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CENTRAL NERVOUS SYSTEM HEMORRHAGE IN THROMBOCYTOPENIC PATIENTS

Computed tomographic findings in 21 cases

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ABSTRACT - *Objective:* To describe the CT scan findings of 21 thrombocytopenic patients with central nervous system (CNS) hemorrhage. *Method:* Retrospective study of the computed tomography (CT) of 21 platelet-depleted patients with CNS hemorrhage. One patient presented two episodes of hemorrhagic episode with different intervals. The clinical data were obtained by the review of the medical records. Two radiologists analyzed the films and reached the decisions by consensus. The following findings were studied: type of bleeding, number of lesions, topography, laterality, size and associated findings. *Results:* Intraparenchymal hemorrhage (IPH) was the most common findings, found in 20 cases, being six of them associated with subarachnoid and intraventricular hemorrhages. The size of the lesions varied between 1.8 and 10.5 cm. The parietal lobes were more commonly affected (n=11, 50%), followed by the temporal (n=7, 31.8%), frontal (n=7, 31.8%) and occipital (n=2, 9.09%) lobes. In 15 cases (68.2%) there was a single area of hemorrhage and in the remaining cases there were multiple hemorrhages. Associated findings were found in 20 cases. The most prevalent were edema (n=17, 77.3%), hydrocephalus (10, 45.4%) and midline shift (n=9, 41%). *Conclusion:* The most frequent CT scan findings in thrombocytopenic patients with CNS hemorrhage are single IPH, located mostly in the parietal, temporal and frontal lobes, with varied sizes and associated with edema, hydrocephalus and midline shift.

KEY WORDS: computed tomography, thrombocytopenia, cerebral hemorrhage.

Hemorragia do sistema nervoso central em pacientes trombocitopênicos: achados por tomografia computadorizada em 21 casos

RESUMO - *Objetivo:* Descrever os achados tomográficos de 21 pacientes trombocitopênicos com hemorragia no sistema nervoso central (SNC). *Método:* Estudo retrospectivo das tomografias computadorizadas (TC) de 21 pacientes trombocitopênicos que apresentaram hemorragia no SNC. Um dos pacientes apresentou 2 episódios hemorrágicos em épocas diferentes. Os dados clínicos foram obtidos por revisão de prontuários médicos. Dois radiologistas analisaram os exames e estabeleceram os achados por consenso. Os seguintes achados foram estudados: tipo de sangramento, número de lesões, topografia, lateralidade, tamanho e achados associados. *Resultados:* A hemorragia intraparenquimatosa foi o achado mais comum, observada em 20 casos, sendo que em seis deles apresentavam hemorragia subaracnóidea e intraventricular associadas. O tamanho das lesões variou entre 1,8 e 10,5 cm (mediana= 4,5 cm). Os lobos parietais foram mais acometidos (n=11, 50%), seguidos pelos temporais (n=7, 31,8%), frontais (n=7, 31,8%) e occipitais (n=2, 9,09%). Em 15 casos (68,2%) houve uma única área de hemorragia, e nos demais múltiplas áreas foram observadas. Em 20 casos foram encontrados achados associados, sendo mais comum edema (n=17, 77,3%), hidrocefalia (n=10, 45,4%) e desvio da linha média (n=9, 41%). *Conclusão:* Os achados tomográficos mais freqüentes em pacientes trombocitopênicos com hemorragia cerebral são lesões intraparenquimatosas únicas acometendo principalmente os lobos parietais, temporais e frontais, com tamanhos variados e associadas a edema, hidrocefalia e desvio da linha média.

PALAVRAS-CHAVE: tomografia computadorizada, plaquetopenia, hemorragia cerebral.

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Spontaneous intracranial hemorrhage (ICH) accounts for 10% to 15% of all causes of stroke. It is defined as a nontraumatic abrupt onset of severe headache, altered level of consciousness and/or focal neurologic deficit, which are associated with a focal collection of blood within the brain parenchyma[1-3]. Excluding cases of vascular anomaly, most of the patients with ICH have hypertension as the main cause of the event. In addition, nontraumatic intracerebral hemorrhage may occur because hemostatic disorder, such as thrombocytopenia[1,4]. The incidence of ICH in this group of patients is around 2%, with 47% of mortality rate[5]. Noncontrast computed tomographic (CT) scan is currently the gold standard imaging method for initial evaluation of patients with suspected stroke. The major aim of this exam is to differentiate hemorrhagic and non-hemorrhagic strokes, which can define the correct therapy[6].

