian artery, arteria lusoria or a right sided aortic arch. Left RLN anomaly should be suspected in all cases of dextrocardia [31]. A preoperative suspicion is suggested by the presence of retroesophageal subclavian artery on CT imaging.

The inferior laryngeal nerve (ILN) supplies the sixth branchial arch, the fifth arch becomes rudimentary and disappears, the fourth arch on the right develop into the brachiocephalic and the subclavian arteries while on the left forms the definitive aortic arch. Differential neck growth of the embryo with inferior migration of the developing heart and its vessels away from the larynx drags the RLN along with the vessels into the thorax. The distal part of the sixth arch disappears on the right forcing the RLN to contact the fourth arch (subclavian artery) while the distal arch on the left persists as the ligamentum arteriosum [31-32]. The abnormalities of fourth arch on the right permits a further cephalad origin of the ILN directly from the vagus at the level of cricoid cartilage. Toniato et al. [30] classified the RLN anomalies into the following:

Type 1: Nonrecurrent laryngeal nerve arising directly from the cervical vagus and coursing along the branches of the superior thyroid peduncle.

Type 2A: Follows a course over and parallel to inferior thyroid artery.

Type 2B: Follows a course parallel to and under or between branches of the inferior thyroid artery.

The Galen's loop and anastomotic branch between the cervical sympathetic plexus and the RLN can be the cause of misidentification with the non-RLN [30]. The nonrecurrent nerve is at high risk of injury during thyroid, parathyroid, cervical esophageal surgeries and anterior approaches to the cervical spine [32–33]. Several techniques have been suggested to identify non-RLN and include imaging studies like barium swallow, CT/ MR angiography and USG these rely on the detection of associated vascular anomalies [34]. Numerous techniques have been described to identify or avoid injuring the non-RLN. Liu et al. [33] has recommended delaying division



Figure 4: Anomalous hepatic artery (yellow arrow pointer).



Figure:5: Non-recurrent laryngeal nerve (yellow star).

of any horizontal bond between vascular structures and the larynx except the middle thyroid vein until the RLN is identified. The use of nerve monitors have been advocated by some [34]. Nevertheless an awareness and thorough anatomical knowledge is essential to prevent damage.

Spinal Accessory Nerve Anomalies

The spinal accessory nerve is the most important structure in the posterior triangle of the neck. Damage to this structure results in the shoulder syndrome an important morbidity of radical neck dissection. Functional neck dissections specifically seek to prevent this complication by preserving the spinal accessory nerve. The spinal accessory nerve arises by several anterior cervical nerve roots which ascend as a single trunk to enter the posterior fossa through the foramen magnum then unites with the cranial division at variable locations. The nerve then exits the skull through the jugular foramen posterior to the vagus and anteromedial to the Internal Jugular Vein (IJV). It then divides into an internal branch containing the cranial fibers which then joins the vagus nerve. The external division assumes a lateral relation to IJV and descends into the posterior triangle to supply the trapezius and sternomastoid muscles. Several anomalies have been described these are generally rare and occur along with an abnormal upper IJV [35-36].

Partial duplication or fenestration of the IJV is a well described anomaly and results from anomalous condensation of developing venous plexuses posterior to the precardinal veins, this is associated with a medially placed or more commonly with a transvenous passage of the spinal accessory nerve [35, 36]. This arrangement predisposes to high risk of nerve injury while IJV ligation during neck dissections. Even in functional neck dissections a thorough awareness of the different anomalous positions of the nerve are required to avoid injury at level 2b and 5.

Anomalies and Breast Surgery

Most anomalies encountered at breast surgery are the result of abnormal chest wall musculature. They are nonfunctional and are considered vestiges. A plethora of anomalies has been described in the literature most involving the pectoralis major muscle and the rest supernumerary chest wall muscles. In our series we encountered the sternalis, axillary arch (Figure 6) and an accessory pectoralis major muscle [37].

The sternalis is a bilateral, fleshy longitudinal band arising from sheaths of rectus abdominis, external oblique and pectoralis major muscle, after a cephalad parasternal course inserts into upper costal cartilages, manubrium and sternomastoid muscle [37]. There is considerable confusion in literature regarding the



Figure 6: Axillary arch shown with the instrument, thoracodorsal pedicle (yellow star).

description of the muscle which has an incidence ranging from 4–11.5% with a strong Asian racial predilection. The embryological origin is unclear with several explanations. It is thought as a remnant of panniculus carnosus, the ventral longitudinal column of muscles, cuticular muscle of mammals, or as a result of atavism of cutaneous pectoralis muscle. The clinical significance is that the muscle is imaged during mammography, CT/MRI of the breast and could be misinterpreted as a mass lesion prompting a biopsy [37, 38].

Three supernumerary muscles have been described with importance in the context of breast and axillary surgery the axillary arch, pectoralis quadrates and chondroepitrochlearis. The axillary arch (7% of the population) or Langer muscle or axillo-pectoral muscle occurs as a single or multiple, fibrous or muscular band arising from the latissimus dorsi or the serratus anterior muscles and passing through the axillary cavity over the axillary vessels to insert between the pectoralis major insertion and the coracoid process. The pectoralis quadratus (11–16%) is a muscular slip bridging the fifth and sixth costal cartilages to the pectoralis tendon and it passes deep to the lateral margin of pectoralis major muscle. The dorsoepitrochlearis is the rarest (0.2%), this long muscular band originates from the aponeurosis of external oblique or costal cartilages and inserts into the medial humerus distal to the pectoral tendon [37].

The anomalies of the Pectoralis major Muscle (1:5000–1:11000) vary from complete deficiency to absence of clavicular or sternal heads [38]. These may be syndromic (Poland's) or isolated.

These subtle anomalies present several challenges

to the unwary. The axillary arch restricts the axillary exposure and obscures the level 1 node. The margins of dissection can be restricted if the arch is misinterpreted as the anterior border of latissimus dorsi and the arch may mislead the surgeon to a level above the axillary vein with potential for injury [38]. Failure to divide the arch can predispose to high incidence of lymphedema by compressing the axillary vein and lateral lymphatic channels. Non-recognition of pectoralis major anomalies can cause faulty development of planes, a hypoplastic or absent pectoralis major leaves the reconstructive breast surgeon with little or no tissue to cover implants/ prosthesis [38].

CONCLUSION

Congenital anomalies are rare, but present diverse problems to the oncologist. Some predispose to cancers while others have no relation to malignancy but generate challenges in management. A majority are anatomical variations noticed at surgery; an awareness and early recognition prevents surgical morbidity. For some a pretreatment diagnosis is possible based on clinical and imaging information and helps in selecting appropriate management strategy. The surgeon requires a thorough knowledge and understanding of anatomic variations to interpret imaging, plan treatment and lessen perioperative morbidity. Most anomalies do not result in adverse surgical outcome.

Author Contributions

Shanmugam Subbiah – Substantial contributions to conception and design, Acquisition of data, Analysis and interpretation of data, Drafting the article, Revising it critically for important intellectual content, Final approval of the version to be published

Rajaraman – Analysis and interpretation of data, Revising it critically for important intellectual content, Final approval of the version to be published

Noushad Navin – Analysis and interpretation of data, Revising it critically for important intellectual content, Final approval of the version to be published

Guarantor

The corresponding author is the guarantor of submission.

Conflict of Interest

Authors declare no conflict of interest.

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