Despite the higher rates of morbidity and mortality of ICH in patients with thrombocytopenia, there are a few papers discussing the CT scan findings in this group of patients. Shih et al.[5] described the CT scan findings of spontaneous ICH in 13 patients; however, only four of them had thrombocytopenia or platelet dysfunction. Pierce et al.[7] presented the CT scan features of acute ICH in three anemic platelet-depleted patients. In summary, these studies do not clarify the most common CT scan findings in thrombocytopenic patients with ICH.

The authors aim to present the most common CT scan findings in 21 thrombocytopenic patients with spontaneous ICH.

METHOD

The Institutional Review Board of our hospital approved the study, which retrospectively included 21 platelet-depleted patients with central nervous system (CNS) hemorrhage, who were investigated with CT scan. One patient presented two episodes of ICH with different intervals, totalizing 22 events analyzed. There were nine male and 12 female patients, with ages ranging from 2 to 48 years (median=20.5 years).

The clinical and laboratorial data were obtained by medical reports review (Table 1). The main clinical diagnoses prior to the CNS hemorrhage were: severe aplastic anemia (n=10), acute myeloid leukemia (n=4), Fanconi's anemia (n=2), haemophilia A (n=1), chronic myeloid leukemia (n=1), myelodysplasia (n=1), idiopathic thrombocytopenic purpura (n=1) and acute lymphocytic leukemia (n=1). The most common clinical presentations were headache (52%), vomiting (38%), seizure (33%), focal neurological deficit (28.5%), altered mental status (23%), irritability (14%), speech disorder (9,5%) and nausea (9.5%). The platelet count at the day of the episode of ICH ranged from 5,000/μL to 20,000 μl/L (median=12,000 μl/L). The clinical data are summarized in Table 1.

All the CT scans were performed within 12 hours of the initial symptoms, and were obtained in same equipment (Somaton ART, Siemens, Germany, 1988). The exams were performed with 2.5 mm collimation at 5 mm intervals at the posterior fossa, and 5mm collimation at 10 mm intervals in the remaining brain. Two radiologists analyzed the CT scans and reached final decisions regarding the findings by consensus. The following CT findings were assessed: type of bleeding (intraparenchymal, subarachnoid, subdural, epidural and intraventricular), number of lesions, topography, laterality, diameters and associated findings (hydrocephalus, edema and midline shift).

RESULTS

Twenty two CT scans of patients with ICH were studied (Table 2). Intraparenchymal hemorrhage was found in 20 cases. In six of them, there were also subarachnoid and intraventricular hemorrhages associated. In the remaining two cases, subarachnoid and subdural hemorrhage were found isolated in each patient.

The size of the lesions (the largest diameter) var-

Table 1. Clinical data of thrombocytopenic patients with CNS hemorrhage.

Patient	Sex/Age	Underlying disease	Platelet count
1	F/13	AML	5000
2	M/44	AML	9000
3	M/48	Myelodysplasia	19000
4	M/31	AML	5000
5	M/24 and 30	Haemophilia A	19000
6	F/11	Fanconi	19000
7	F/44	ITP	9000
8	M/13	SAA	12000
9	F/14	SAA	4000
10	F/17	SAA	20000
11	F/40	CML	12000
12	F/8	SAA	12000
13	M/18	SAA	7000
14	F/17	SAA	5000
15	M/27	SSA	15000
16	F/9	Fanconi	9000
17	F/4	SSA	19000
18	F/12	SSA	12000
19	M/10	SSA	19000
20	F/2	ALL	12000
21	F/4	AML	9000

AML, acute myelogenous leukemia; Fanconi, Fanconi anemia; ITP, idiopathic thrombocytopenic purpura; SAA, severe aplastic anemia; CML, chronic myelogenous leukemia; ALL, acute lymphocytic leukemia; F, female; M, male.

Table 2. CT findings of thrombocytopenic patients with CNS hemorrhage.

Case	Location	Type of bleeding	Nº of lesions	Side	Associated findings	Size (cm)	Follow-up
1	T, P	SAH, IPH	5	R + L	Edema ++	2.5	
2	F	IPH	1	L	Midline shift / edema ++	5.5	
3	P	IPH	1	R	Midline shift / edema +++ / hydrocephalus +	5.0	
4	T	SAH, IPH, IVH	1	R	Midline shift / edema + / hydrocephalus +	5.0	
5*	F	IPH	1	R	Midline shift / edema ++	5.2	
5**	T, F, basal ganglia	IPH	1	L	Midline shift / edema +++ / hydrocephalus ++	8.2	
6	P, F	SDH	1	L	Midline shift / hydrocephalus +	10.5	
7	T, P, F	IPH	3	R + L	Edema +++	3.5	
8	F	IPH	3	R + L	Edema ++	4.0	
9	F	IPH	1	L	Midline shift / edema ++	4.0	> in 4 days
10	T, P	IPH	2	R	Midline shift / edema +++ / hydrocephalus +	8.5	
11	P	IPH	1	L	Edema ++	2.8	> in 5 days
12	P	SAH, IPH, IVH	1	L			same in 5 days
13	cistern, sulcus	SAH	1	L	Hydrocephalus +		
14	P, O	IPH	1	R	Edema ++ / hydrocephalus ++	4.0	Hydrocephalus > in 4 days
15	O	IPH	1	R	Edema ++	3.0	
16	P	IPH	2	L	Edema ++	3.0	< in 14 days
17	P	IPH, IVH	1	L	Midline shift / hydrocephalus ++	6.0	
18	T	IPH, IVH	1	R	Edema + / hydrocephalus +++	5.5	
19	P	SAH, IPH	2	R + L		1.8	
20	T	IPH	1	R	Midline shift / edema ++ / hydrocephalus ++	6.0	
21	difuse	IPH	>5	R + L	Edema +	2.1	

T, temporal; F, frontal; P, parietal; O, occipital; SAH, subarachnoid hemorrhage; IPH, intraparenchymal hemorrhage; IVH, intraventricular hemorrhage; SDH, subdural hemorrhage; R, right; L, left. Size was considered as the largest diameter of the largest lesion. Edema and hydrocephalus were graduated according with the severity: + (discrete), ++ (moderate) and +++ (severe); *first hemorrhagic event; **second hemorrhagic event.

ied between 1.8 and 10.5 cm (median=4.5 cm). Considering the density of the IPH (n=20), in fourteen (70%) cases the lesions were heterogeneous (Figs 1 and 2) and in the remaining six (30%) homogeneous. The hemorrhages were more commonly located at the parietal regions (n=11, 50%), followed by the temporal (n=7, 31.8%), frontal (n=7, 31.8%) and occipital (n=2, 9.1%) regions. In 15 cases (68.2%) there was a single area of hemorrhage (Figs 3 and 4) and in the remaining seven cases (31.8%) there were multiple hemorrhages. The lesions were located in the left hemisphere in nine cases (41%), in the right in eight (36.4%) and there were bilateral hemorrhages in five patients (22.6%). The hemorrhages were also classified considering the profound or superficial location. Most of the cases were superficial (16 of 22, 72.7%), and in six (27.3%) patients the hemorrhages were superficial and profound (Figs 1-4)

In only two cases there were no additional findings associated with the hemorrhages at the CT scans. In the remaining twenty cases, the most prevalent associated CT findings were edema, encountered in 17 cases (77.3%), hydrocephalus in 10 cases (45.4%) and midline shift in 9 cases (41%). Table 2 summarizes the CT scan findings.

Five of the 21 patients (23.8%), had follow-up CT scans performed between four and 14 days after the initial exam. In two cases the hemorrhages enlarged (2.2 cm in four days and 1.3 cm in five days). One case had hydrocephalus enlargement in a period of two days. In the remaining two cases, the hemorrhage was stable in one and diminished in the other (five and

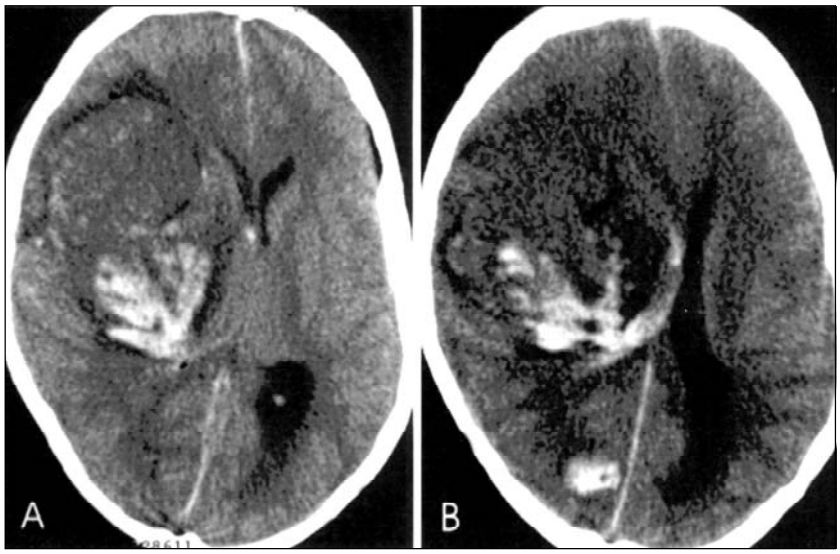

Fig 1. In A, CT scan demonstrates a large heterogeneous hematoma in the right fronto-temporal region, with hypo and hyperdense components. In B, CT scan shows an additional small parietal hematoma at the right, and severe midline shift.

Fig 2. CT scan demonstrates a large ill-defined hematoma in left frontal and temporal lobes, with extension into the ventricles and severe midline shift.

Fig 3. CT scan shows a well-defined heterogeneous hemorrhage in the left frontal lobe, with adjacent vasogenic edema.

Fig 4. CT scan demonstrates a left frontal round hematoma, with surrounding vasogenic edema.

fourteen days after the first CT scan, respectively).

Seven patients underwent bone marrow transplantation (BMT) before the hemorrhage event. The most common CT findings in this group of patients were: IPH in six cases, parietal location in four, single lesion in 6 cases and edema and hydrocephalus as the commonest associated findings in four patients each one.

DISCUSSION

Although ICH accounts for 10 to 15% of all cases of stroke, it is associated with high mortality rate[1-3]. Spontaneous ICH is an unusual and potentially disastrous event that might complicate primary and secondary hemostatic abnormalities. Among secondary alterations in hemostasis, thrombocytopenia, platelet function abnormalities, or factor consumption contribute to the risk of ICH in patients with disseminated intravascular coagulation, myeloproliferative or myelodysplastic disorders, and exposure to certain medication[3,8-16]. Strokes occur more frequently in patients who have undergone BMT than in the general population. Coplin et al.[10] studied 1245 patients who underwent BMT and found 36 cases (2.9%) of stroke. The most common cause of the stroke was intracranial hemorrhage related with thrombocytopenia (39.8%). In our series, intraparenchymal hemorrhage was found in six of seven patients (85.7%) who underwent BMT. It is well known that thrombocytopenia secondary chemotherapy or radiother-

aphy, or secondary to a decreased in megakaryocytes have been considered a major risk factor for CNS bleeding post-BMT[11,12].

Koide et al.[13] studied 96 patients who had hemorrhagic cerebrovascular disease. Among them, only 16 patients (16.7%) had thrombocytopenia, half of them presented subarachnoid hemorrhage (SAH), and the remaining showed IPH. In this study, there were five cases of SAH, four of them associated with intraparenchymal or intraventricular hemorrhage. Intraparenchymal hemorrhage was seen in 20 of the 22 events of the current casuistic.

The same type of bleeding distribution was observed by Shih et al.[5] when they described the CT features of spontaneous intracranial hemorrhage in 13 patients with haemostatic disorder. Four patients had thrombocytopenia (due to aplastic anemia and rubella) or congenital platelet dysfunction. Three of them had ICH, being the frontal lobes affected in two cases and the thalamus in the other. In one of the cases, there was subarachnoid hemorrhage associated with the IPH. No associated findings were found in one of the patients, and in the remaining two cases there was edema.

Most of the non-thrombocytopenic patients with spontaneous CNS hemorrhage present lesions at the profundity of the brain, usually with homogeneous high density at the CT scans[14,15]. However, in the current study, 72.7% of the hemorrhages were superficial, and the remaining patients showed superficial and profound lesions. In addition, in most of the cases (70%) the hemorrhages had heterogeneous density. We state that the hemorrhages in thrombocytopenic patients usually begin at the periphery of the brain, progressing then to the profundity. Also, because these patients frequently present several consecutive episodes of CNS bleeding, the lesions usually have heterogeneous density, demonstrating the different ages of the hemorrhage.

In conclusion, the most frequent CT scan findings in thrombocytopenic patients with spontaneous ICH are single IPH with lobar topography, mainly parietal followed by temporal and frontal lobes, presenting varied size and commonly associated with midline shift, edema and hydrocephalus. In contrast with the spontaneous episodes of CNS hemorrhage in non-thrombocytopenic patients, our study showed that those thrombocytopenic patients usually had superficial and heterogeneous CNS bleedings.

REFERENCES

1. Woo D, Broderick JP. Spontaneous intracerebral hemorrhage: epidemiology and clinical presentation. Neurosurg Clin N Am 2002;13:265-279.
2. Kamal AK, Dyke JP, Katz JM, et al. Temporal evolution of diffusion after spontaneous supratentorial intracranial hemorrhage. Am J Neuroradiol 2003;24:895-901.
3. Quinones-Hinojosa A, Gulati M, Singh V, Lawton MT. Spontaneous intracerebral hemorrhage due to coagulation disorders. Neurosurg Focus 2003;15:1-17.
4. Hill MD, Silver FL, Austin PC, Tu JV. Rate of stroke recurrence in patients with primary intracerebral hemorrhage. Stroke 2000;31:123-127.
5. Shih SL, Lin JCT, Liang DC, Huang JK. Computed tomography of spontaneous intracranial haemorrhage due to haemostatic disorders in children. Neuroradiology 1993;35:619-621.
6. Packard AS, Kase CS, Aly AS, Barest GD. "Computed tomography - negative" intracerebral hemorrhage: case report and implications for management. Arch Neurol 2003;60:1156-1159.
7. Pierce JN, Taber KH, Hayman LA. Acute intracranial hemorrhage secondary to thrombocytopenia: CT appearances unaffected by absence of clot retraction. Am J Neuroradiol 1994;15:213-215.
8. Zoppo GJ, Mori E. Hematologic causes of intracerebral hemorrhage and their treatment. Neurosurg Clin N Am 1992;3:637-658.
9. Rogers LR. Cerebrovascular complications in cancer patients. Oncology 1994;8:23-30.
10. Coplin WM, Cochran MS, Levine SR, Crawford SW. Stroke after bone marrow transplantation: frequency, etiology and outcome. Brain 2001;124:1043-1051.
11. Graus F, Saiz A, Sierra J, et al. Neurologic complications of autologous and allogenic bone marrow transplantation in patients with leukemia: a comparative study. Neurology 1996;46:1004-1009.
12. Mehta J, Powles R, Singhal S, et al. Early identification of patients at risk of death due to infections, hemorrhage, or graft failure after allogeneic bone marrow transplantation on the basis of the leukocyte counts. Bone Marrow Transplant 1997;19:349-355.
13. Koide D, Manaka S, Takagi K, et al. Clinical significance of thrombocytopenia associated with hemorrhagic cerebrovascular disease. No Shinkei Geka 1991;19:729-734.
14. Soares CM, Carvalho ACP, Rodrigues AJ. Spontenous intraparenchymatous hemorrhage: findings at computed tomography. Arq Neuropsiquiatr 2004;62:682-688.
15. Wiggins WS, Moody DM, Toole JF, Laster DW, Ball MR. Clinical and computerized tomography study of hypertensive intracerebral hemorrhage. Arch Neurol 1978;35:832–833.
16. Francisco S, Reis-Filho JB, Neves AC. Subarachoinal hemorrhage with cranial tomography without bleeding signals. Arq Neuropsiquiatr 1997; 55:413-419.